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Sequencing Therapies in Peripheral T-Cell Lymphoma

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Introduction

Peripheral T-cell lymphomas (PTCLs) are a heterogeneous group of clinically aggressive mature T-cell neoplasms that represent approximately 10% of all non-Hodgkin lymphoma cases.[1] According to the most recent World Health Organization (WHO) classification and the International Consensus Classification (ICC),[2,3] there are over 30 distinct T and natural killer (NK) cell lymphomas. Although genetic and environmental factors are implicated in certain subtypes (e.g., *HTLV-1* in adult T-cell leukemia/lymphoma [ATLL]), most PTCLs are associated with genomic alterations acquired during normal T-cell development and differentiation.[1] The most common nodal PTCL subtypes, which will be the focus of this review, are PTCL-not otherwise specified (NOS), nodal T-follicular helper (TFH) lymphoma, including angioimmunoblastic T-cell lymphoma (AITL), and anaplastic large cell lymphoma (ALCL).

TFH lymphomas are defined by the expression of at least two markers characteristic of normal TFH cells (CD10, BCL6, CXCL13, PD1, and ICOS).[2] This group comprises 3 distinct entities (angioimmunoblastic-type, follicular-type, and NOS) that have unique histologic patterns but share a common genetic landscape characterized by mutations in genes that regulate DNA and histone methylation, including *TET2, DNMT3A*, and *IDH2*.[4] Based on their pathogenesis involving epigenome dysregulation, these lymphomas appear particularly sensitive to epigenetic therapies, such as histone deacetylase (HDAC) inhibitors and azacitidine.[5,6]

PTCL-NOS encompasses a heterogeneous group of diseases and remains a diagnosis of exclusion. Among cases not classified as TFH lymphomas, two molecularly defined subgroups have been identified: PTCL-GATA3 and PTCL-TBX21, which resemble T helper 1 (Th1) and T helper 2 (Th2) cells, respectively.[4] These subgroups are associated with distinct clinical outcomes, with PTCL-GATA3 conferring a particularly poor prognosis. Importantly, these signatures may have treatment implications, as PTCL-GATA3 is associated with activation of the PI3K pathway, whereas PTCL-TBX21 appears more closely linked to STAT3 pathway activation. Ongoing research in this area will hopefully facilitate the development of more biologically targeted therapies and ultimately improve outcomes for these distinct PTCL subsets.

ALCLs are composed of large, pleomorphic CD30-positive T cells and are classified into four distinct entities: ALK-positive ALCL, ALK-negative ALCL, breast-implant-associated ALCL, and primary cutaneous ALCL. ALK-positive ALCL generally carries a more favourable prognosis than ALK-negative ALCL, in part due to the younger age at presentation.[7] Given the uniform expression of CD30 in ALCL, brentuximab vedotin (BV) has become a cornerstone of front-line therapy following the landmark ECHELON-2 trial, discussed below, which demonstrated both progression-free survival (PFS) and overall survival (OS) benefits with the incorporation of BV into an anthracycline-based regimen (BV-CHP).[8]

Historically, PTCL has been associated with inferior outcomes compared with aggressive B-cell lymphomas, with multiple national and international registry studies reporting 5-year PFS rates of approximately 20%–30% and 5-year OS rates of 30%–40%.[9] However, recent advances in identifying molecular biomarkers and understanding disease biology are increasingly enabling more individualized treatment approaches. This review will discuss an evidence-based approach to sequencing therapies for PTCL in both the front-line and relapsed/refractory settings.

Approach to Front-Line Therapy

As with the management of any malignancy, several factors must be considered when selecting a treatment approach for PTCL. Specifically, these include the histological subtype, immunohistochemistry (particularly CD30 expression), patient fitness, and transplant eligibility. This section outlines the approach to fit patients, which typically involves combination chemotherapy with or without immunotherapy (BV). For patients deemed unfit for intensive systemic chemotherapy, palliative-intent approaches may include single agents (e.g., oral etoposide or cyclophosphamide) with or without corticosteroids.

Chemotherapy

CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone) has been compared with multiple alternative regimens in the front-line treatment of PTCL.[10-12] Despite retrospective studies demonstrating cure rates of <50%,[13,14] CHOP has remained the backbone of therapy for most PTCL subtypes, often with the addition of etoposide (CHOEP).[15,16] CHOEP is preferred in younger patients, largely based on an analysis of 7 prospective studies that demonstrated improved 3-year event-free survival (EFS) (75% vs. 51%) among younger (<60 years), good-risk patients (normal lactate dehydrogenase) treated with CHOEP compared with CHOP alone.[16] Notably, the benefit was most pronounced in ALK-positive ALCL, although a trend toward improved outcomes was also observed in other nodal PTCL subtypes.[16]

The landmark ECHELON-2 trial significantly changed the front-line treatment landscape for PTCL.[8] ECHELON-2 was an international phase III study investigating the use of BV, a CD30-directed antibody-drug conjugate linked to monomethyl auristatin E, a microtubule inhibitor. The study enrolled 452 patients with CD30-positive PTCL (>10% by immunohistochemistry), who were randomized to receive either BV-CHP or CHOP. With extended follow-up, patients treated with BV-CHP demonstrated estimated 5-year PFS and OS rates of 51% and 71%, respectively, compared with 43% and 61% with CHOP.[17] Importantly, approximately 70% of enrolled patients had ALCL. Although the study was underpowered to evaluate the efficacy in non-ALCL subtypes, no statistically significant improvement in PFS or OS was observed among patients with AITL or PTCL-NOS.[8,17] Based on these data, BV, in combination with CHP, has been approved by Health Canada for the front-line treatment of ALCL, as well as CD30-positive PTCL-NOS and AITL.

Several additional studies have evaluated the incorporation of novel targeted therapies into front-line treatment, including romidepsin,[18] azacitidine,[19] and belinostat.[20] Collectively, these studies demonstrated mixed efficacy results along with increased toxicity compared with CHOP alone. Therefore, these approaches have not yet been incorporated into standard front-line management.

Consolidation

Given the historically poor outcomes for PTCL and the high risk of relapse (5-year risk of 23% based on long-term follow-up),[9,21] numerous studies have evaluated the role of consolidation with autologous stem cell transplant (ASCT) or allogeneic stem cell transplant (allo-SCT).[22-27]

Although consolidative ASCT is considered standard practice at some institutions,[4] particularly for high-risk patients or those achieving complete remission (CR), this approach has largely been investigated through retrospective and single-arm phase II studies, with conflicting results. The largest prospective study was conducted by the Nordic group, in which 160 patients with newly diagnosed PTCL were treated with CHOP or CHOEP, followed by ASCT for those who achieved a partial or complete response.[22] At a median follow-up of 5 years, the estimated 5-year PFS and OS were 44% and 51%, respectively. Outcomes appeared most favourable in patients with ALK-negative ALCL (5-year PFS 61%), compared with AITL (49%) and PTCL-NOS (38%).[22] Similarly, several more recent retrospective studies have demonstrated improvements in EFS, PFS, and OS with consolidative ASCT among patients who responded to front-line therapy, particularly those who achieved CR.[15,23,24,26] In a nationwide Dutch registry study evaluating the role of etoposide and ASCT, the authors performed a sensitivity analysis restricted to patients who achieved CR and demonstrated a significantly improved 5-year OS in patients undergoing consolidation compared with those who did not (82% vs. 47%; $p<0.01$).[15]

In contrast, a propensity score-matched analysis by the LYSA group of patients with nodal PTCL demonstrated no significant benefit in either PFS or OS with consolidation ASCT.[28] Similarly, a subgroup analysis of patients achieving CR following BV-CHP enrolled on the ECHELON-2

study demonstrated improved PFS with ASCT consolidation (65% vs. 46%); however, this benefit was not observed among patients treated with CHOP.[29] To date, no randomized controlled trial has definitively established the benefit of ASCT consolidation, and this remains a subject of ongoing controversy and investigation.

Allo-SCT consolidation is often considered in eligible patients with PTCL. A randomized phase III trial compared ASCT and allo-SCT as consolidation strategies following front-line therapy in younger patients with PTCL.[27] Patients received four cycles of CHOEP followed by one cycle of DHAP (dexamethasone, high-dose cytarabine, and cisplatin) prior to proceeding to either ASCT or allo-SCT. Although a robust graft-versus-lymphoma effect was observed, with a 0% relapse rate at 3 years in the allo-SCT group, this was offset by substantially higher non-relapse mortality (23% vs. 0%).[27] The study was ultimately terminated early due to futility. Long-term follow-up of the AATT study similarly demonstrated a strong graft-versus-lymphoma effect, with a 7-year relapse rate of 8%, although this was again counterbalanced by high rates of non-relapse mortality (23%).[25]

Taken together, these studies suggest consolidative ASCT may be considered in patients with chemosensitive disease given the potential for improved long-term outcomes, particularly among higher-risk patients. Some guidelines recommend restricting this approach to patients achieving CR following front-line chemotherapy. However, this strategy is not uniformly adopted across Canadian institutions due to the absence of definitive randomized data. Two ongoing clinical trials are investigating the role of ASCT in patients with PTCL who achieve CR following front-line therapy (NCT05444712 and NCT06724237),[30,31] including the US-based ECOG study, in which Canadian centres are participating.[30]

Approach to Relapsed/Refractory PTCL

As previously discussed, more than 50% of patients with nodal PTCL, with the exception of ALK-positive ALCL, will ultimately experience disease relapse.[9] The median OS in the relapsed/refractory setting is less than 6 months, highlighting the need for novel therapies and the importance of considering clinical trial enrollment at each line of therapy.[32] Allo-SCT remains the only potentially curative treatment option in this setting.[33] As such, the choice of second-line therapy should take into account whether the patient is fit for an allo-SCT. Additional considerations include prior BV exposure, PTCL subtype (which may predict differential response to therapy), chemosensitivity, timing of relapse, and patient fitness.

In fit, transplant-eligible patients, most available evidence supports the use of allo-SCT over ASCT, except for ALCL and potentially late relapses post-front-line therapy. Patients with relapsed ALCL appear to have particularly favourable outcomes from ASCT, with reported 3-year PFS and OS rates of 53% and 65%, respectively, compared with 29% and 42% in PTCL-NOS.[34-37] Importantly, allo-SCT may provide durable disease control even in patients who relapse following ASCT or those with refractory disease, highlighting its curative potential. Collectively, these studies suggest that ASCT should be considered in relapsed ALCL when not previously utilized in the front-line setting, whereas allo-SCT should generally be favoured in patients with AITL and PTCL-NOS given the potential for long-term disease control and cure.[33-38]

Multi-agent chemotherapy, most commonly gemcitabine, cisplatin, and dexamethasone (GDP), is a frequently used salvage regimen in relapsed PTCL, particularly as a bridge to stem cell transplant. This approach is supported by a subset analysis of the LY.12 study, which demonstrated an overall response rate (ORR) of 38% in patients with PTCL intended to proceed to ASCT.[39] Among patients who ultimately underwent ASCT, the 2-year EFS and OS were 21% and 42%, respectively.[39] Given the limited treatment options in this setting, GDP-based salvage therapy remains a common approach in many Canadian institutions, including in patients ultimately planned for allo-SCT.

In patients who are not candidates for allo-SCT, several novel agents, as highlighted in **Table 1**, adapted from Moskowitz et al.,[4] may be considered. However, these therapies are generally unlikely to produce durable long-term remissions or a cure. Thus, treatments that can be continued without significant cumulative toxicity are generally preferred in this setting.[4] Single-agent approaches are generally favoured to minimize toxicity while preserving quality of life.

Pralatrexate is a folate analog metabolic inhibitor that competitively inhibits dihydrofolate reductase. In the phase II single-arm PROPEL study, pralatrexate demonstrated modest efficacy in relapsed/refractory PTCL with an ORR of 29%

Drug	Target	n	ORR, CR	Comments	Public access in Canada
GDP (gemcitabine, dexamethasone, cisplatin)[39]	Multi-agent chemotherapy	Salvage/bridge to transplant	ORR 38%	Commonly used as a bridging regimen prior to consolidative ASCT or allo-SCT in relapsed setting	Yes
Pralatrexate[40]	Folate	109	ORR 29%, CR 11%	Lower response rates observed in AITL	Yes
Brentuximab vedotin[41]	CD30	34	ORR 41% (54% in AITL), CR 24%	Most active in ALCL; re-treatment may be considered in select patients, particularly if relapse >6 months	Yes (ALCL)
Romidepsin[42]	HDAC inhibitor	130	ORR 25%, CR 15%	Durable responses reported in AITL (median PFS 29 months); withdrawn from Canadian market	No
Azacitidine[43]	Hypomethylating agent	86	ORR 33% (3 months)	Activity appears greater in TFH lymphomas, may be better used in combination with other agents.	No
Valemetostat[44]	EZH1/2 inhibitor	133	ORR 43%, CR 14%	Novel therapeutic strategy, most active in TFH lymphomas.	No
Belinostat[45]	HDAC inhibitor	129	ORR 26%, CR 11%	Most active in AITL	No

Table 1. Subtype-specific activity of drugs in relapsed/refractory nodal PTCLs[4]; *courtesy of Danyal Ladha, MD and Anca Prica, MD.*

Abbreviations: AITL: angioimmunoblastic T-cell lymphoma; **ALCL:** anaplastic large cell lymphoma; **allo-SCT:** allogeneic stem cell transplant; **ASCT:** autologous stem cell transplant; **CR:** complete response; **HDAC:** histone deacetylase; **ORR:** overall response rate; **PFS:** progression-free survival; **TFH:** T follicular helper.

and a CR rate of 11%.[40] The median PFS was 3.5 months, and responses were notably lower in patients with AITL (ORR: 8%).[40] Despite these limitations, pralatrexate remains a common standard-of-care option in Canada based on current funding algorithms.

HDAC inhibitors, including romidepsin, belinostat, and chidamide, have demonstrated varying degrees of efficacy in relapsed PTCL. Romidepsin was initially approved by the FDA based on a phase II study demonstrating durable responses in a subset of patients, particularly those with AITL (ORR 33%, with 19% of patients maintaining a response for >12 months).[42] However, a subsequent phase III study evaluating CHOP with or without romidepsin in the front-line setting failed to meet its primary endpoint, leading to the withdrawal of romidepsin from the Canadian market.[18] Belinostat has similarly demonstrated activity in phase II studies, with particularly favourable responses observed in AITL (ORR: 45.5% vs. 23.3% with PTCL-NOS).[45] A phase III trial incorporating belinostat in the front-line setting is ongoing.[46]

BV also remains active in the relapsed setting. A phase II study demonstrated efficacy with single-agent BV regardless of prior front-line BV exposure.[41] The greatest benefit was observed in patients with ALCL, with long-term follow-up demonstrating a 5-year PFS of 39% and a CR rate

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of 14% in the absence of a transplant, suggesting that durable remission and potential cure may be achievable in a minority of patients.[47] Based on these data, BV is a preferred second-line option for patients with ALCL relapsing more than 6 months following front-line therapy, particularly as a bridge to transplant alongside ALK inhibitors, such as alectinib or crizotinib, in ALK-positive disease.[4,38,47]

Azacitidine, another epigenetic therapy, has also demonstrated activity in TFH lymphomas. Although an initial retrospective series reported an ORR of 75% and CR of 50%, a subsequent phase III trial comparing azacitidine with investigator's choice therapy demonstrated more modest single-agent activity, with a 3-month ORR of 33% and median PFS of 5.6 months.[6,43] As such, azacitidine may ultimately be most effective in combination-based approaches rather than as monotherapy.

Valemetostat is an oral dual inhibitor of the histone methyltransferases EZH1 and EZH2, thereby increasing the expression of pro-apoptotic and tumour suppressor genes by altering histone methylation.[4] This is considered a promising therapeutic approach, given that epigenetic dysregulation is a hallmark of T-cell lymphomas. In a phase II single-arm study evaluating valemetostat in relapsed or refractory PTCL, the ORR and CR rates, as assessed by PET imaging, were 52.1% and 26.9%, respectively.[44] Responses were observed across all PTCL subtypes, with a trend towards greater efficacy in TFH lymphomas (ORR: 54%), compared with PTCL-NOS (31.7%) and ALCL (33%).[44]

References: 1. DARZALEX® SC (daratumumab injection) Product Monograph. Janssen Inc. November 18, 2025. **2.** DARZALEX® (daratumumab for injection) Product Monograph. Janssen Inc. April 30, 2024.

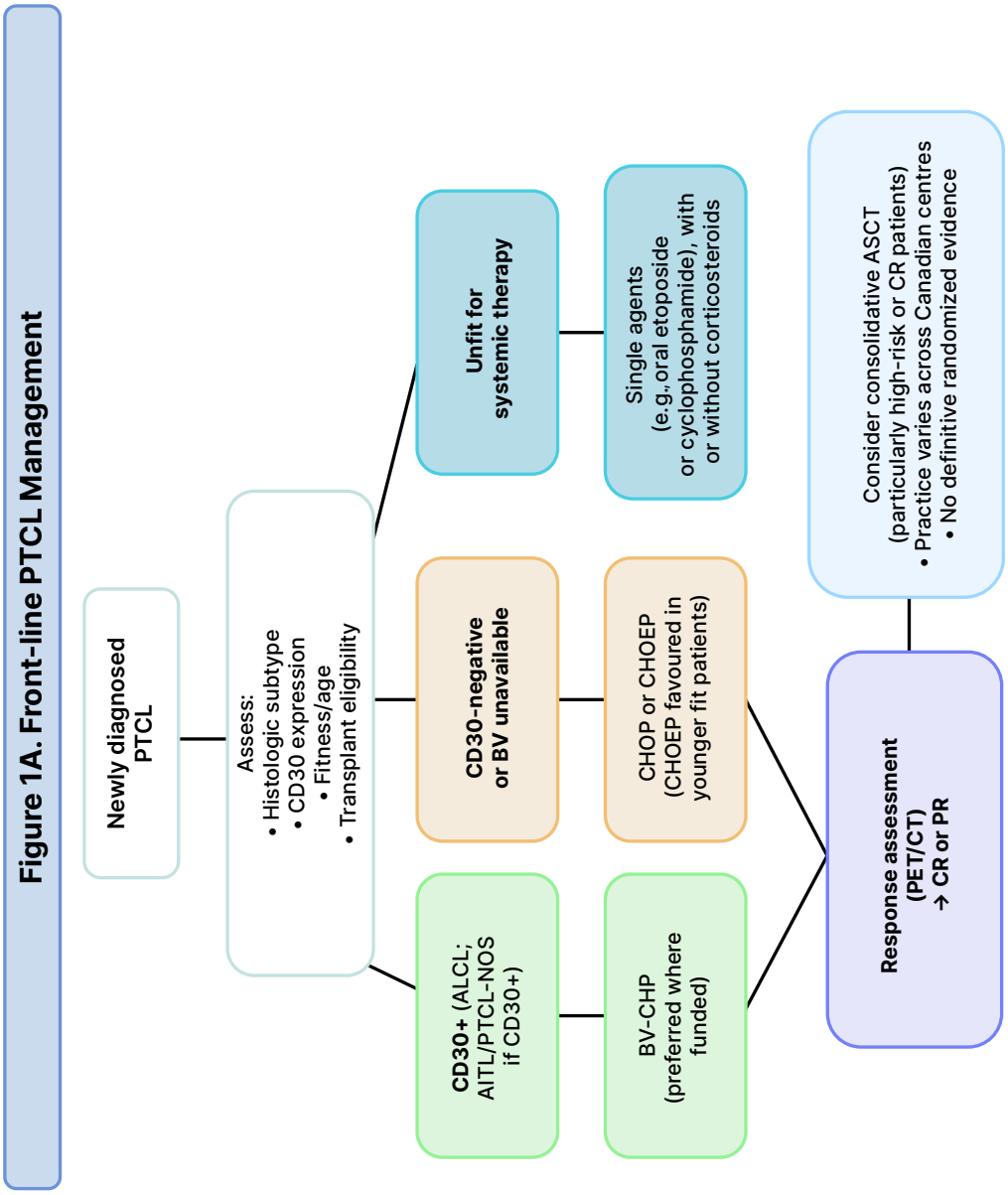
Figure 1A. Front-line PTCL Management
Newly diagnosed PTCL
Assess:
• Histologic subtype
• CD30 expression
• Fitness/age
• Transplant eligibility
Unfit for systemic therapy
Single agents (e.g., oral etoposide or cyclophosphamide), with or without corticosteroids
CD30-negative or BV unavailable
CHOP or CHOEP (CHOEP favoured in younger fit patients)
CD30+ (ALCL; AITL/PTCL-NOS if CD30+)
BV-CHP (preferred where funded)
Response assessment (PET/CT) → CR or PR
Consider consolidative ASCT (particularly high-risk or CR patients)
• Practice varies across Canadian centres
• No definitive randomized evidence

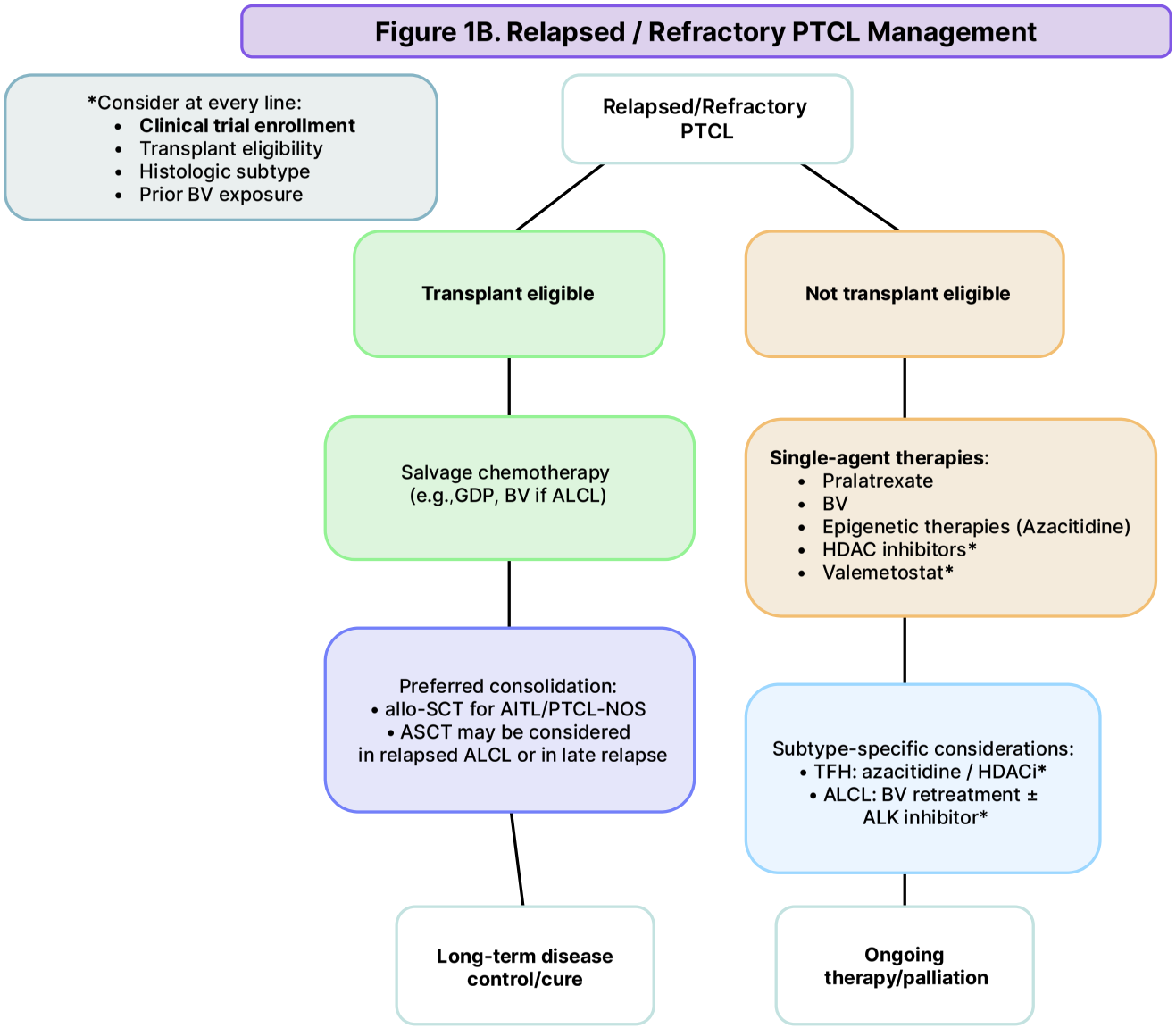

Figure 1. Approach to treatment of PTCL in the Canadian landscape in 2026; *courtesy of Danyal Ladha, MD and Anca Prica, MD.*
*Not funded in Canadian public healthcare system
Abbreviations: AITL: angioimmunoblastic T-cell lymphoma; **ALCL:** anaplastic large cell lymphoma; **allo-SCT:** allogeneic stem cell transplant; **ASCT:** autologous stem cell transplant; **BV:** brentuximab vedotin; **CHOP:** cyclophosphamide, doxorubicin, vincristine, and prednisone **CHOEP:** cyclophosphamide, doxorubicin, vincristine, prednisone, and etoposide; **CHP:** cyclophosphamide, doxorubicin, and prednisone; **HDAC:** histone deacetylase; **GDP:** gemcitabine/dexamethasone/cisplatin; **NOS:** not otherwise specified; **PET/CT:** positron emission tomography/computed tomography; **PTCL:** peripheral T-cell lymphoma; **TFH:** Follicular helper T cell.

Putting It All Together: The Canadian Landscape

As outlined in **Figure 1a**, front-line treatment approaches for PTCL in Canada primarily include CHOP, CHOEP, or BV-CHP. Treatment selection depends on several factors, including immunohistochemistry (BV is publicly funded only for patients whose tumour cells are CD30-positive, with some jurisdictions requiring at least 10% expression), patient age, and comorbidities. Consolidation with ASCT is controversial in the Canadian landscape, given the lack of randomized data to support this practice; some centres routinely consolidate patients in CR, while others do not, depending on how the data are interpreted. The aforementioned ongoing randomized controlled trials will hopefully provide more clarity to guide decision-making.

In the relapsed/refractory setting (**Figure 1b**), enrollment in clinical trials should be considered whenever feasible to facilitate access to novel therapies that are not publicly funded. Outside of a clinical trial setting, patients who are candidates for allo-SCT should be referred early to a transplant program and treated with an appropriate bridging strategy to achieve disease control. Pralatrexate remains a commonly utilized standard-of-care option in Canada; however, as previously discussed, its modest single-agent activity makes durable disease control unlikely in most patients.[40] In patients with ALCL, BV retreatment may be considered, particularly in those relapsing more than 6 months after front-line therapy,[38] followed by ASCT if not previously utilized in the front-line setting. For TFH lymphomas, preference should be given to epigenetic therapies, such as azacitidine, or HDAC inhibitors, where available, although HDAC inhibitors are currently not accessible in Canada.

Future Directions

A number of other strategies are currently being investigated, including the use of immune checkpoint inhibitors,[48] bispecific antibodies (AFM13),[49] and chimeric antigen receptor T-cell therapy (CAR T).[50] However, CAR T therapy in PTCL is associated with unique biologic and manufacturing challenges, including T-cell aplasia, fratricide, and contamination of CAR T products with malignant T cells.[50] Ongoing studies are evaluating strategies to overcome these limitations and improve the feasibility of cellular therapies in PTCL.

In conclusion, the treatment landscape for PTCL continues to evolve rapidly, and substantial advances over the past decade. Recent developments in the understanding of disease biology and molecular subtypes have enabled a more individualized approach to therapy selection and sequencing. Despite these advances, outcomes in relapsed/refractory disease remain poor, highlighting the importance of clinical trial enrollment whenever possible.

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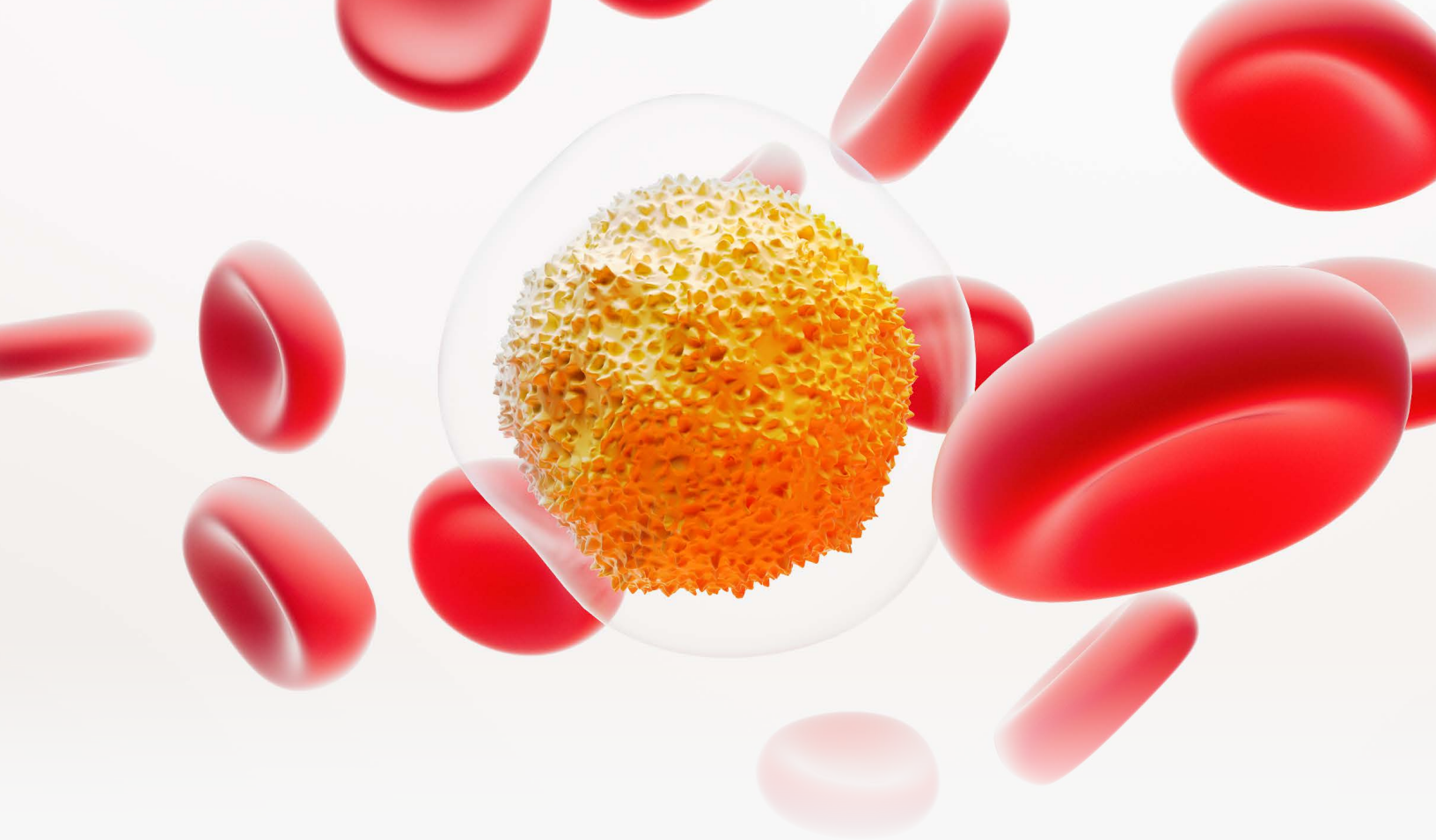
References

1. Iqbal J, Inghirami G, Chan WC. New insights into the biology of T-cell lymphomas. Blood. 2024;144(18):1873-86.
2. Alaggio R, Amador C, Anagnostopoulos I, Attygalle AD, Araujo IBDO, Berti E, et al. The 5th edition of the World Health Organization Classification of Haematolymphoid Tumours: Lymphoid Neoplasms. Leukemia. 2022;36(7):1720-48.
3. Campo E, Jaffe ES, Cook JR, Quintanilla-Martinez L, Swerdlow SH, Anderson KC, et al. The International Consensus Classification of Mature Lymphoid Neoplasms: a report from the Clinical Advisory Committee. Blood. 2022;140(11):1229-53.
4. Moskowitz AJ, Stuver RN, Horwitz SM. Current and upcoming treatment approaches to common subtypes of PTCL (PTCL, NOS; ALCL; and TFHs). Blood. 2024;144(18):1887-97.
5. Ghione P, Faruque P, Mehta-Shah N, Seshan V, Ozkaya N, Bhaskar S, et al. T follicular helper phenotype predicts response to histone deacetylase inhibitors in relapsed/refractory peripheral T-cell lymphoma. Blood Advances. 2020;4(19):4640-7.
6. Lemonnier F, Dupuis J, Sujobert P, Tournillhac O, Cheminant M, Sarkozy C, et al. Treatment with 5-azacytidine induces a sustained response in patients with angioimmunoblastic T-cell lymphoma. Blood. 2018;132(21):2305-9.
7. Chiattone C, Civallero M, Fischer T, Miranda E, Manni M, Zing NPC, et al. Characteristics and clinical outcomes of patients with ALK-positive anaplastic large cell lymphoma: Report from the prospective international T-cell lymphoma project. Hematological Oncology. 2022;40(5):953-61.

8. Horwitz S, O'Connor OA, Pro B, Illidge T, Fanale M, Advani R, et al. Brentuximab vedotin with chemotherapy for CD30-positive peripheral T-cell lymphoma (ECHELON-2): a global, double-blind, randomised, phase 3 trial. The Lancet. 2019;393(10168):229-40.
9. Shea L, Mehta-Shah N. Peripheral T-cell lymphoma: are all patients high risk? Blood. 2024;144(25):2604-12.
10. Gleeson M, Peckitt C, To YM, Edwards L, Oates J, Wotherspoon A, et al. CHOP versus GEM-P in previously untreated patients with peripheral T-cell lymphoma (CHEMO-T): a phase 2, multicentre, randomised, open-label trial. The Lancet Haematology. 2018;5(5):e190-e200.
11. Li L, Duan W, Zhang L, Li X, Fu X, Wang X, et al. The efficacy and safety of gemcitabine, cisplatin, prednisone, thalidomide versus <scp>CHOP</scp> in patients with newly diagnosed peripheral T-cell lymphoma with analysis of biomarkers. British Journal of Haematology. 2017;178(5):772-80.
12. Simon A, Peoch M, Casassus P, Deconinck E, Colombat P, Desablens B, et al. Upfront VIP-reinforced-ABVD (VIP-rABVD) is not superior to CHOP/21 in newly diagnosed peripheral T cell lymphoma. Results of the randomized phase III trial GOELAMS-LTP95. British Journal of Haematology. 2010;151(2):159-66.
13. Savage KJ, Chhanabhai M, Gascoyne RD, Connors JM. Characterization of peripheral T-cell lymphomas in a single North American institution by the WHO classification. Annals of Oncology. 2004;15(10):1467-75.
14. Vose J, Armitage JO, Weisenburger DD. International Peripheral T-Cell and Natural Killer/T-Cell Lymphoma Study: Pathology Findings and Clinical Outcomes. Journal of Clinical Oncology. 2008;26(25):4124-30.
15. Brink M, Meeuwes FO, Van Der Poel MWM, Kersten MJ, Wondergem M, Mutsaers PGNJ, 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. 2022;140(9):1009-19.
16. Schmitz N, Trümper L, Ziepert M, Nickelsen M, Ho AD, Metzner B, et al. Treatment and prognosis of mature T-cell and NK-cell lymphoma: an analysis of patients with T-cell lymphoma treated in studies of the German High-Grade Non-Hodgkin Lymphoma Study Group. Blood. 2010;116(18):3418-25.
17. Horwitz S, O'Connor OA, Pro B, Trümper L, Iyer S, Advani R, et al. The ECHELON-2 Trial: 5-year results of a randomized, phase III study of brentuximab vedotin with chemotherapy for CD30-positive peripheral T-cell lymphoma. Annals of Oncology. 2022;33(3):288-98.
18. Bachy E, Camus V, Thieblemont C, Sibon D, Casasnovas R-O, Ysebaert L, 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). Journal of Clinical Oncology. 2022;40(3):242-51.
19. Ruan J, Moskowitz AJ, Mehta-Shah N, Sokol L, Chen Z, Kotlov N, et al. Multicenter Phase 2 Study of Oral azacitidine (CC-486) plus CHOP as initial treatment for peripheral T-cell lymphoma. Blood. 2023.
20. Johnston PB, Cashen AF, Nikolinakos PG, Beaven AW, Barta SK, Bhat G, et al. Belinostat in combination with standard cyclophosphamide, doxorubicin, vincristine and prednisone as first-line treatment for patients with newly diagnosed peripheral T-cell lymphoma. Experimental Hematology & Oncology. 2021;10(1).
21. Maurer MJ, Ellin F, Srour L, Jerkeman M, Bennani NN, Connors JM, et al. International Assessment of Event-Free Survival at 24 Months and Subsequent Survival in Peripheral T-Cell Lymphoma. Journal of Clinical Oncology. 2017;35(36):4019-26.
22. D'Amore F, Relander T, Lauritzsen GF, Jantunen E, Hagberg H, Anderson H, et al. Up-Front Autologous Stem-Cell Transplantation in Peripheral T-Cell Lymphoma: NLG-T-01. Journal of Clinical Oncology. 2012;30(25):3093-9.
23. Zhang Y, Rose A, Khadka S, Cao B, Eatrides J, Saeed H, et al. Autologous Hematopoietic Cell Transplantation Consolidation for First Response is Associated With Longer Survival Among Patients With Nodal Peripheral T Cell Lymphoma. Transplantation and Cellular Therapy. 2024;30(9):887.e1-.e9.
24. Fulati W, Ma J, Wu M, Qian W, Chen P, Hu Y, et al. Consolidation therapy with autologous stem cell transplantation after remission of induction chemotherapy prolongs the survival of patients with peripheral T-cell lymphoma. Frontiers in Immunology. 2024;15.
25. Tournilhac O, Altmann B, Friedrichs B, Bouabdallah K, Leclerc M, Cartron G, et al. Long-Term Follow-Up of the Prospective Randomized AATT Study (Autologous or Allogeneic Transplantation in Patients With Peripheral T-Cell Lymphoma). Journal of Clinical Oncology. 2024;42(32):3788-94.
26. Yang P, Cai M, Cao Y, Fan S, Tang W, Ji M, et al. Up-front autologous stem cell transplant in peripheral T-cell lymphoma patients achieving complete response after first-line treatment: A multicentre real-world analysis. British Journal of Haematology. 2024;204(4):1414-21.
27. Schmitz N, Truemper LH, Bouabdallah K, Ziepert M, Leclerc M, Cartron G, et al. A randomized phase 3 trial of auto vs. allo transplantation as part of first-line therapy in poor-risk peripheral T-NHL. Blood. 2020.
28. Fossard G, Broussais F, Coelho I, Bailly S, Nicolas-Virelizier E, Toussaint E, et al. Role of up-front autologous stem-cell transplantation in peripheral T-cell lymphoma for patients in response after induction: an analysis of patients from LYSA centers. Annals of Oncology. 2018;29(3):715-23.
29. Savage KJ, Horwitz SM, Advani R, Christensen JH, Domingo-Domenech E, Rossi G, et al. Role of stem cell transplant in CD30+ PTCL following frontline brentuximab vedotin plus CHP or CHOP in ECHELON-2. Blood Advances. 2022;6(19):5550-5.
30. Eastern Cooperative Oncology Group. Testing Whether High Dose Chemotherapy and Infusion of the Patients' Own Stem Cells Improves Survival in Patients With Peripheral T-cell Lymphoma Who Achieved a Complete Response at the End of the Initial Chemotherapy (NCT06724237) 2026 [Available from: https://clinicaltrials.gov/study/NCT06724237.

31. Hospices Civils de Lyon. Transplantation After Complete Response In Patients With T-cell Lymphoma (TRANSCRIPT) (NCT05444712) 2023 [Available from: https://clinicaltrials.gov/study/NCT05444712.
32. Mak V, Hamm J, Chhanabhai M, Shenkier T, Klasa R, Sehn LH, et al. Survival of Patients With Peripheral T-Cell Lymphoma After First Relapse or Progression: Spectrum of Disease and Rare Long-Term Survivors. Journal of Clinical Oncology. 2013;31(16):1970-6.
33. Mehta-Shah N, Kommalapati A, Teja S, Cashen AF, Dahi PB, Sauter CS, et al. Successful Treatment of Mature T-Cell Lymphoma with Allogeneic Stem Cell Transplantation: The Largest Multicenter Retrospective Analysis. Blood. 2020;136(Supplement 1):35-6.
34. Smith SM, Burns LJ, Van Besien K, Lerademacher J, He W, Fenske TS, et al. Hematopoietic Cell Transplantation for Systemic Mature T-Cell Non-Hodgkin Lymphoma. Journal of Clinical Oncology. 2013;31(25):3100-9.
35. Epperla N, Ahn KW, Litovich C, Ahmed S, Battiwalla M, Cohen JB, et al. Allogeneic hematopoietic cell transplantation provides effective salvage despite refractory disease or failed prior autologous transplant in angioimmunoblastic T-cell lymphoma: a CIBMTR analysis. Journal of Hematology & Oncology. 2019;12(1).
36. Hamadani M, Ngoya M, Sureda A, Bashir Q, Litovich CA, Finel H, et al. Outcome of allogeneic transplantation for mature T-cell lymphomas: impact of donor source and disease characteristics. Blood Advances. 2022;6(3):920-30.
37. Le Gouill S, Milpied N, Buzyn A, Peffault De Latour R, Vernant J-P, Mohty M, et al. Graft-Versus-Lymphoma Effect for Aggressive T-Cell Lymphomas in Adults: A Study by the Société Française de Greffe de Moëlle et de Thérapie Cellulaire. Journal of Clinical Oncology. 2008;26(14):2264-71.
38. Ngu HS, Savage KJ. Past, present and future therapeutic approaches in nodal peripheral T-cell lymphomas. Haematologica. 2023;108(12):3211-26.
39. Skamene T, Crump M, Savage KJ, Reiman T, Kuruvilla J, Good D, et al. Salvage chemotherapy and autologous stem cell transplantation for peripheral T-cell lymphoma: a subset analysis of the Canadian Cancer Trials Group LY.12 randomized phase 3 study. Leukemia & Lymphoma. 2017;58(10):2319-27.
40. O'Connor OA, Pro B, Pinter-Brown L, Bartlett N, Popplewell L, Coiffier B, et al. Pralatrexate in Patients With Relapsed or Refractory Peripheral T-Cell Lymphoma: Results From the Pivotal PROPEL Study. Journal of Clinical Oncology. 2011;29(9):1182-9.
41. Horwitz SM, Advani RH, Bartlett NL, Jacobsen ED, Sharman JP, O'Connor OA, et al. Objective responses in relapsed T-cell lymphomas with single-agent brentuximab vedotin. Blood. 2014;123(20):3095-100.
42. Coiffier B, Pro B, Prince HM, Foss F, Sokol L, Greenwood M, et al. Romidepsin for the treatment of relapsed/refractory peripheral T-cell lymphoma: pivotal study update demonstrates durable responses. Journal of Hematology & Oncology. 2014;7(1):11.
43. Dupuis J, Bachy E, Morschhauser F, Cartron G, Fukuhara N, Daguindau N, et al. Oral azacitidine compared with standard therapy in patients with relapsed or refractory follicular helper T-cell lymphoma (ORACLE): an open-label randomised, phase 3 study. The Lancet Haematology. 2024;11(6):e406-e14.
44. Zinzani PL, Izutsu K, Mehta-Shah N, Barta SK, Ishitsuka K, Córdoba R, et al. Valemetostat for patients with relapsed or refractory peripheral T-cell lymphoma (VALENTINE-PTCL01): a multicentre, open-label, single-arm, phase 2 study. The Lancet Oncology. 2024;25(12):1602-13.
45. O'Connor OA, Horwitz S, Masszi T, Van Hoof A, Brown P, Doorduijn J, et al. Belinostat in Patients With Relapsed or Refractory Peripheral T-Cell Lymphoma: Results of the Pivotal Phase II BELIEF (CLN-19) Study. Journal of Clinical Oncology. 2015;33(23):2492-9.
46. Tiger YK, Atmuri U, Iyer SP. Trial in Progress: A Phase 3, Randomized, Open-Label Study Comparing the Efficacy and Safety of the Combination of Beleodaq-CHOP or Folotyn-Cop to the CHOP Regimen Alone in Newly Diagnosed Patients with Peripheral T- Cell Lymphoma - Crescendo. Blood. 2024;144(Supplement 1):3123.1-.1.
47. Pro B, Advani R, Brice P, Bartlett NL, Rosenblatt JD, Illidge T, et al. Five-year results of brentuximab vedotin in patients with relapsed or refractory systemic anaplastic large cell lymphoma. Blood. 2017;130(25):2709-17.
48. Bennani NN, Kim HJ, Pederson LD, Atherton PJ, Micallef IN, Thanarajasingam G, et al. Nivolumab in patients with relapsed or refractory peripheral T-cell lymphoma: modest activity and cases of hyperprogression. Journal for ImmunoTherapy of Cancer. 2022;10(6):e004984.
49. Kim W-S, Shortt J, Luigi Zinzani P, Mikhaylova N, Marin-Niebla A, Radeski D, et al. P1142: AFM13 IN PATIENTS WITH R/R PERIPHERAL T CELL LYMPHOMA (PTCL): A POST-HOC SUBGROUP ANALYSIS FROM THE REDIRECT STUDY. HemaSphere. 2023;7(S3):e6843062.
50. Fleischer LC, Spencer HT, Raikar SS. Targeting T cell malignancies using CAR-based immunotherapy: challenges and potential solutions. Journal of Hematology & Oncology. 2019;12(1).



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Committed to delivering new innovations in Hematology

GSK prioritizes the development of targeted medicines to bring groundbreaking cancer therapies to patients. We are focused on developing innovative medicines both as monotherapies and in combinations to get ahead of blood cancers together.

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