CoLab Network

Emerging Drugs for Relapsed or Refractory Peripheral T-Cell Lymphoma

Author
Michael Law, PhD

May 2023

Table of Contents

About This Document 03

Objective 03

Selection Criteria and Methods 03

Results 04

Summary 05

References 08

About This Document

This report provides information on advanced pipeline drugs intended to treat relapsed or refractory peripheral t-cell lymphoma (RR-PTCL). Specifically, it identifies therapies that have published phase II or III trial results and are not either approved for use or are under review by Health Canada. In addition, it also identifies several drugs and therapies that have currently ongoing phase II trials. It is important to note that this report is not a systematic review and does not include a critical appraisal of studies, nor is it intended to provide any recommendations.

Objective

To identify and describe the trial characteristics of recently completed phase II and III trials with published results that evaluated drugs to treat RR-PTCL that are not currently approved by or undergoing Health Canada review.

Selection Criteria and Methods

Drugs for RR-PTCL that have completed and published phase II or III trials were identified using several sources, including:

- ClinicalTrials.gov: A search was conducted on the clinicaltrials.gov study registration platform using the keywords and conditions “peripheral t-cell lymphoma” and “peripheral t-cell lymphoma refractory,” limiting the results to phase II or III studies. The study titles were then used to narrow the list to studies specific to RR-PTCL.
- Other horizon scan documents: We identified candidate ingredient names from other horizon scan documents, including summaries of commercially available scans. These drug names were then searched on clinicaltrials.gov to identify potential candidates.
- Published abstracts: We used PubMed and Google Scholar to search for published manuscripts or abstracts describing phase II or III trials of treatments for RR-PTCL. This was conducted using similar keywords and Medical Subject Headings (MeSH) headings to the searches on clinicaltrials.gov. We then used the clinicaltrials.gov National Clinical Trial (NCT) number reported in the article to identify the relevant trial, which was available in all cases.

Based on this candidate list of drugs:

- We excluded drugs that had already been approved in Canada, either for RR-PTCL or another indication. Approved drugs were identified using the Health Canada Drug Product Database.[1]
- We excluded drugs that have currently active submissions that were under review by Health Canada. These were identified using the Health Canada website.[2]
- From this final list, we used PubMed, Google Scholar, and internet searches to identify published articles and/or abstracts that reported the results of these trials. We excluded trials for which we could not identify a publication. We have included a separate table of these excluded drugs to show other activity in earlier clinical development stages and to assess the degree of development activity in this clinical area.

For the final list of drugs, we used clinicaltrials.gov to identify information on the population(s) that were studied, the names of the drugs, any comparators that were used, the basic study design, and the estimated or actual primary completion date of each trial. We also searched for the approval status of these drugs in other countries, including using the US Drugs@FDA database,[3] online corporate pipeline reports, and corporate press releases.

Results

Table 1 shows the characteristics of the 10 drugs for which we identified completed phase II or III trials with published results. As shown in the table, all of the drugs we identified were studied in phase II trials that were nonrandomized, open-label studies, and had comparatively small sample sizes. The studies reported in the publications were conducted in a number of countries, with a large number including trial sites in countries in East Asia, particularly Japan and Korea. The sample sizes in these trials ranged from 25 to 160 participants and all required treatment with 1 or more prior lines of therapy.

The approval status for these 10 drugs in other countries and notes on their progress toward approval are shown in Table 2. As shown in the table, several of these 10 drugs have been granted breakthrough or orphan review designations by the US FDA. In addition, some have been approved or are under review in Japan and Korea.

Table 3 shows the names and clinicaltrials.gov identifiers for the 15 drugs that were listed as having phase II trials in progress and for which we did not identify published results. This table shows active assessment of a number of new treatments, including 2 chimeric antigen receptor (CAR) T-cell therapies that are currently under study.

In terms of limitations, it is important to note that there is no central repository of drugs under development, so it is possible that this list is incomplete and missing 1 or more drugs that would fulfill our inclusion criteria had they been identified. This review would also not include drugs that might be already approved for other indications and potentially used for RR-PCTL in the future. In addition, it also did not cover the potential repurposing of already approved and/or failed therapies in new combinations. Finally, the assessment of their approval prospects could only account for information that was posted on corporate websites and press releases, so may not fully reflect their current status.

Summary

As seen by the number of drugs under study for RR-PCTL, this is a clinical space with a large amount of drug development in progress. This is likely the result of a comparatively high need for additional treatments for relapsed and/or refractory disease.[4] As several of these drugs are approved in other countries or moving in that direction, it seems highly likely that some will appear in the Canadian market in coming years. This suggests that it will become a clinical area to monitor for drug plans across the country.

Table 1

Drugs to Treat Relapsing or Refractory Peripheral T-Cell Lymphoma: Phase II Trials With Published Results

Experimental drug	Study design and location(s)	Estimated or actual trial primary completion date	Sample size and key inclusion criteria	ClinicalTrials.gov reference	Study reference
AFM13	Nonrandomized, open label, multinational (69 locations across 10 countries)	December 2022	145 participants who had treatment with 1 prior line of therapy	NCT04101331	Nieto et al.[5]
Copanlisib	Single-group assignment, open label, Korea	July 2021	28 participants with histologically confirmed relapsed or refractory PTCL or NK/T-cell lymphomas	NCT03052933	Yhim et al.[6]
Darinaparsin (SP-02L)	Single-group assignment, open label, 4 countries (Hong Kong, Japan, Korea, Taiwan)	October 2020	67 participants of Japanese, Korean, Taiwanese, or Chinese background with a treatment history of 1 prior regimen	NCT02653976	Kim et al.[7]
Geptanolimab	Single-group assignment, open label, China	August 2021	86 participants with histologically confirmed relapsed or refractory PTCL who had received systemic treatment at least once	NCT03502629	Shi et al.[8]
Golidocitinib	Single-group assignment, open label, multinational (US, Korea, Australia, China)	January 2023	160 participants who relapsed after or were refractory or intolerant to ≥ 1 (but not > 3) prior systemic therapy(ies) for PTCL	NCT04105010	Kim et al.[9]
Tenalisib (RP6530)	Single-group assignment, open label, US	March 2018	58 participants who were refractory to or relapsed after at least 1 prior treatment line	NCT02567656	Iyer et al.[10]
Tipifarnib	Single-group assignment, open label, 3 countries (US, Spain, Korea)	March 2021	65 participants who relapsed or were refractory to at least 1 prior systemic cytotoxic therapy	NCT02464228	Witzig et al.[11]
Tislelizumab	Single-group assignment, open label, 6 countries (Canada, China, France, Germany, Italy, Taiwan)	April 2021	77 participants who were relapsed or refractory to at least 1 prior systemic therapy	NCT03493451	Bachy et al.[12]
Tucidinostat (HBI-8000)	Single-group assignment, open label, 2 countries (Japan and Korea)	February 2022	40 participants with relapsed or refractory disease after receiving ≥ 1 prior systemic therapy with antitumor drugs(s)	NCT02953652	Rai et al.[13]
Valemetostat (DS-3201b)	Single-group assignment, open label, Japan	April 2021	25 participants with relapsed or refractory ATL who had a history of treatment with mogamulizumab or were mogamulizumab intolerant	NCT04102150	Izutsu et al.[14]

ATL = adult T-cell leukemia or lymphoma; NK = natural killer; PTCL = peripheral T-cell lymphoma.

Table 2

Advanced Pipeline Drugs to Treat Relapsing or Refractory Peripheral T-Cell Lymphoma: Approval Status in Other Countries

Experimental drug	Approval status in other countries
AFM13	Granted orphan drug designation by the US FDA in 2020 In process of completing an Investigational New Drug application with the US FDA in early 2023[15]
Copanlisib	Approved in the US in 2017 for a different indication (relapsed follicular lymphoma)[3]
Darinaparsin (SP-02L)	Approved in Japan in June 2022, granted orphan drug designation by US FDA[16]
Geptanolimab	New Drug Application under review in China[17]
Golidocitinib	Granted US FDA fast track designation in 2022[18]
Tenalisib (RP6530)	Granted US FDA fast track designation in 2017, orphan designation in 2018[19]
Tipifarnib	Granted US FDA breakthrough designation for another indication[20]
Tislelizumab	Likely US FDA submission in 2023 for another indication[21]
Tucidinostat (HBI-8000)	Under review in Korea and Japan[22]
Valemetostat (DS-3201b)	Approved in Japan in September 2022, granted orphan drug status in the US in 2021[23]

Table 3

Drugs to Treat Relapsing or Refractory Peripheral T-Cell Lymphoma: Ongoing Phase II Trials

Experimental drug	Estimated trial primary completion date	ClinicalTrials.gov reference
AZD4573	November 2023	NCT05140382
CAR T-Cell (AUTO4)	July 2023	NCT03590574
CAR T-Cell (ATLCAR.CD30)	August 2023	NCT04083495
CFT7455	September 2024	NCT04756726
Devimistat (CPI 613)	March 2023	NCT04217317
Duvelisib (Copiktra)	September 2023	NCT03372057
Lacutamab (IPH4102)	January 2025	NCT04984837
Linperlisib	January 2023	NCT05274997
MT-101	November 2023	NCT05138458
Nanatinostat	July 2024	NCT05011058
SHR 2554	March 2024	NCT05559008
Sintilimab (Tyvyt)	September 2023	NCT04512534
ST-001	July 2021	NCT02495415
Tolinapant	December 2025	NCT05403450

References

1. Health Canada. Health Canada Drug Product Database (DPD). 2023]. http://www.hc-sc.gc.ca/dhp-mps/prodpharma/databasdon/index-eng.php Accessed 2023 Oct 23.
2. Health Canada. Drug and Health Product Submissions Under Review (SUR): New drug submissions under review. 2021. https://www.canada.ca/en/health-canada/services/drug-health-product-review-approval/submissions-under-review/new-drug-submissions-under-review.html Accessed 2023 Feb 12.
3. US Food and Drug Administration. Drugs@FDA: FDA-Approved Drugs. 2023. https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm Accessed 2023 Feb 27.
4. Foster C, Kuruvilla J. Treatment approaches in relapsed or refractory peripheral T-cell lymphomas [version 1; peer review: 3 approved]. F1000Research. 2020;9:1091.
5. Nieto Y, Banerjee P, Kaur I, Bassett R, Kerbauy L, Basar R, et al. Innate cell engager (ICE®) AFM13 combined with preactivated and expanded cord blood (CB)-derived NK cells for patients with refractory/relapsed CD30+ lymphoma. Cancer Research. 2022 Jun 15;82(12_Supplement):CT003–CT003.
6. Yhim HY, Kim T, Kim SJ, Shin HJ, Koh Y, Kim JS, et al. Combination treatment of copanlisib and gemcitabine in relapsed/refractory PTCL (COSMOS): an open-label phase I/II trial. Ann Oncol. 2021 Apr 1;32(4):552–9.
7. Kim WS, Fukuhara N, Yoon DH, Yamamoto K, Uchida T, Negoro E, et al. Darinaparsin in Patients with Relapsed or Refractory Peripheral T-Cell Lymphoma: Results of an Asian Phase 2 Study. Blood Adv. 2023 Jan 20;bloodadvances.2022008615.
8. Shi Y, Wu J, Wang Z, Zhang L, Wang Z, Zhang M, et al. Efficacy and safety of geptanolimab (GB226) for relapsed or refractory peripheral T cell lymphoma: an open-label phase 2 study (Gxplore-002). J Hematol Oncol. 2021 Jan 12;14(1):12.
9. Kim WS, Yoon DH, Song Y, Yang H, Cao J, Ji D, et al. A phase I/II study of golidocitinib, a selective JAK1 inhibitor, in refractory or relapsed peripheral T-cell lymphoma. JCO. 2022 Jun 1;40(16_suppl):7563–7563.
10. Iyer SP, Huen A, Ai WZ, Jagadeesh D, Lechowicz MJ, Okada C, et al. Safety and Efficacy of Tenalisib Given in Combination with Romidepsin in Patients with Relapsed/Refractory T-Cell Lymphoma: Final Results from a Phase I/II Open Label Multi-Center Study. Blood. 2021 Nov 23;138:1365.
11. Witzig TE, Sokol L, Kim WS, de la Cruz Vicente F, Caballero D, Advani R, et al. Final Results from a Phase 2 Study of Tipifarnib in Subjects with Relapsed or Refractory Peripheral T-Cell Lymphoma. Blood. 2021 Nov 5;138(Supplement 1):621–621.
12. Bachy E, Savage KJ, Huang H, Kwong YL, Gritti G, Zhang Q, et al. Tislelizumab, a PD-1 inhibitor for relapsed/refractory mature T/NK-cell neoplasms: Results from a phase 2 study. JCO. 2022 Jun 1;40(16_suppl):7552–7552.
13. Rai S, Kim WS, Ando K, Choi I, Izutsu K, Tsukamoto N, et al. Oral HDAC inhibitor tucidinostat in patients with relapsed or refractory peripheral T-cell lymphoma: phase IIb results. Haematologica. 2022 Oct 6;108(3).
14. Izutsu K, Makita S, Nosaka K, Yoshimitsu M, Utsunomiya A, Kusumoto S, et al. An Open-Label, Single-Arm, Phase 2 Trial of Valemetostat in Relapsed or Refractory Adult T-Cell Leukemia/Lymphoma. Blood. 2022 Sep 23;blood.2022016862.
15. Affirmed. Affimed Reports on Corporate Progress and Provides Regulatory Update for AFM13. 2023. https://www.affimed.com/affimed-reports-on-corporate-progress-and-provides-regulatory-update-for-afm13/ Accessed 2023 Feb 27.
16. Solasia Pharma K.K. Pipeline Information. https://solasia.co.jp/en/pipeline/ Accessed 2023 Feb 11.
17. Genor Biopharma Co. Ltd. Pipeline. https://www.genorbio.com/en/research-development/pipeline/ Accessed 2023 Feb 27.
18. PR Newswire. Pharmaceutical D. Dizal Pharmaceutical Receives U.S. FDA Fast Track Designation for DZD4205 (Golidocitinib) for the Treatment of Refractory or Relapsed Peripheral T-Cell Lymphoma. https://www.prnewswire.com/news-releases/dizal-pharmaceutical-receives-us-fda-fast-track-designation-for-dzd4205-golidocitinib-for-the-treatment-of-refractory-or-relapsed-peripheral-t-cell-lymphoma-301485596.html Accessed 2023 Feb 27.

19. Rhizen. Our Pipeline. https://rhizen.com/our-pipeline/ Accessed 2023 Feb 27.
20. Kura Oncology Inc. Kura Oncology Receives FDA Breakthrough Therapy Designation for Tipifarnib in Head and Neck Squamous Cell Carcinoma. https://ir.kuraoncology.com/news-releases/news-release-details/kura-oncology-receives-fda-breakthrough-therapy-designation Accessed 2023 Feb 27.
21. BeiGene. Development Pipeline. https://www.beigene.com/our-science-and-medicines/pipeline 2023 Feb 27.
22. HUYABIO International. Pipeline. https://huyabio.com/pipeline/ Accessed 2023 Feb 27.
23. Daiichi-Sankyo. EZHARMIA® Approved in Japan as First Dual EZH1 and EZH2 Inhibitor Therapy for Patients with Adult T-Cell Leukemia/ Lymphoma. 2022 https://www.daiichisankyo.com/files/news/pressrelease/pdf/202209/20220926_E.pdf Accessed 2023 Feb 27.

For more information on CoLab and its work visit **colab.cadth.ca**

Canada's Drug and Health Technology Agency

CoLab Network

This work was supported by CADTH and its Post-Market Drug Evaluation Program, through funding provided by Health Canada.

About CADTH: CADTH is a not-for-profit organization responsible for providing Canada's health care decision-makers with objective evidence to help make informed decisions about the optimal use of drugs and medical devices in our health care system.

About CoLab: CoLab is a pan-Canadian network of experts in applied research, scientific methods, and data analysis. CoLab members work with CADTH's Post-Market Drug Evaluation Program to produce credible and timely evidence on post-market drug safety and effectiveness.