ZYNLONTA® (loncastuximab tesirine-lpyl) – Bulky Disease and Burkitt Lymphoma

Overview

- LOTIS-1 was a Phase 1, open-label, single-arm, multicenter study that evaluated the safety and tolerability of ZYNLONTA monotherapy in 183 adult patients with relapsed or refractory (R/R) B-cell Non-Hodgkin Lymphoma (B-NHL).[1]
    - Eighteen patients (9.8%) had presence of bulky disease and the overall response rate (ORR) in this patient population was 22.2% (95% CI: [6.4, 47.6]).[2]
    - One patient (0.5%) was diagnosed with Burkitt Lymphoma and received 1 dose of Loncastuximab tesirine-lpyl. Treatment was withdrawn due to disease progression and no additional action was taken with the study drug. The outcome of the event was fatal, and the event was considered not related to study drug.[1,3]
- LOTIS-2 was a pivotal Phase 2, multicenter, open-label single-arm study that evaluated the efficacy and safety of ZYNLONTA used as monotherapy in 145 adult patients with R/R diffuse large B-cell lymphoma (DLBCL) following ≥2 lines of prior systemic therapy.[4]
    - Patients with bulky disease (tumor ≥10 cm in longest dimension) were included in the study until a protocol amendment subsequently excluded this patient population due to low ORR in an interim analysis of the Phase 1 study.[4]
    - Eight patients (6%) had bulky disease and the ORR was 25% (95% CI: [3.2, 65.1]).[5]
    - Pathologic diagnosis of Burkitt Lymphoma was a key exclusion criterion.[5]
- ADC Therapeutics does not make recommendations outside the Prescribing Information. ZYNLONTA is indicated for the treatment of adult patients with relapsed or refractory large B-cell lymphoma after two or more lines of systemic therapy, including diffuse large B-cell lymphoma (DLBCL) not otherwise specified, DLBCL arising from low-grade lymphoma, and high-grade B-cell lymphoma.[6] See Relevant Prescribing Information for additional information.

Literature Search

- A PubMed biomedical literature search conducted on March 12, 2025, yielded no relevant data regarding ZYNLONTA and bulky disease or Burkitt Lymphoma.

Relevant Prescribing Information

1 INDICATIONS AND USAGE[7]

- ZYNLONTA is indicated for the treatment of adult patients with relapsed or refractory large B-cell lymphoma after two or more lines of systemic therapy, including diffuse large B-cell lymphoma (DLBCL) not otherwise specified, DLBCL arising from low-grade lymphoma, and high-grade B-cell lymphoma.
- This indication is approved under accelerated approval based on overall response rate [see Clinical Studies (14.1)]. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).

6.1: Adverse Reactions[7]

Section 6.1: Clinical Trials Experience

- Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.
- The pooled safety population described in the WARNINGS AND PRECAUTIONS reflect exposure to ZYNLONTA as a single agent at an initial dose of 0.15 mg/kg in 215 patients with DLBCL in studies ADCT-402-201 (LOTIS-2) and ADCT-402-101, which includes 145 patients from LOTIS-2 treated with 0.15 mg/kg x 2 cycles followed by 0.075 mg/kg for subsequent cycles. Among 215 patients who received ZYNLONTA, the median number of cycles was 3 (range 1 to 15) with 58% receiving three or more cycles and 30% receiving five or more cycles.
- In this pooled safety population of 215 patients, the most common (>20%) adverse reactions, including laboratory abnormalities, were thrombocytopenia, increased gamma-glutamyltransferase, neutropenia, anemia, hyperglycemia, transaminase elevation, fatigue, hypoalbuminemia, rash, edema, nausea, and musculoskeletal pain.

14: Clinical Studies[7]

Section 14.1: Relapsed or Refractory Diffuse Large B-cell Lymphoma

- The efficacy of ZYNLONTA was evaluated in LOTIS-2 (NCT03589469), an open-label, single-arm trial in 145 adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) after at least 2 prior systemic regimens. The trial excluded patients with bulky disease and active central nervous system lymphoma. Patients received ZYNLONTA 0.15 mg/kg every 3 weeks for 2 cycles, then 0.075 mg/kg every 3 weeks for subsequent cycles and received treatment until progressive disease, or unacceptable toxicity.

References

[1] Hamadani M, Radford J, Carlo-Stella C, et al. Final results of a phase 1 study of loncastuximab tesirine in relapsed/refractory B-cell non-Hodgkin lymphoma. *Blood*. 2021;137(19):2634-2645. doi:10.1182/blood.2020007512

[2] Hamadani M, Radford J, Carlo-Stella C, et al. Final results of a phase 1 study of loncastuximab tesirine in relapsed/refractory B-cell non-Hodgkin lymphoma [Supplementary Appendix]. *Blood*. 2021;137(19):2634-2645. doi:10.1182/blood.2020007512

[3] Data on File, LOTIS-1 Clinical Study Report. ADC Therapeutics

[4] Caimi PF, Ai WZ, Alderuccio JP, et al. Loncastuximab tesirine in relapsed/refractory diffuse large B-cell lymphoma: long-term efficacy and safety from the phase 2 LOTIS-2 study. Haematol. Published online August 31, 2023. doi: 110.3324/haematol.2023.283459

[5] Caimi PF, Ai W, Alderuccio JP, et al. Loncastuximab tesirine in relapsed or refractory diffuse large B-cell lymphoma (LOTIS-2): a multicentre, open-label, single-arm, phase 2 trial [Supplementary Appendix]. *Lancet Oncol*. 2021;22(6):790-800. doi:10.1016/S1470-2045(21)00139-X

[6] Data on File, Bulky Disease and Burkitt Lymphoma Memo. ADC Therapeutics

[7] ZYNLONTA® (loncastuximab tesirine-lpyl) for injection Prescribing Information, October 2022

ADC Therapeutics encourages all health care professionals to report any adverse events and product quality complaints to medical information at 855-690-0340. Please consult the ZYNLONTA Prescribing Information.