ZYNLONTA® (loncastuximab tesirine-lpyl) – Incidence and Management of Hypersensitivity

Summary

- LOTIS-1 was a Phase 1, open-label, single-arm, multicenter study which evaluated the safety and tolerability of ZYNLONTA monotherapy in 183 patients (≥18 years of age) with relapsed or refractory (R/R) B-Cell Non-Hodgkin's Lymphoma (B-NHL).[1,3]
    - Patients with a known history of immunogenicity or hypersensitivity to a CD19 antibody were excluded from the study.
    - There were no treatment-emergent adverse events (TEAEs) of hypersensitivity, or anaphylaxis, in the LOTIS-1 study.
- 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 relapsed or refractory diffuse large B-cell lymphoma (R/R DLBCL) following ≥2 lines of prior systemic therapy.[2,4]
    - Patients with a known history to or positive serum human anti-drug antibody (ADA) to a CD19 antibody were excluded from the study.
    - One patient (0.7%) experienced Grade 2 drug hypersensitivity after the first infusion of ZYNLONTA which led to interruption of the infusion. The hypersensitivity resolved on the same day after treatment, and the patient continued the study.
        - Treatment of the drug hypersensitivity included diphenhydramine hydrochloride, famotidine, and methylprednisolone sodium succinate.
- See Relevant Prescribing Information for additional information.

Background

- LOTIS-1 was a Phase 1, open-label, dose-escalation (Part 1) and expansion (Part 2) study that evaluated the safety and tolerability of ZYNLONTA, used as monotherapy, in 183 adult patients with relapsed or refractory B-cell Non-Hodgkin's Lymphoma (R/R B-NHL).[1]
- 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 relapsed or refractory diffuse large B-cell lymphoma (R/R DLBCL) following ≥2 lines of prior systemic therapy.[2]

Clinical Data

LOTIS-1 (Phase 1)[1,3]

- Patients with a known history of immunogenicity or hypersensitivity to a CD19 antibody were excluded from the study.
- Premedication was administered if Grade ≥2 infusion-related hypersensitivity reactions were observed in one patient at any time during Part 1 of the study. All subsequent patients were to receive prophylactic treatment on Day 1 of each cycle thereafter to reduce the risk of hypersensitivity reaction. During Part 2, all patients received dexamethasone, unless contraindicated.
- There were no TEAEs of hypersensitivity, or anaphylaxis, presented in the LOTIS-1 study.

LOTIS-2 (Phase 2)[2,4]

- Patients with a known history to or positive serum human ADA to a CD19 antibody were excluded from the study.
- Medications for the treatment of severe hypersensitivity reactions, including anaphylaxis, were available for immediate use and were administered according to site standard treatment protocols.
- Any patient who experienced an infusion-related hypersensitivity reaction received prophylactic treatment in subsequent cycles according to the guidelines below or institutional standard of care.
    - On Day 1 of each cycle, patients were instructed to take dexamethasone 20 mg orally 12 and 6 hours before ZYNLONTA treatment.
    - On Day 1 of each cycle, patients were administered diphenhydramine hydrochloride 50 mg intravenously 30 minutes before ZYNLONTA treatment.
    - On Day 1 of each cycle, patients were administered ranitidine (or pharmaceutical equivalent) 50 mg intravenously 30 minutes before ZYNLONTA treatment.
    - For 2 days following ZYNLONTA treatment, patients were given dexamethasone 4 mg orally, twice daily.
- One patient (0.7%) experienced Grade 2 drug hypersensitivity (described as an allergic reaction to the infusion) after the first infusion of ZYNLONTA which in turn led to infusion interruption. The investigator's assessment concluded that this was drug related. The event resolved the same day after treatment and the patient continued the study.
    - Treatment for the patient's drug hypersensitivity included diphenhydramine hydrochloride, famotidine, and methylprednisolone sodium succinate.

Literature Search

- A PubMed biomedical literature search conducted on March 26, 2025, yielded no relevant data regarding the incidence and management of hypersensitivity of ZYNLONTA.

Relevant Prescribing Information

Section 2 Dosage and Administration[5]

2.1 Recommended Premedication

- Unless contraindicated, administer dexamethasone 4 mg orally or intravenously twice daily for 3 days beginning the day before administering ZYNLONTA. If dexamethasone administration does not begin the day before ZYNLONTA, dexamethasone should begin at least 2 hours prior to administration of ZYNLONTA.

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. 2020. https://doi.org/10.1182/blood.2020007512.
[2] 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
[3] Data on File, LOTIS 1 Clinical Study Report. ADC Therapeutics.
[4] Data on File, LOTIS 2 Clinical Study Report. ADC Therapeutics.
[5] ZYNLONTA® (loncastuximab tesirine-lpyl) FDA-approved 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.