ZYNLONTA® (loncastuximab tesirine-lpyl) – Use in Overweight/Obese Patients

Summary

- LOTIS-1 was a Phase 1, open-label, single-arm, multicenter study which 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]
  - Mean body mass index (BMI) of the patient population was 27.93 kg/m^2 (range 16.5 to 50.1).[3]
  - No safety or efficacy subgroup analyses were performed in patients who were obese (≥ 30 kg/m^2).
- LOTIS-2 was a Phase 2, open-label, single-arm, multicenter study which evaluates the efficacy and safety of ZYNLONTA monotherapy in 145 patients (≥18 years of age) with R/R diffuse large B-cell Lymphoma (DLBCL) following ≥2 lines of prior systemic therapy.[2]
  - Mean BMI of the overall population was 26.93 kg/m^2 (range 17.2 to 50.5).
  - For patients with a body mass index (BMI) ≥35 kg/m^2, their dose was calculated based on an adjusted body weight (ABW).
    - Only nine patients had a BMI of 35 kg/m^2 or greater, therefore it was not possible to compare safety with patients with BMI less than 35 kg/m^2.
  - No safety or efficacy subgroup analyses were performed in patients who were obese (≥ 30 kg/m^2).
- For patients with a BMI ≥35 kg/m^2, calculate the dose based on an ABW.[Error! Bookmark not defined.] See **Relevant Prescribing Information** for additional information.

Background

- LOTIS-1 was a Phase 1, open-label, single-arm, multicenter study which evaluated the safety and tolerability of ZYNLONTA monotherapy in 183 adult patients with relapsed or refractory (R/R) B-Cell Non-Hodgkin's Lymphoma (B-NHL). The study was conducted in two parts, dose-escalation (Part 1) followed by dose-expansion (Part 2). Male or female patients (≥18 years of age) with histologically confirmed R/R B-NHL were enrolled if they failed or became intolerant to established therapies or if they had no other treatment options available.[1]
- LOTIS-2 was a Phase 2, open-label, single-arm, multicenter study which evaluates the efficacy and safety of ZYNLONTA monotherapy in 145 patients (≥18 years of age) with R/R DLBCL following ≥2 lines of prior systemic therapy.[2]

Clinical Data

LOTIS-1 (Phase 1)

- In Part 1 of LOTIS-1, patients were assigned to dose cohorts using a 3+3 dose-escalation study design, starting with ZYNLONTA 15 µg/kg once every 3 weeks (Day 1 of each 21-day cycle) and administered as an intravenous (IV) infusion over 60 minutes. The maximum administered dose of ZYNLONTA in Part 1 was 200 µg/kg.[3]
- In Part 2, patients were assigned to recommended dose level(s) and regimen(s) of ZYNLONTA identified from Part 1 based on safety, efficacy, and pharmacokinetic data.
- Patients received ZYNLONTA at a dose of 120 µg/kg every 3 weeks or 150 µg/kg every 3 weeks. Some patients in the 150 µg/kg treatment arm had their doses reduced to 75 µg/kg every 3

weeks after 3 cycles.[1] In LOTIS-1, the mean body mass index of the patient population (safety analysis set) was 27.93 kg/m^2 (range 16.5 to 50.1).

- No safety or efficacy subgroup analyses based on patient weight were performed.

LOTIS-2 (Phase 2)

- In LOTIS-2, ZYNLONTA was administered as an IV infusion over 30 minutes on Day 1 of each cycle (every 3 weeks) at a dose of 150 µg/kg for 2 cycles and then 75 µg/kg for subsequent cycles.[2]
- The mean body mass index of the overall population was 26.93 kg/m^2 (range 17.2 to 50.5).
- For patients with a body mass index (BMI) ≥35 kg/m^2, their dose was calculated based on an adjusted body weight (ABW).[2] ABW in kg=35 kg/m^2 × (height in meters)^2 Dose to administer (mg)=dosage (µg/kg) × ABW/1000
    - Only nine patients had a BMI of 35 kg/m^2 or greater, therefore it was not possible to compare safety with patients with BMI less than 35 kg/m^2.[4]
- In the LOTIS-2 study, one patient with a BMI >35 was administered ZYNLONTA based on their actual weight instead of ABW for the first infusion. The dose was 19.6% higher than the planned dose according to ABW.[2]
- In the LOTIS-2 study one patient was administered ZYNLONTA at a dose which was 18% lower than the planned dose according to ABW for all 3 cycles.
- Subgroup analyses for safety and efficacy were not performed based on patient weight.

Literature Search

- A PubMed biomedical literature search conducted on May 22, 2025, yielded no relevant data regarding the use of ZYNLONTA in overweight/obese patients.

Relevant Prescribing Information

Section 2: Dosage and Administration[5]

2.1 *Recommended Dosage*

ZYNLONTA is to be administered as an IV infusion over 30 minutes on Day 1 of each cycle (every 3 weeks). Administer IV infusion as follows:

- 0.15 mg/kg every 3 weeks for 2 cycles
- 0.075 mg/kg every 3 weeks for subsequent cycles

2.4 Reconstitution and Administration Instructions[5]

Dose Calculation

Calculate the total dose (mg) required based on the patient's weight and prescribed dose

- For patients with a BMI ≥35 kg/m^2, calculate the dose based on an ABW as follows: ABW in kg = 35 kg/m^2 × (height in meters)^2
- More than one vial may be needed to achieve the calculated dose.
- Convert the calculated dose (mg) to volume using 5 mg/mL, which is the concentration of ZYNLONTA after reconstitution.

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. DOI: 10.1182/blood.2020007512.

[2] Data on File, LOTIS 2 Clinical Study Report. ADC Therapeutics.

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

[4] 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. Lancet Oncol. 2021;22(6):790-800. doi:10.1016/S1470-2045(21)00139-X

[5] ZYNLONTA® (loncastuximab tesirine-lpyl) FDA-approved Prescribing Information. October 2022.