ZYNLONTA® (loncastuximab tesirine-lpyl) – Rationale for Adjusted Body Weight Calculation

Summary

- The adjusted body weight (ABW) formula was derived from the pharmacokinetic model in the LOTIS-1 (Phase 1) study which identified body mass index (BMI) as a significant covariate for ZYNLONTA exposure. Only body weight was included as a size factor in the covariate model building.[4]
    - The cutoff for a BMI of ≥35 kg/m^2 was chosen earlier during clinical development to mitigate the potential toxicity associated with treatment in patients who were obese.[5]
- The dose of ZYNLONTA is calculated based on an ABW formula for patients with a BMI of ≥35 kg/m^2.
    - 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.[6]
- See **Relevant Prescribing Information** for additional information.

Background

- LOTIS-1 was a Phase 1, open-label, dose-escalation (Part 1) and dose-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 Lymphoma (R/R B-NHL).[1]
- LOTIS-2 was a pivotal, Phase 2, open-label, single-arm, multicenter study that evaluated 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]

Overview

LOTIS-1 (Phase 1)

- Body weight (BW) was highly correlated with body surface area (BSA) and BMI. The correlation coefficient between body weight and BSA was 0.96. Only body weight was included as a size factor in the covariate model building.[3]

LOTIS-2 (Phase 2)

- In LOTIS-2, patients with a BMI ≥35 mg/kg^2 were dosed using ABW based on pharmacokinetic modeling analyses of the Phase 1 trial. Data from the Phase 1 trial showed that BMI was a significant covariate for ZYNLONTA exposure.[4]
    - Dosing based on BW is associated with a physiological bias which, for therapeutic proteins, can lead to higher exposures in obese patients and lower exposures in patients with a lower body weight. The cutoff for a BMI of ≥35 kg/m^2 was chosen earlier during clinical development to mitigate the potential toxicity associated with treatment in patients who were obese.[5]

- The formula for ABW used for the calculation specified in the prescribing information was derived from the Phase 1 pharmacokinetic model.[5]

Literature Search

- A PubMed biomedical literature search conducted on April 11, 2024, yielded no relevant information regarding alternative dosing for ZYNLONTA.

Relevant Prescribing Information

Section 2: Dosage and Administration[6]

2.4: Reconstitution and Administration Instructions

Dose Calculation

- Calculate the total dose (mg) required based on the patient's weight and prescribed dose [see Dosage and Administration (2.1)].
    - For patients with a body mass index (BMI) ≥35 kg/m^2, calculate the dose based on an adjusted body weight (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] Data on File, LOTIS-1 Clinical Study Report. ADC Therapeutics.
[2] Data on File, LOTIS-2 Clinical Study Report. ADC Therapeutics.
[3] Data on File, Population Pharmacokinetics Report. ADC Therapeutics.
[4] Data on File, Pharmacokinetics Memo. ADC Therapeutics.
[5] Data on File, Adjusted Body Weight Memo. ADC Therapeutics.
[6] 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.