ZYNLONTA® (loncastuximab tesirine-lpyl)-Use in Patients with Renal Impairment

Summary

- LOTIS-1 was a Phase 1, open-label, single-arm, multicenter study which evaluated the safety and tolerability of ZYNLONTA monotherapy in adult patients with relapsed or refractory (R/R) B-Cell Non-Hodgkin's Lymphoma (B-NHL).[1]
    - Patients were required to have a plasma creatinine ≤1.5 mg/dL. If a patient's serum creatinine was >1.5 mg/dL, a measured creatinine clearance of >60 mL/min as calculated by the Cockcroft and Gault equation for study inclusion was required.[3]
- LOTIS-2 is a Phase 2, open-label, single-arm, multicenter study which evaluates the efficacy and safety of ZYNLONTA monotherapy in male or female patients (≥18 years of age) with R/R DLBCL following ≥2 lines of prior systemic therapy.[2]
    - To be included in the study, a patient's blood creatinine was required to be ≤1.5×ULN, or the patient's calculated creatinine clearance had to be ≥60 mL/min by the Cockcroft and Gault equation.[4]
- No clinically significant differences in the pharmacokinetics of ZYNLONTA were observed in patients with mild to moderate renal impairment (creatinine clearance 30 to <90 mL/min using the Cockcroft-Gault equation).[5]
- The effect of severe renal impairment (creatinine clearance 15 to 29 mL/min), and end-stage renal disease with or without hemodialysis on ZYNLONTA pharmacokinetics is unknown.
- See **Relevant Prescribing Information** for additional information regarding use of ZYNLONTA in patients with renal impairment.

Background

- LOTIS-1 was a Phase 1, open-label, single-arm, multicenter study which evaluated the safety and tolerability of ZYNLONTA monotherapy in adult patients with relapsed or refractory (R/R) B-Cell Non-Hodgkin Lymphoma (B-NHL). The study was conducted in two parts, dose-escalation (Part 1) followed by dose-expansion (Part 2).[1]
- LOTIS-2 is a Phase 2, open-label, single-arm, multicenter study which evaluates the efficacy and safety of ZYNLONTA monotherapy in male or female patients (≥18 years of age) with R/R DLBCL following ≥2 lines of prior systemic therapy.[2]

Clinical Data

LOTIS 1 (Phase 1)

- In LOTIS-1 (Phase 2, dose expansion), patients were required to have a plasma creatinine ≤1.5 mg/dL. If a patient's serum creatinine was >1.5 mg/dL, a measured creatinine clearance of >60 mL/min as calculated by the Cockcroft-Gault equation was required. Additionally, patients were excluded from study enrollment if they had any significant medical illness, abnormality, or condition that could, in the investigator's opinion, make the patient inappropriate for study participation.[3]

LOTIS 2 (Phase 2)

- To be included in LOTIS-2, patients were required to have adequate organ function. A patient's blood creatinine was required to be ≤1.5 × upper limit of normal (ULN) or the patient's creatinine clearance had to be ≥60 mL/min by the Cockcroft-Gault equation.[4]

Literature Search

- A PubMed biomedical literature search conducted on March 27, 2025, yielded no relevant data regarding use of ZYNLONTA in patients with renal impairment.

Relevant Prescribing Information

Section 12: Clinical Pharmacology[5]

Section 12.3 Pharmacokinetics, Specific Populations

- No clinically significant differences in the pharmacokinetics of ZYNLONTA were observed in patients with mild to moderate renal impairment (creatinine clearance 30 to <90 mL/min using the Cockcroft-Gault equation).
- The effect of severe renal impairment (creatinine clearance 15 to 29 mL/min), and end-stage renal disease with or without hemodialysis on ZYNLONTA pharmacokinetics is unknown.
- The major excretion pathways of SG3199, a pyrrolobenzodiazepine (PBD) dimer cytotoxic alkylating agent, have not been studied in humans. SG3199 is expected to be minimally renally excreted.

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] 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.