ZYNLONTA® (loncastuximab tesirine-lpyl)-Drug Interactions

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). The study was conducted in two parts, dose-escalation (Part 1) followed by dose-expansion (Part 2). The primary endpoint of Part 1 was to investigate the safety and tolerability of Lonca in R/R B-NHL and to determine the maximum tolerated dose (MTD) to recommend dose(s) for Part 2. The primary endpoint for Part 2 was to evaluate safety and tolerability at the recommended dose(s). [1]
- LOTIS-2 was a Phase 2, open-label, single-arm, multicenter study which evaluated 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. The primary endpoint was ORR according to the 2014 Lugano classification in all-treated patients.[2]
- No specific analyses of drug-drug interactions were performed for ZYNLONTA.[3,4]
- See **Relevant Prescribing Information** for additional information.

Literature Search

- A PubMed biomedical literature search conducted on December 2, 2025, yielded no relevant data regarding potential drug-drug interactions of ZYNLONTA.

Relevant Prescribing Information

Section 11: Description[6]

- Loncastuximab tesirine-lpyl is a CD19-directed antibody and alkylating agent conjugate, consisting of a humanized IgG1 kappa monoclonal antibody conjugated to SG3199, a pyrrolobenzodiazepine (PBD) dimer cytotoxic alkylating agent, through a protease-cleavable valine-alanine linker.
- SG3199 attached to the linker is designated as SG3249, also known as tesirine.

Section 12: Clinical Pharmacology[6]

Section 12.3 *Pharmacokinetics, Drug Interaction Studies*

- In Vitro Studies: Cytochrome P450 (CYP) Enzymes: SG3199 does not inhibit CYP1A2, CYP2A6, CYP2B6, CYP2C8, CYP2C9, CYP2C19, CYP2D6, CYP2E1, or CYP3A4/5 at clinically relevant unconjugated SG3199 concentrations.
- Transporter Systems: SG3199 is a substrate of P-glycoprotein (P-gp), but not a substrate of breast cancer resistance protein (BCRP), organic anion-transporting polypeptide (OATP)1B1, or organic cation transporter (OCT)1.
- SG3199 does not inhibit P-gp, BCRP, OATP1B1, OATP1B3, organic anion transporter (OAT)1, OAT3, OCT2, OCT1, multi-antimicrobial extrusion protein (MATE)1, MATE 2-K, or bilesalt export pump (BSEP) at clinically relevant unconjugated SG3199 concentrations.

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] Derenzini, E., Gibb, A., Kwiatek, M., & Strati, P. (2025). Loncastuximab tesirine in relapsed/refractory diffuse large B-cell lymphoma: drug profile and expert opinion on the prevention and management of adverse events. *Leukemia & lymphoma*, *66*(11), 1990–2002. https://doi.org/10.1080/10428194.2025.2520440

[6] ZYNLONTA® (loncastuximab tesirine) 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.