ZYNLONTA® (loncastuximab tesirine-lpyl)–Concomitant Use with Vaccines

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/refractory (R/R) B-Non-Hodgkin lymphoma (NHL).[1]
  - Administration of live vaccines was not permitted during the study, while inactivated vaccines were allowed.
  - A total of 7 (3.8%) and 1 (0.5%) patient received influenza and pneumococcal vaccinations, respectively.
- LOTIS-2 was a Phase 2, open-label, single-arm, multicenter study which evaluated the efficacy and safety of ZYNLONTA monotherapy in patients (≥18 years of age) with R/R diffuse large B-cell lymphoma (DLBCL) following ≥2 lines of prior systemic therapy.[2]
  - Live vaccines were prohibited in the study, but inactivated vaccines were permitted.
  - A total of three patients received influenza vaccines.
- Additional information regarding this subset of patients in LOTIS-1 and LOTIS-2 is not available.
- The ZYNLONTA Prescribing Information does not contain any information regarding the concomitant use of ZYNLONTA with vaccines.
- ADC Therapeutics does not have any data regarding the concomitant use of ZYNLONTA with US approved vaccines and cannot make any recommendations beyond what is provided in the US FDA prescribing 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-NHL. The study was conducted in two parts, dose-escalation (Part 1) followed by dose-expansion (Part 2).[1]
- LOTIS-2 was a Phase 2, open-label, single-arm, multicenter study which evaluated the efficacy and safety of ZYNLONTA monotherapy in patients (≥18 years of age) with R/R diffuse large B-cell lymphoma (DLBCL) following ≥2 lines of prior systemic therapy.[2]
- ADC Therapeutics does not have any data regarding the concomitant use of ZYNLONTA with US approved vaccines and cannot make any recommendations beyond what is provided in the US FDA prescribing information.

Clinical Data

LOTIS-1 (Phase 1)

- In LOTIS-1, administration of live vaccines was not permitted. However, inactivated vaccines were permitted. A total of 7 (3.8%) and 1 (0.5%) patient received influenza and pneumococcal vaccinations, respectively.[3] Additional information regarding the subset of these patients is not available. Table 1 contains additional information regarding the proportion of patients who received immunizations in LOTIS-1.

Table 1. Proportion of Patients Receiving Concomitant Vaccine. Adapted from LOTIS 1 Data on File.[3]

TEAE, n (%)	Dose (µg/kg)				
	≤90	120	150	200	
	Part 1 (n = 17)	Part 1+2 (n = 42)	Part 1+2 (n = 88)	Part 1 (n = 36)	Total (N=183)
Vaccine					
Influenza Vaccine	0 (0)	5 (11.9)	2 (2.3)	0 (0)	7 (3.8)
Pneumococcal Vaccine	0 (0)	1 (2.4)	0 (0)	0 (0)	1 (0.5)

Concomitant medications' are coded using World Health Organization (WHO) drug dictionary version Mar2019.
Part 1, dose escalation; Part 2, dose expansion

LOTIS-2 (Phase 2)

- In LOTIS-2, planned live vaccine administration after starting study drug (Cycle 1, Day 1) was an exclusion criterion of the study; inactivated vaccines were permitted. A total of three patients received the influenza vaccine.[4] Additional information regarding these patients is not available.

Literature Search

- A PubMed biomedical literature search conducted on March 24, 2025, yielded no relevant data regarding concomitant use of ZYNLONTA and vaccines.

Relevant Prescribing Information

Section 11: Description[5]

- 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[5]

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 bile salt 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] 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.