ZYNLONTA® (loncastuximab tesirine-lpyl) – Incidence of Extravasation and Management

Summary

- LOTIS-1 was a phase 1, open-label, dose-escalation (Part 1) and 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's Lymphoma (R/R B-NHL).[2]
    - One patient experienced 2 serious treatment emergent adverse events (TEAE's) of Grade 3 injection site extravasation which included worsening swelling, pain, and a new ulceration. Both events resolved, however they were considered related to treatment. The patient discontinued treatment with ZYNLONTA.
- LOTIS-2 was a Phase 2, open-label, single-arm, multicenter study which 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.[3]
    - Out of 145 patients included in the study, 1 patient (0.7%) experienced a TEAE of infusion site extravasation.
- The pyrrolobenzodiazepine (PBD) dimer portion of the drug (tesirine) is an alkylating agent, many of which are considered either vesicants or irritants.[6]
- Extravasation of ZYNLONTA may be associated with local irritation, swelling, pain, or tissue damage. Suspected extravasation of ZYNLONTA should be managed according to institutional protocol for management of extravasation of cytotoxic chemotherapy.[4]
- Administration of vesicant agents should be carried out through a central line whenever possible, especially if continuous infusion is required.[1]
- Monitor the infusion site for possible subcutaneous infiltration during drug administration.[6]
- ADC Therapeutics does not make recommendations outside of what is provided in the approved FDA prescribing information. See **Relevant Prescribing Information** for additional information.

Background

- LOTIS-1 was a phase 1, open-label, dose-escalation (Part 1) and expansion (Part 2) study that evaluated the safety and tolerability of ZYNLONTA, used as monotherapy, in 183 adult patients with R/R B-NHL. [2]
- LOTIS-2 was a Phase 2, open-label, single-arm, multicenter study which 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.[3]

Clinical Data

LOTIS-1 (Phase 1)

- One patient experienced 2 serious TEAE's of Grade 3 injection site extravasation which included worsening swelling, pain, and a new ulceration at a dose of 200 µg/kg. Both events resolved, however they were considered related to treatment. Symptoms of extravasation continued for

approximately 12 days and resolved thereafter. The patient discontinued treatment after the latter injection site extravasation event.[2]

- The first Grade 3 injection site extravasation (described as worsened injection site extravasation) was diagnosed approximately 4 days after the last dose of treatment (cycle 2, day 1).[2.]
    - The TEAE was categorized initially as a grade 2 injection site extravasation and lasted for about 12 days before worsening to a Grade 3 injection site extravasation.
    - The Grade 3 TEAE resolved after approximately 13 days from the onset of worsened symptoms (May 23, 2017- June 5, 2017).
- The second Grade 3 injection site extravasation (described as worsened injection site extravasation) was diagnosed approximately 4 days after the first event resolved.[2]
    - The TEAE resolved after approximately 6 days from onset of symptoms (June 9, 2017- June 15, 2017).

Management of Injection Site Extravasation in LOTIS-1

- The patient was treated with vancomycin, daptomycin, and prednisone for the first extravasation event.
- The patient was treated with vancomycin and sulfadiazine silver for the second extravasation event.

LOTIS-2 (Phase 2)

- Out of 145 patients included in the study, 1 patient (0.7%) experienced a Grade 1 TEAE of infusion site extravasation.[3]
- No further follow up information is available regarding this patient.

Management of Injection Site Extravasation[4,5]

- Extravasation of ZYNLONTA may be associated with local irritation, swelling, pain, or tissue damage.[4]
- Monitor the IV infusion for signs of IV infiltration or drug extravasation.
- Instruct patients to report any signs of IV infiltration or drug extravasation during or after the infusion.
- Suspected extravasation from ZYNLONTA should be managed according to institutional protocol for management of extravasation of cytotoxic chemotherapy.[5]

Literature Search

- A PubMed biomedical literature search conducted on November 18, 2025, yielded no relevant data regarding incidence of extravasation and management of ZYNLONTA in adult patients with R/R DLBCL.

Relevant Prescribing Information

Section 2: Dosage and Administration[6]

2.4: Reconstitution and Administration Instructions

Administration

- Administer by intravenous infusion over 30 minutes using a dedicated infusion line equipped with a sterile, non-pyrogenic, low-protein binding in-line or add-on filter (0.2- or 0.22-micron pore size) and catheter.
- Extravasation of ZYNLONTA has been associated with irritation, swelling, pain, and/or tissue damage, which may be severe. Monitor the infusion site for possible subcutaneous infiltration during drug administration.
- Do not mix ZYNLONTA with or administer as an infusion with other drugs.

References

[1] Boschi R, Rostagno E. Extravasation of antineoplastic agents: prevention and treatments. *Pediatr Rep*. 2012;4(3): e28. doi:10.4081/pr.2012.e28
[2] Data on File. LOTIS-1 Clinical Study Report. ADC Therapeutics.
[3] Data on File. LOTIS-2 Clinical Study Report. ADC Therapeutics.
[4] Data on File. IND/EAP Pharmacy Manual. ADC Therapeutics.
[5]ASCO/ONS (2025). Joint Guideline on the Management of Antineoplastic Extravasation. JCO Oncol Pract. November 2025
[6]ZYNLONTA® (loncastuximab tesirine-lpyl) FDA-approved Prescribing Information. October 2022.