ZYNLONTA® (loncastuximab tesirine-lpyl) – Prophylactic Use of Growth Factors

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]
    - Four patients (2.2%) received a granulocyte growth factor prior to being treated with ZYNLONTA.
    - Fifty patients (27.3%) received a granulocyte growth factor as a concomitant medication during treatment with ZYNLONTA.
- LOTIS-2 was a pivotal phase 2, multicenter, open-label single-arm study that evaluated the efficacy and safety of ZYNLONTA used as monotherapy in 145 adult patients with R/R diffuse large B-Cell lymphoma (DLBCL) following ≥2 lines of prior systemic therapy.[3]
    - Four patients (2.8%) received a granulocyte growth factor prior to being treated with ZYNLONTA.
    - Forty-eight patients (33.1%) received a granulocyte growth factor as a concomitant medication during treatment with ZYNLONTA.
    - Forty-two patients (29%) received growth factors for neutropenia at the discretion of the investigator that aligned with protocols at the clinical site.[4]
- See **Relevant Prescribing Information** for additional information.
- Please see the ASCO guidelines regarding recommendations for prophylactic use of hematopoietic growth factors https://ascopubs.org/doi/10.1200/jco.2015.62.3488

Background

- Myelosuppression may be secondary to treatment from cytotoxic agents. The prophylactic use of G-CSF prior to treatment has been widely accepted to reduce the risk of febrile neutropenia, specifically when the incidence is ≥20%.[1]
- Primary prophylaxis is recommended for the prevention of febrile neutropenia in high-risk patients based on age, disease characteristics, or cytotoxicity from the treatment regimen.[1]

Clinical Data

LOTIS-1 (Phase 1)[2]

- 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).
    - In the Part 2 expansion, patients required an absolute neutrophil count (ANC) of $\geq 1.0 \times 10^3/\mu L$ to be included in the study.
- Hematopoietic growth factors were permitted as per American Society of Clinical Oncology guidelines, however prophylactic use of growth factors was not allowed during the first treatment cycle.

- Two patients (1.1%) received Pegfilgrastim, 1 patient (0.5%) received Filgrastim, and 1 patient (0.5%) received G-CSF prior to ZYNLONTA treatment.
- Twenty-nine patients (15.8%) received Filgrastim, 11 patients (6.0%) received Pegfilgrastim, 6 patients (3.3%) received G-CSF, and 4 patients (2.2%) received Filgrastim SNDZ as a concomitant medication during treatment with ZYNLONTA.
- Please see the ASCO guidelines regarding recommendations for prophylactic use of hematopoietic growth factors https://ascopubs.org/doi/10.1200/jco.2015.62.3488

<u>LOTIS-2 (Phase 2)</u>[3,4]

- LOTIS-2 (NCT03589469) was a pivotal Phase 2, multicenter, open-label single-arm study that evaluated the efficacy and safety of ZYNLONTA used as monotherapy in 145 adult patients with relapsed or refractory diffuse large B-cell lymphoma (R/R DLBCL) following ≥2 lines of prior systemic therapy.
    - Patients required an ANC of $\geq 1.0x10^3/\mu L$ and were required to be off growth factors for at least 72 hours to be included in the study.
- Hematopoietic growth factors were to be permitted as per American Society of Clinical Oncology guidelines.
    - Three patients (2.1%) received Filgrastim, and 1 patient (0.7%) received Filgrastim SNDZ prior to ZYNLONTA treatment.
    - Thirty-one patients (21.4%) received Filgrastim, 9 patients (6.2%) received Filgrastim SNDZ, 5 patients (3.4%) received G-CSF, and 3 patients (2.1%) Pegfilgrastim as a concomitant medication.
    - Forty-two patients (29%) received growth factors for neutropenia at the discretion of the investigator that aligned with protocols at the clinical site.[4]
        - 33 patients (22.8%) received growth factors for treatment of neutropenia.
        - 20 patients (13.8%) received growth factors for prophylaxis of neutropenia.
    - No specific recommendations were made regarding the prophylactic use of G-CSF in LOTIS-2.

Literature Search

- A PubMed biomedical literature search conducted on December 2, 2025, yielded no relevant data regarding ZYNLONTA and the prophylactic use of growth factors.

Relevant Prescribing Information

<u>Section 2: Dosage and Administration</u>[5]

2.3: Dosage Modifications and Delays

Table 1: Recommended Dosage Modification for Adverse Reactions. Adopted from Prescribing Information.[5]

Adverse Reactions	Severity	Dosage Modification
Hematologic Adverse Reactions		
Neutropenia [see Warnings and Precautions (5.2)]	Absolute neutrophil count less than $1x10^9/L$	Withhold ZYNLONTA until neutrophil counts returns to $1x10^9/L$ or higher

Section 5: Warnings and Precautions[5]

5.2: Myelosuppression

- Treatment with ZYNLONTA can cause serious or severe myelosuppression, including neutropenia, thrombocytopenia, and anemia. Grade 3 or 4 neutropenia occurred in 32%, thrombocytopenia in 20%, and anemia in 12% of patients. Grade 4 neutropenia occurred in 21% and thrombocytopenia in 7% of patients. Febrile neutropenia occurred in 3% [see Adverse Reactions (6.1)].
- Monitor complete blood counts throughout treatment. Cytopenias may require interruption, dose reduction, or discontinuation of ZYNLONTA. Consider prophylactic granulocyte colony-stimulating factor administration as applicable [see Dosage and Administration (2.3)].

Section 6: Adverse Reactions[5]

6.1: Clinical Trials Experience

- In this pooled safety population of 215 patients, the most common (>20%) adverse reactions, including laboratory abnormalities, were thrombocytopenia, increased gamma-glutamyltransferase, neutropenia, anemia, hyperglycemia, transaminase elevation, fatigue, hypoalbuminemia, rash, edema, nausea, and musculoskeletal pain.
- Serious adverse reactions occurred in 28% of patients receiving ZYNLONTA. The most common serious adverse reactions that occurred in ≥2% receiving ZYNLONTA were febrile neutropenia, pneumonia, edema, pleural effusion, and sepsis. Fatal adverse reactions occurred in 1%, due to infection.
- Permanent treatment discontinuation due to an adverse reaction of ZYNLONTA occurred in 19% of patients. Adverse reactions resulting in permanent discontinuation of ZYNLONTA in ≥2% were gamma-glutamyltransferase increased, edema, and effusion.
- Dose reductions due to an adverse reaction of ZYNLONTA occurred in 8% of patients. Adverse reactions resulting in dose reduction of ZYNLONTA in ≥4% was gamma-glutamyltransferase increased.
- Dosage interruptions due to an adverse reaction occurred in 49% of patients receiving ZYNLONTA. Adverse reactions leading to interruption of ZYNLONTA in ≥5% were gamma-glutamyltransferase increased, neutropenia, thrombocytopenia, and edema.
- Clinically relevant adverse reactions in <10% of patients (all grades) who received ZYNLONTA included:
  - Blood and lymphatic system disorders: Febrile neutropenia (3%)

References

[1] Smith T, Bohlke K, Lyman GH, et al. Recommendations for the Use of WBC Growth Factors: American Society of Clinical Oncology Clinical Practice Guideline Update. J Clin Oncol. 2015; 33(28): 3199-212.
[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. Summary of Growth factor for Neutropenia Memo. ADC Therapeutics.
[5]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.