ZYNLONTA® (loncastuximab tesirine-lpyl) – Incidence of Nausea and Vomiting

Summary

- According to the American Society of Clinical Oncology (ASCO) antiemetic guidelines, the emetic risk of antineoplastic mediations was classified by using four levels based on the likelihood of emesis in the absence of antiemetic prophylaxis: high (>90%), moderate (30% to 90%), low (10% to 30%), and minimal (<10%).[1]
- LOTIS-1 was a Phase 1, open-label, single-arm, multicenter study that evaluated the safety and tolerability of loncastuximab tesirine-lpyl (Lonca) monotherapy in 183 adult patients with relapsed or refractory (R/R) B-cell Non-Hodgkin Lymphoma (B-NHL).[2]
    - Twenty-eight (32%) patients who received 150 µg/kg reported Grades 1-3 treatment-emergent adverse event (TEAE) of nausea, and 17 (19%) patients reported Grades 1-2 TEAE of vomiting.[2,3]
- 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 relapsed or refractory diffuse large B-cell lymphoma (R/R DLBCL) following >2 lines of prior systemic therapy.[4]
    - In LOTIS-2, 34 patients (23%) reported TEAE of nausea and 19 patients (13%) reported TEAE of vomiting, all Grades 1-2.
    - Patients received ZYNLONTA as monotherapy without traditional chemotherapy. Traditional chemotherapy-induced nausea and vomiting (CINV) was not reported.[5]
- Patients received routine dexamethasone treatment for the management of edema and effusion, so the incidence of emesis in the absence of premedication is unknown.[5]
- ADC Therapeutics does not make recommendations outside the Prescribing Information. Please defer to your clinical judgement for the management of nausea and vomiting. See Relevant Prescribing Information for additional information.

Background

- According to the ASCO antiemetic guidelines, the emetic risk of antineoplastic mediations was classified by using four levels based on the likelihood of emesis in the absence of antiemetic prophylaxis: high (>90%), moderate (30% to 90%), low (10% to 30%), and minimal (<10%).[1]

Clinical Data

- LOTIS-1 was a Phase 1, open-label, single-arm, multicenter study that evaluated the safety and tolerability of ZYNLONTA monotherapy in 183 adult patients with R/R B-NHL. The study was conducted in two parts, dose-escalation (Part 1), followed by dose-expansion (Part 2).[2]
    - In LOTIS-1, 88 patients received ZYNLONTA monotherapy at 150 µg/kg.[2]
    - Twenty-eight (32%) patients who received 150 µg/kg reported Grades 1-3 TEAE of nausea, and 17 (19%) patients reported Grades 1-2 TEAE of vomiting.[2,3]
- 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 DLBCL following >2 lines of prior systemic therapy.[4]
    - In LOTIS-2, 34 patients (23%) reported TEAE of nausea and 19 patients (13%) reported TEAE of vomiting, all Grades 1-2.

- Patients received ZYNLONTA as monotherapy without traditional chemotherapy. Traditional CINV was not reported.[5]

Literature Search

- A PubMed biomedical literature search conducted on April 5, 2025, yielded no further relevant data regarding incidence of nausea, and vomiting with the use of ZYNLONTA.

Relevant Prescribing Information

Section 2: Dosage and Administration[6]

2.2: Recommended Premedication

- Unless contraindicated, administer dexamethasone 4 mg orally or intravenously twice daily for 3 days beginning the day before administering ZYNLONTA. If dexamethasone administration does not begin the day before ZYNLONTA, dexamethasone should begin at least 2 hours prior to administration of ZYNLONTA.

Section 6: Adverse Reactions[6]

6.1: Clinical Trials Experience

- The pooled safety population described in the WARNINGS AND PRECAUTIONS reflect exposure to ZYNLONTA as a single agent at an initial dose of 0.15 mg/kg in 215 patients with DLBCL in studies ADCT-402-201 (LOTIS-2) and ADCT-402-101, which includes 145 patients from LOTIS-2 treated with 0.15 mg/kg x 2 cycles followed by 0.075 mg/kg for subsequent cycles. Among 215 patients who received ZYNLONTA, the median number of cycles was 3 (range 1 to 15) with 58% receiving three or more cycles and 30% receiving five or more cycles.
- 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.

Table 1: Adverse Reactions (≥10%) in Patients with Relapsed or Refractory DLBCL who received ZYNLONTA in LOTIS-2.
Adopted from Prescribing Information.[6]

Adverse Reaction	ZYNLONTA (N=145)	
	All Grades (%)	Grades 3 or 4 (%)
Gastrointestinal Disorders		
Nausea	23	0
Vomiting	13	0

References

[1] Hesketh PJ, Kris MG, Basch E, et al. Antiemetics: American Society of Clinical Oncology Clinical Practice Guideline Update. *J Clin Oncol*. 2017;35(28):3240-3261. doi:10.1200/JCO.2017.74.4789
[2] 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. https://doi.org/10.1182/blood.2020007512.
[3] Data on File, LOTIS 1 Clinical Study Report. ADC Therapeutics.
[4] 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
[5] Data on File, Antiemetic Memo. ADC Therapeutics.
[6] 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.