Characterization and Management of Cutaneous Reactions in Patients With Relapsed or Refractory Diffuse Large B-cell Lymphoma Treated With Loncastuximab Tesirine in the LOTIS-2 Trial

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INTRODUCTION

- Loncastuximab tesirine (loncastuximab tesirine-lypl; Lonca), an FDA-approved antibody-drug conjugate comprising a CD19-targeted antibody conjugated to a pyrrolobenzodiazepine (PBD)-dimer cytotoxin, is indicated for the treatment of relapsed or refractory diffuse large B-cell lymphoma (DLBCL) after 2 or more prior systemic therapies.[1]
- In the pivotal open-label, single-arm phase 2 trial (LOTIS-2), Lonca demonstrated single-agent antitumor activity in patients with heavily pretreated relapsed or refractory DLBCL.[2] The overall response rate was 48.3%, and the complete response rate was 24.8%.[2,3]
- Treatment-emergent adverse events (AEs) were reported in 99% (n=143) of patients, and grade ≥3 AEs were reported in 72.4% (n=105) of patients treated with Lonca.[2]
- Some cutaneous reactions are among AEs considered likely related to the PBD cytotoxin.[4,5]
- Knowledge of potential adverse cutaneous reactions that may impact a patient's quality of life is necessary for healthcare professionals to counsel and manage patients on treatment effectively.[6]

OBJECTIVE

- To describe the incidence, duration, and management of cutaneous reactions, including photosensitivity and non-photosensitivity reactions, in the LOTIS-2 trial (NCT03589469).[7]

METHODS

- The methodology for LOTIS-2 was previously published.[2] In the LOTIS-2 trial, eligible patients received Lonca administered intravenously over 30 minutes on day 1 of each 21-day cycle—at 0.15 mg/kg for the first 2 cycles followed by 0.075 mg/kg for all remaining cycles for up to 1 year or until disease relapse or progression.[2]
- Dexamethasone premedication (4 mg orally) was administered twice daily beginning the day before Lonca administration for 3 days to reduce the incidence and severity of PBD toxicities.[2] Patients were advised to avoid prolonged skin exposure to sunlight to prevent light-sensitive skin rashes seen in earlier phase studies of Lonca.[2,8]
- Patients were monitored for new or worsening cutaneous reactions (regardless of causality), including photosensitivity reactions.[1]
  - Non-photosensitivity reactions included rash and pruritus. Rash includes rash, rash erythematous, rash maculopapular, rash pruritic, rash pustular, erythema, generalized erythema, dermatitis, dermatitis acneiform, dermatitis bullous, dermatitis exfoliative generalized, and palmar-plantar erythrodysesthesia syndrome.[1] Lonca was withheld for severe (grade ≥3) cutaneous reactions until resolution to grade ≤1.[1] Dermatologic consultation was considered if skin reaction or rash developed.[1]

Statistical Analysis

- Primary safety analyses were carried out in the all-treated population (patients that received ≥1 dose of Lonca).
- For this analysis (data cutoff: March 1, 2021), the number (%) of photosensitivity and non-photosensitivity cutaneous reactions, time to treatment-emergent AEs (TEAEs), action taken, and duration of cutaneous reactions were included.
- To determine the duration of cutaneous reactions, missing AE end dates were imputed using the new anticancer therapy, end of study, or data cutoff dates.

RESULTS

Incidence, Onset, and Duration

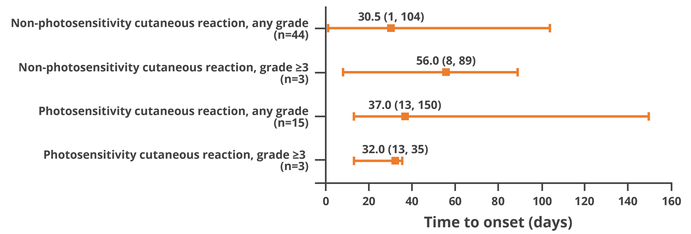
- Of the 145 patients who received Lonca in LOTIS-2, 10.3% had photosensitivity reactions (2.1% of patients experienced grade ≥3) and 30.3% had non-photosensitivity reactions (2.1% of patients experienced grade ≥3) (**Table 1**).

Table 1. Incidence of cutaneous reactions

	LOTIS-2 (N=145)
Photosensitivity cutaneous reaction, any grade, n (%)	15 (10.3)
Photosensitivity cutaneous reaction, grade ≥3	3 (2.1)
Non-photosensitivity cutaneous reaction, any grade	44 (30.3)
Non-photosensitivity cutaneous reaction, grade ≥3	3 (2.1)

- The median time to onset was 37.0 days for any grade and 32.0 days for grade ≥3 photosensitivity reactions and 30.5 days for any grade and 56.0 days for grade ≥3 non-photosensitivity reactions (**Figure 1**).

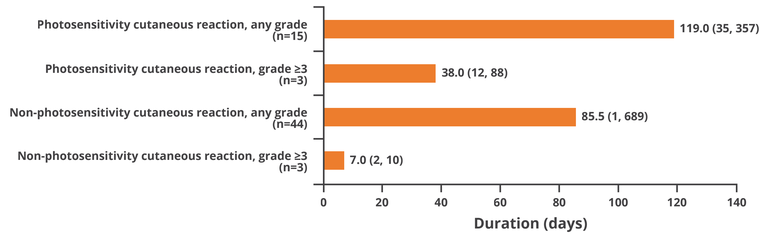
Figure 1. Median time to onset of any grade and grade ≥3 cutaneous reactions



Data labels represent median (min, max).

- The median duration of any grade photosensitivity reactions was 119.0 days and 38.0 days for grade ≥3 events. The median duration of any grade non-photosensitivity reactions was 85.5 days and 7.0 days for grade ≥3 events (**Figure 2**).

Figure 2. Median duration of any grade and grade ≥3 cutaneous reactions



Data labels represent median (min, max).

RESULTS (continued)

Cutaneous Reaction Dose Modification

- Dose modifications to manage grade ≥3 cutaneous reactions (dose delays, modifications, or withdrawals) occurred in <5% of patients (**Table 2**).

Table 2. Actions taken (dose delay, reduction, or discontinuation), N=145

	Dose Delay	Dose Reduced	Discontinuation
Photosensitivity cutaneous reaction (any grade)	2.8% (n=4)	0% (n=0)	0.7% (n=1)
Non-photosensitivity cutaneous reaction (any grade)	4.8% (n=7)	0% (n=0)	0% (n=0)

CONCLUSIONS

- In LOTIS-2, the incidence of grade ≥3 cutaneous reactions was low.
- Cutaneous reactions typically occurred within 60 days of starting treatment, and infrequently resulted in dose modification or treatment discontinuation.
- Patients should be advised to minimize and protect skin from sun exposure.

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References

1. ADC Therapeutics SA. ZYNLONTA Prescribing Information. https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/761196s000lbl.pdf. Updated April, 2021. Accessed January 6, 2022.
2. Caimi PF, Ai W, Alderuccio JP, et al. *Lancet Oncol*. 2021;22(6):790-800.
3. Caimi PF, Ai W, Alderuccio JP, et al. *J Clin Oncol*. 2021;39:15_suppl, 7546-7546.
4. Saber H, Simpson N, Ricks TK, Leighton JK. *Regul Toxicol Pharmacol*. 2019;107:104429.
5. Hartley JA. *Expert Opin Biol Ther*. 2021;21(7):931-943.
6. Sanlorenzo M, Vujic I, Daud A, et al. *JAMA Dermatol*. 2015;151(11):1206-1212.
7. ClinicalTrials.gov.https://clinicaltrials.gov/ct2/show/NCT03589469. Updated July 29, 2021. Accessed January 6, 2022.
8. Hamadani M, Radford J, Carlo-Stella C, et al. *Blood*. 2021;137(19):2634-2645.

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