Onset, Duration, and Management of Edema and Effusion in Patients Treated With Loncastuximab Tesirine for R/R DLBCL: Updated Results From the LOTIS-2 Clinical Trial

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INTRODUCTION

- Loncastuximab tesirine (loncastuximab tesirine-lpyl; Lonca) is an FDA-approved antibody-drug conjugate (ADC) comprising a CD19-targeted antibody conjugated to a pyrrolobenzodiazepine (PBD)-dimer cytotoxin.[1]
- Lonca is indicated for the treatment of relapsed/refractory diffuse large B-cell lymphoma (R/R DLBCL) after ≥2 prior systemic therapies.[1]
- Lonca demonstrated substantial single-agent activity in the pivotal phase 2 LOTIS-2 clinical trial in patients with R/R DLBCL, with an overall response rate of 48.3% and a complete response rate of 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]
- Edema and effusion are among AEs considered likely related to the PBD cytotoxin.[4,5]
- While rare, peripheral edema (3% [n=4]), localized edema (2% [n=3]), and pleural effusion (2% [n=3]) were some of the most common adverse events (AEs) leading to treatment discontinuation in the LOTIS-2 trial.[2]

OBJECTIVE

- To characterize the onset and management of edema and effusion in the pivotal LOTIS-2 trial in patients with R/R DLBCL.

INTERVENTIONS

Study Design

- In the open-label, single-arm, phase 2 LOTIS-2 trial (NCT03589469), Lonca was administered intravenously every 3 weeks at a dose of 0.15 mg/kg for 2 cycles and then 0.075 mg/kg for subsequent cycles.
- Dexamethasone premedication (4 mg, orally, twice daily) was administered beginning the day before Lonca administration (if possible), the day of Lonca administration, and the day after Lonca administration, unless contraindicated.
  - Dexamethasone was administered to reduce the incidence and severity of PBD-related toxicities.[2]
- Lonca was held for patients that experienced grade ≥2 edema or effusion until toxicity resolved to grade ≤1.
  - AEs were graded according to the Common Terminology Criteria for Adverse Events, Version 4.0.
- Standard doses of spironolactone were recommended for the initial management of edema or effusion in patients with weight gain of >1 kg from day 1 cycle 1, new or worsening edema, and/or new or worsening pleural effusion.
  - Additional diuretic support was added if a further increase in weight, edema, or pleural effusion occurred.
  - Patients were advised to monitor their weight daily around the same time of day and to notify the study site if they gained >1 kg (2.2 lbs) over baseline.

Statistical Analysis

- In this analysis (data cutoff: March 1, 2021), missing AE end dates were imputed using the date of new anticancer therapy, the end of study, or data cutoff.
- Partial AE end dates were imputed using the last month or last day of the month, bounded by the end of study, data cutoff, or new anticancer therapy.

RESULTS

Incidence, Time to Onset, and Duration

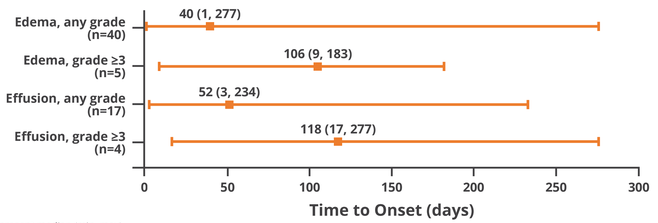
- In LOTIS-2 (N=145), any grade edema occurred in 27.6% of patients, and grade ≥3 edema occurred in 3.4% of patients (**Table 1**).
- Any grade effusion occurred in 11.7% of patients, and grade ≥3 effusion occurred in 2.8% of patients (**Table 1**).

Table 1. Incidence of edema and effusion

	LOTIS-2 (N=145)
Edema, any grade, n (%)	40 (27.6)
Edema, grade ≥3, n (%)	5 (3.4)
Effusion, any grade, n (%)	17 (11.7)
Effusion, grade ≥3, n (%)	4 (2.8)

- The onset of any grade edema and effusion typically occurred within the first 2 and 3 treatment cycles, respectively, and the onset of grade ≥3 edema and effusion typically occurred within the first 6 treatment cycles (**Figure 1**).

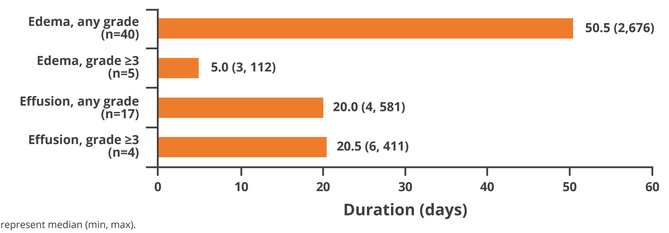
Figure 1. Median time to onset of edema and effusion



Data labels represent median (min, max).

- Any grade and grade ≥3 edema lasted a median of 50.5 days and 5 days, respectively; any grade and grade ≥3 effusion lasted a median of 20 days and 20.5 days, respectively (**Figure 2**).

Figure 2. Median duration of edema and effusion



Data labels represent median (min, max).

RESULTS (continued)

Dose Modifications

- In the total trial population, dose delays, reductions, and withdrawal occurred due to edema in 4.8%, 0.7%, and 2.8% of patients, respectively, and due to effusion in 1.4%, 0%, and 2.8% of patients, respectively (**Table 2**).

Table 2. Dose modifications due to edema or effusion

	LOTIS-2 (N=145)		
	Dose delay	Dose reduction	Dose withdrawal
Edema, n (%)	7 (4.8)	1 (0.7)	4 (2.8)
Effusion, n (%)	2 (1.4)	0 (0)	4 (2.8)

CONCLUSIONS

- Dexamethasone premedication was administered to reduce the incidence and severity of PBD-related adverse events, such as edema and effusion.
- The median time to onset of any grade edema and effusion was approximately 2 and 3 treatment cycles, respectively.
- Incidences of grade ≥3 edema and effusion were low and typically occurred later in therapy, with a median time to onset of approximately 6 treatment cycles.
- Edema and effusion were generally manageable with dose delays and modifications, as recommended for grade ≥2 events.

Acknowledgments

- ADC Therapeutics; medical writing support: CiTRUS Health Group.
- The authors also acknowledge Kirit Ardeshna, John Radford, Matt Lunning, Muneet Burke, and Luqiang Wang for their contributions.

Disclosures

C Grandas: no disclosures. **L Hendrickson:** no disclosures. **JP Alderuccio:** immediate family member has served on advisory boards for Puma Biotechnology, Inovio Pharmaceuticals, Agios Pharmaceuticals, Forma Therapeutics, and Foundation Medicine; honoraria from OncLive and OncInfo; consult for and research funding from ADC Therapeutics. **B Hess:** speakers' bureau member for Bristol-Myers Squibb; advisory board member for ADC Therapeutics; speakers' bureau member for AstraZeneca. **D Ungar:** employee of ADC Therapeutics with ownership interests. **M Solh:** consultant for Amgen and Bristol-Myers Squibb; research funding from ADC Therapeutics and Partner Therapeutics; speakers' bureau member for Bristol-Myers Squibb, GlaxoSmithKline, AbbVie, and Celgene.

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Poster presented at the 47th Annual ONS Congress. April 27–May 1, 2022, Anaheim, CA USA