Incidence, onset, and management of myelosuppression in patients treated with loncastuximab tesirine for R/R DLBCL in a pooled safety analysis

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INTRODUCTION

- An unmet need remains for the treatment of relapsed/refractory (R/R) diffuse large B-cell lymphoma (DLBCL), as although a number of treatments have been approved in this indication, they are associated with substantial toxicities.[1-4]
- Loncastuximab tesirine (Loncastuximab tesirine-lpyl; Lonca), a novel antibody-drug conjugate comprising an anti-CD19 antibody conjugated to a potent pyrrolobenzodiazepine dimer cytotoxin, is indicated for the treatment of R/R DLBCL after ≥2 systemic treatments.[5]
- Both phase 1 (LOTIS-1; NCT02669017) and phase 2 (LOTIS-2; NCT03589469) trials have evaluated the antitumor activity and safety of Lonca as a single agent in patients with R/R B-cell non-Hodgkin lymphoma.[6,7]
  - In LOTIS-1, treatment-emergent adverse events (TEAEs) occurred in 98.9% of patients with R/R B-cell NHL who received Lonca (0.15 mg/kg), the majority of which were hematological TEAEs. In the subset of patients with R/R DLBCL, the overall response rate (ORR) was 42.3%.[6]
  - In LOTIS-2 (data-cut off, April 6, 2020), the ORR in patients with R/R DLBCL was 48.3%. TEAEs occurred in 98.6% of patients. The most common TEAEs were increased gamma-glutamyltransferase (40.7%), neutropenia (39.3%), and thrombocytopenia (33.1%).[7]

OBJECTIVE

- To characterize the occurrence and management of myelosuppression events (neutropenia, thrombocytopenia, and anemia) in patients with R/R DLBCL, treated with single-agent Lonca.

METHODS

- Patients with R/R DLBCL (WHO 2016 classification) in the completed phase 1 LOTIS-1 trial and the ongoing pivotal phase 2 LOTIS-2 trial (data cutoff: 06 August 2020) received IV Lonca every 3 weeks.
  - LOTIS-1 used doses ranging from 0.015 to 0.2 mg/kg.
  - LOTIS-2 used the approved dose of 0.15 mg/kg for 2 doses followed by 0.075 mg/kg for subsequent doses.
- Growth factor was allowed according to ASCO guidelines.
- This safety analysis used pooled data from patients with R/R DLBCL in the LOTIS-1 trial treated with an initial Lonca dose of 0.15 mg/kg and all patients in the LOTIS-2 trial.

Myelosuppression Events (neutropenia, thrombocytopenia, anemia)

- Incidence of Grade 3/4 AEs based on laboratory abnormalities (**Table 1**).
- Time to onset of AEs.
- Dose delay due to AEs.
- Dose reduction due to AEs.
- Treatment discontinuation due to AEs.

Table 1. Myelosuppression event definitions*

Neutropenia	
Grade 3	<1.0 - 0.5 x 10e9/L
Grade 4	<0.5 x 10e9/L
Thrombocytopenia	
Grade 3	<50.0 - 25.0 x 10e9/L
Grade 4	<25.0 x 10e9/L
Anemia	
Grade 3	hemoglobin <80 g/L or transfusion indicated
Grade 4	life-threatening consequences or urgent intervention

*based on Common Terminology Criteria for Adverse Events (CTCAE) criteria

Statistical Analysis

- Safety analyses were conducted in the all-treated population, who received ≥1 dose of Lonca.
- Time to event analyses were performed for Grade 3/4 neutropenia, thrombocytopenia, and anemia.
  - Analyses assessed time to first onset of Grade 3 or 4 decreases in hemoglobin, neutrophil count and platelet count.
- Incidence of hematologic abnormalities was based on laboratory reporting, whereas therapy modification was based on adverse event reporting.

RESULTS

Patient Population

- In total, 215 patients received at least one dose of Lonca (0.15 mg/kg) in the LOTIS-1 and LOTIS-2 trials and were included in this analysis.
- The extent of exposure to Lonca is shown in (**Table 2**).

Table 2. Lonca administration and extent of exposure in patients with R/R DLBCL

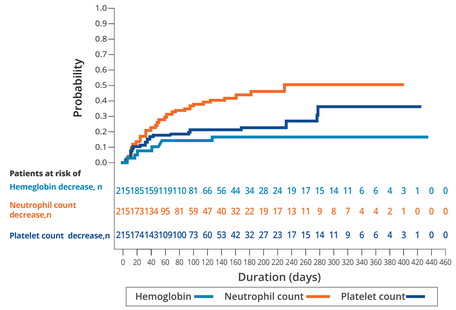
	Lonca 0.15 mg/kg (n=215)
Total Lonca cycles, n (range)	3.0 (1, 18)
Duration of treatment, days	45.0 (1, 412)

Data are median (min, max)

Myelosuppression Events

- Grade 3/4 neutropenia occurred in 32.1% (n=69), thrombocytopenia in 20.0% (n=43), and anemia in 12.6% (n=27, all Grade 3) of patients.
- The time to onset of Grade 3/4 myelosuppression is shown in (**Figure1**).

Figure 1. Time to first onset of Grade 3/4 anemia, neutropenia, and thrombocytopenia in patietns who received at least one dose of Lonca (0.15 mg/kg)



  - Most patients with Grade 3/4 anemia and thrombocytopenia had onset within the first 2 months, by treatment cycle 4.
  - Most patients with Grade 3/4 neutropenia had onset within the first 4 months, by treatment cycle 7.
- Dose delay occurred due to Grade 3/4 neutropenia in 10.2% (n=22), Grade 3/4 thrombocytopenia in 8.4% (n=18), and Grade 3 anemia in 1.4% (n=3) of patients.
- Dose reduction occurred due to Grade 3/4 thrombocytopenia in 0.5% (n=1) of patients and due to Grade 3/4 neutropenia in 0.5% (n=1) of patients.
- No dose reductions occurred due to anemia.
- Treatment discontinuation occurred due to Grade 3/4 thrombocytopenia in 2.3% (n=5) of patients and due to Grade 3/4 neutropenia in 0.5% (n=1) of patients.
- No treatment discontinuations occurred due to anemia.
- Febrile neutropenia occurred in 3.3% (n=7) of patients.

CONCLUSIONS

- The incidence of Grade ≥3 myelosuppression with Lonca was moderate.
  - Most patients with Grade 3/4 anemia and thrombocytopenia had onset within the first 2 months, by treatment cycle 4.
- Most myelosuppression events were manageable with dose delays and did not result in dose reduction or treatment discontinuation.
- The percentage of patients with febrile neutropenia was very low.

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Disclosures

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SCAN ME

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