LOTIS-2 follow-up analysis: Updated results from a Phase 2 study of loncastuximab tesirine in relapsed or refractory diffuse large B-cell lymphoma

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Introduction

- Patients with relapsed/refractory diffuse large B-cell lymphoma (R/R DLBCL) for whom salvage chemotherapy/stem cell transplant (SCT) is unsuccessful have a poor prognosis and limited treatment options[1,2]
- Loncastuximab tesirine (loncastuximab tesirine-lpyl; Lonca) comprises a humanized anti-CD19 antibody conjugated to a potent pyrrolobenzodiazepine (PBD) dimer toxin[3]
- LOTIS-2 is a Phase 2 study evaluating Lonca in patients with R/R DLBCL (NCT03589469)[4–6]
- Primary efficacy and safety data have been previously published[4] (≥6 months since patients received first dose), and patients are being followed-up; here, we present updated results (≥17 months since patients received their first dose)

Methods

Study design

- This multicenter, open-label, single-arm Phase 2 study of Lonca enrolled adult patients (≥18 years) with pathologically defined R/R DLBCL and ≥2 prior systemic treatments
- Patients received intravenous Lonca at 150 µg/kg every 3 weeks (Q3W) for 2 cycles, then 75 µg/kg Q3W thereafter for up to 1 year
- Follow-up is Q12W for up to 3 years after the end of treatment

Endpoints

- The primary efficacy endpoint was overall response rate (ORR), assessed by central review
- Secondary efficacy endpoints included duration of response (DoR), progression-free survival (PFS), and overall survival (OS)
- Secondary safety endpoints included frequency and severity of treatment-emergent adverse events (TEAEs)

Results

Patients and treatment

- 145 patients with heavily pre-treated R/R DLBCL received at least 1 dose of Lonca; median (range) patient age was 66 years (23–94)
- At data cut-off (March 01, 2021), all patients had completed treatment
- Patients received a mean (standard deviation) of 4.6 cycles (4.3) and median (range) of 3.0 cycles (1.0–26.0) of Lonca
  - Responders (n=70) received a mean of 6.8 cycles (5.0) and median of 5.0 cycles (1.0–26.0)
  - 24 (34.3%) responders received ≥7 cycles
- Median (range) of follow-up for all patients was 7.8 months (0.3–31.0); 37 patients remain in follow-up

Safety

- Grade ≥3 TEAEs were reported in 107 (73.8%) patients (**Table 1**)

Table 1. Overall TEAEs (all-treated population)

TEAE	Patients, n (%) (N=145)
Patients with any TEAE	**143 (98.6)**
Grade ≥3 TEAE	107 (73.8)
TEAE related to Lonca[a]	118 (81.4)
TEAE leading to Lonca dose delay or reduction	75 (51.7)
TEAE leading to Lonca discontinuation	36 (24.8)
Serious TEAE	57 (39.3)
TEAE with a fatal outcome	8 (5.5)

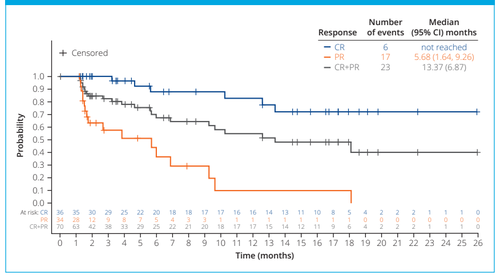
[a]Related defined as possibly related, probably related, or related including missing relationship. Lonca, loncastuximab tesirine; TEAE, treatment-emergent adverse event.

- Most common (≥10%) Grade ≥3 TEAEs were neutropenia (38 [26.2%]), thrombocytopenia (26 [17.9%]), increased gamma-glutamyltransferase (GGT; 25 [17.2%]), and anemia (15 [10.3%])
  - Most Grade ≥3 events were reflective of laboratory abnormalities rather than clinical symptoms
- The rate of febrile neutropenia was low (5 [3.4%])
- All-grade TEAEs considered likely related to the PBD warhead included edema or effusion (45 [31.0%]), skin reactions and nail disorders (63 [43.4%]), and liver enzyme abnormalities (76 [52.4%])
- Treatment-related TEAEs leading to treatment discontinuation and dose delays were reported in 27 (18.6%) and 62 (42.8%) patients, respectively; most common reason for both was increased GGT (17 [11.7%] and 26 [17.9%] patients, respectively)

Efficacy

- ORR by central review was 48.3% (70/145); complete response was 24.8% (36/145) and partial response was 23.4% (34/145)
- Median DoR for the 70 responders was 13.4 months. Median DoR for patients with a complete response was not reached and was 5.7 months for those with a partial response (**Figure 1**)

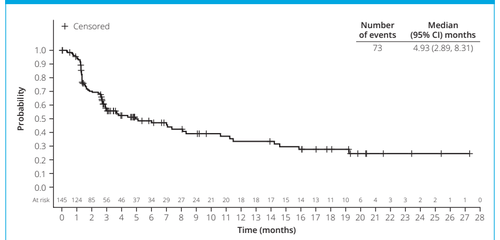
Figure 1. Duration of response by best overall response (all-treated population)



CI, confidence interval; CR, complete response; PR, partial response.

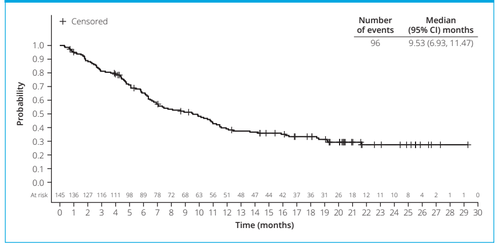
- Median PFS was 4.9 months (**Figure 2**) and median OS was 9.5 months (**Figure 3**)
- Following Lonca treatment, 16 patients received CD19-directed chimeric antigen receptor T-cell therapy, with an investigator-assessed ORR of 43.8%; 11 patients proceeded to SCT as consolidation after responding to Lonca

Figure 2. Progression-free survival (all-treated population)



CI, confidence interval.

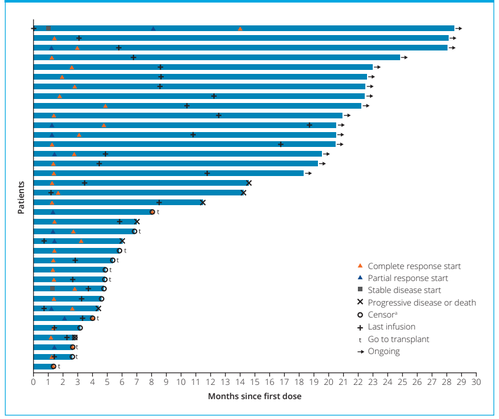
Figure 3. Overall survival (all-treated population)



CI, confidence interval.

- At data cut-off, among patients who had a complete remission, 44.4% (16/36) remained in complete response with no further treatment and 36.1% (13/36) had disease progression or death; corresponding values excluding 10 patients who were censored because of transplant were 61.5% (16/26) and 34.6% (9/26), respectively (**Figure 4**)

Figure 4. Swimmer plot of complete responders



Each bar represents one patient. *Only for censored patients who discontinued the trial due to reasons other than progression or who went onto a different anticancer treatment other than transplant.

Conclusions

- After longer follow-up of patients in LOTIS-2, durable responses (median 13.4 months) to Lonca continue to be observed in heavily pre-treated patients with R/R DLBCL
- No new safety concerns were reported
- Efficacy and safety continue to be monitored

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