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

Pier Luigi Zinzani1, Paolo F. Caimi2, Carmelo Carlo-Stella3, Weiyun Ai4, Juan Pablo Alderuccio5, Kirit M. Ardeshna6, Brian Hess7, Brad S. Kahl8, John Radford9, Melhem Solh10, Anastasios Stathis11, Jay Feinberg12, David Ungar13, Taijuan Qin14, Luqiang Wang14, Mehdi Hamadani14

BACKGROUND

- Patients with relapsed/refractory diffuse large B-cell lymphoma (R/R DLBCL) who are ineligible for, or relapse after, salvage chemotherapy/stem cell transplant have a poor prognosis and limited treatment options.
- Loncastuximab tesirine (Lonca) comprises a humanized anti-CD19 antibody conjugated to a potent pyrrolidinobenzodiazepine (PBD) dimer toxin.
- LOTIS-2 is a Phase 2 study evaluating Lonca in patients with R/R DLBCL (NCT03589469).
- Primary efficacy and safety data have been previously published (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) [SD] of 4.6 cycles (4.3) and median (range) of 3 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).
- Most common (≥10%) Grade ≥3 TEAEs included neutropenia (26 [17.9%]), gamma-glutamyltransferase (GGT) [25 [17.2%]], and anemia (15 [10.3%])
- Most Grade ≥3 events were related to laboratory abnormalities rather than clinical symptoms.
- The rate of febrile neutropenia was low (3 [2.4%]).
- 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 50.0% (95% CI 38.6, 61.5% [16/26]) and 61.5% (95% CI 49.6, 73.0%) with an investigator-assessed ORR of 43.8%; 11 patients proceeded to stem cell transplant as consolidation after responding to Lonca.
- Median PFS was 4.9 months (95% CI 4.3, 7.6) for all patients (≥6 months since patients received first dose), and was 5.7 months for those with a partial response (Figure 1).
- Median DoR for all patients was 13.4 months.
- Complete response start.
- Go to transplant.
- Last infusion.

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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- Dr. Hamadani reports consultancy or advisory roles for ADC Therapeutics, AstraZeneca, and Celgene Corporation.

CONTACT INFORMATION

Prof Pier Luigi Zinzani: zinzani@iogen.it

REFERENCES