LOTIS-5: Study to Evaluate Loncastuximab Tesirine With Rituximab Versus Immunochemotherapy in Participants With Relapsed or Refractory Diffuse Large B-Cell Lymphoma

ADC THERAPEUTICS

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Rationale

Loncastuximab tesirine (Lonca) is a CD19-targeted, antibody–drug conjugate (ADC) that is Food and Drug Administration and European Medicines Agency approved for relapsed/refractory (R/R) diffuse large B-cell lymphoma (DLBCL) after ≥2 systemic therapies.[1,2]

- **Rituximab** is an anti-CD20 monoclonal antibody used in frontline and subsequent DLBCL immunotherapy.[3,4]
- Evidence from preclinical and clinical studies suggests that adding rituximab (R) to anti-CD19 ADC therapy may enhance tumor control.[5,6,a]

Patients

Adults diagnosed with **DLBCL** or high-grade B-cell lymphoma (HGBCL) with *MYC* and *BCL2* and/or *BCL6* rearrangements who have had ≥1 line of prior systemic therapy and are not a candidate for stem cell transplant (SCT).[7]

Trial

LOTIS-5 (NCT04384484) is a **phase 3**, randomized, open-label, 2-part, multicenter trial in patients with R/R DLBCL across sites in North America, South America, Europe, and Asia.[7,8]

- **Part 1** is a nonrandomized safety run-in that will characterize the safety of Lonca-R.
- **Part 2** is a randomized (1:1) study evaluating the efficacy and safety of Lonca-R versus the standard immunochemotherapy, R + gemcitabine + oxaliplatin (R-GemOx).

Status

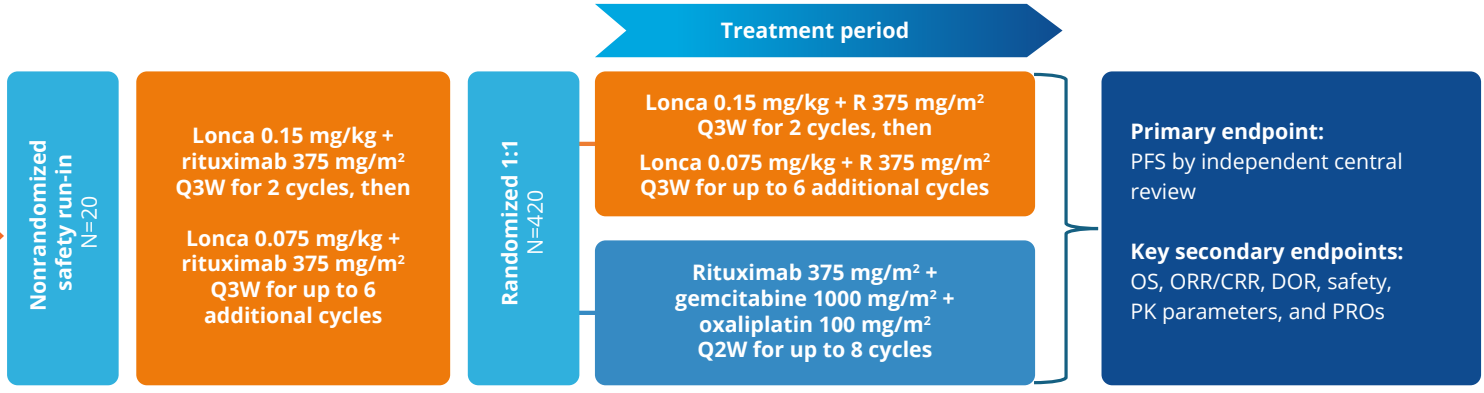
Enrollment for the **nonrandomized safety run-in** (part 1) and the **randomized study** (part 2) of LOTIS-5 is **complete**.[8,9]

Key Inclusion Criteria[7]

- Adults with a pathologic diagnosis of R/R DLBCL (including DLBCL transformed from indolent lymphoma) or HGBCL, with *MYC* and *BCL2* and/or *BCL6* rearrangements
- R/R disease following ≥1 multiagent systemic treatment regimen
- Measurable disease (2014 Lugano Classification[10])
- Not a candidate for SCT based on performance status, advanced age, and/or significant medical comorbidities (as considered by the investigator)
- Eastern Cooperative Oncology Group performance status score of 0-2
- Adequate organ function

Key Exclusion Criteria[7]

- Previous treatment with Lonca or R-GemOx
- Autologous SCT within 30 days before the start of the study drug
- Allogeneic SCT within 60 days before the start of the study drug
- Lymphoma with active central nervous system involvement, including leptomeningeal disease
- Serologic evidence of chronic hepatitis B virus (HBV) infection and inability or unwillingness to receive standard prophylactic antiviral therapy or with detectable HBV viral load
- Serologic evidence of hepatitis C virus (HCV) infection without completion of curative treatment or with detectable HCV viral load
- Clinically significant third-space fluid accumulation (ie, ascites requiring drainage or pleural effusion either requiring drainage or associated with shortness of breath)
- Major surgery within 4 weeks before the start of the study drug, unless approved by the sponsor
- Radiotherapy, chemotherapy, or other antineoplastic therapy within 14 days before the start of the study drug, unless approved by the sponsor

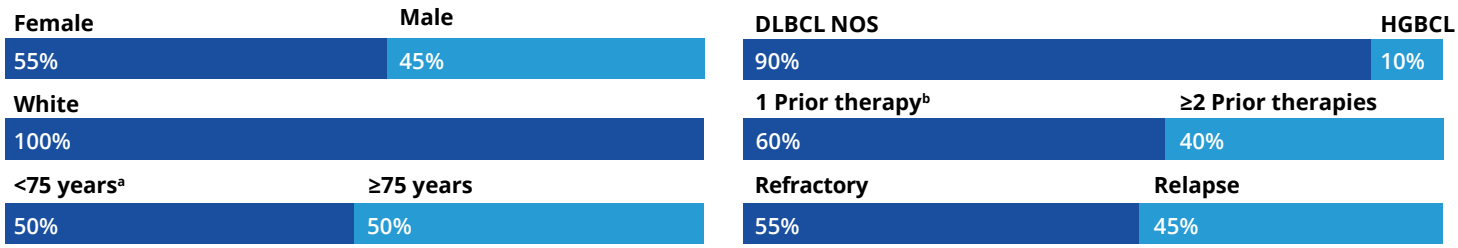


For both parts of the study, irrespective of disease status, patients will be followed for up to 4 years after EOT until withdrawal of consent, loss to follow-up, or death—whichever occurs first.
CRR, complete response rate; DOR, duration of response; Lonca, loncastuximab tesirine; ORR, overall response rate; OS, overall survival; PFS, progression free survival; PK, pharmacokinetic; PRO, patient-reported outcome; QXW, every X weeks; R, rituximab.

[a]The combination of Lonca and rituximab is not currently approved for the treatment of DLBCL.

Baseline characteristics for patients enrolled in LOTIS-5 safety run-in

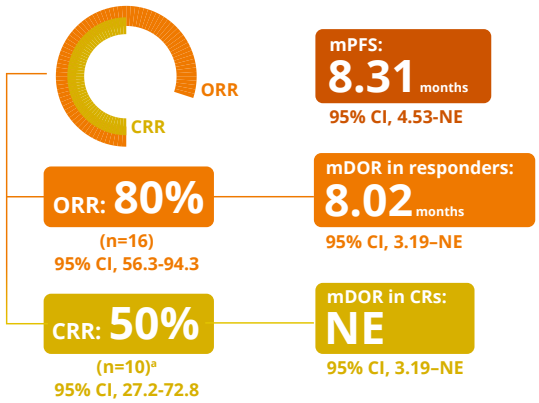
N=20



[a]Age range: 35-93
[b]Median number of prior therapies: 1 (range, 1-7)
DLBCL, diffuse large B-cell lymphoma; HGBCL, high-grade B-cell lymphoma; Lonca, loncastuximab tesirine; NOS, not otherwise specified; R, rituximab.
Data cutoff: October 4, 2024. Median duration of follow-up: 37.2 months (range, 34.1-41.5).

Efficacy outcomes for the LOTIS-5 safety run-in

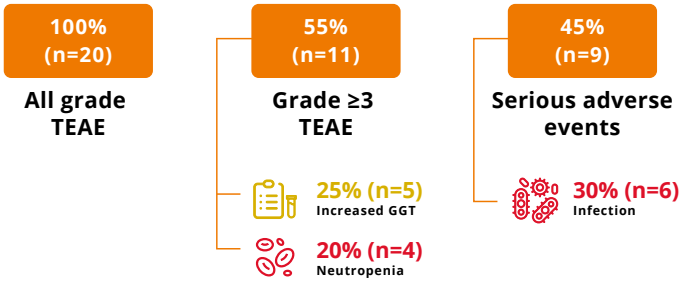
N=20



[a]One patient who achieved CR was refractory to most recent prior treatment.
CRR, complete response rate; mDOR, median duration of response; NE, not estimable; ORR, overall response rate; PFS, progression-free survival.
Data cutoff: October 4, 2024. Median duration of follow-up: 37.2 months (range, 34.1-41.5).
Median number of Lonca-R cycles: 5 (range: 1-8).

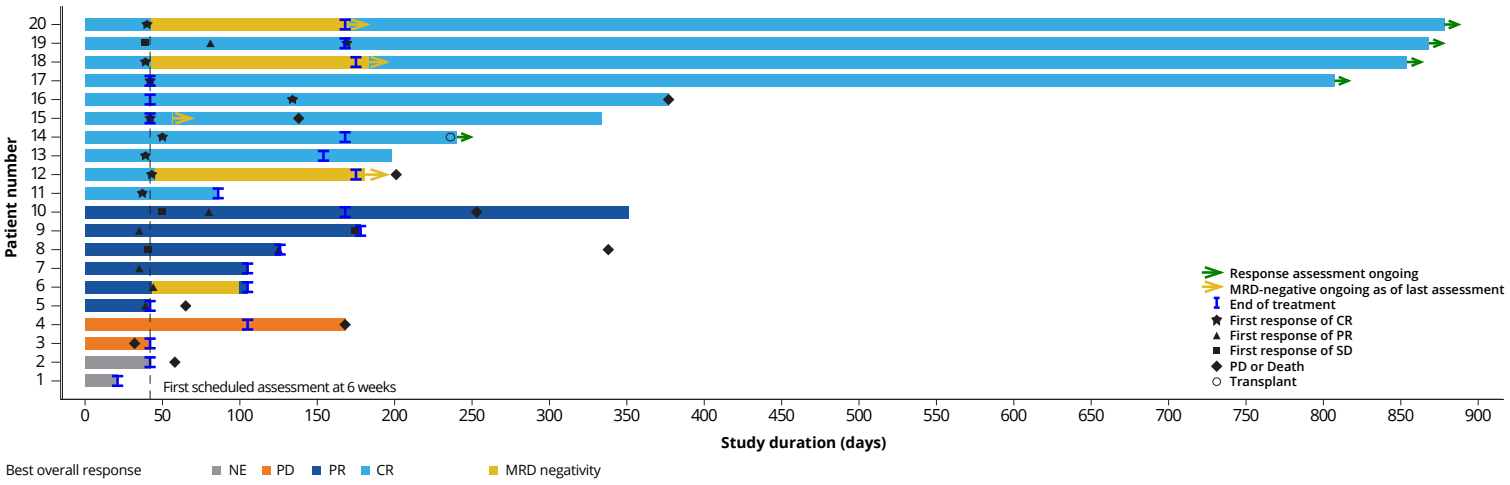
Safety outcomes for the LOTIS-5 safety run-in

N=20



GGT, gamma glutamyl transferase; TEAE, treatment-emergent adverse events.
Listed are the most common (≥20%) grade ≥3 TEAEs and serious adverse events.
Additional adverse events of interest (any grade): photosensitivity, 15% (n=3); pleural effusion, 15% (n=3); and edema, 5% (n=1).
Data cutoff: October 4, 2024. Median duration of follow-up: 37.2 months (range, 34.1-41.5).

Swimmer plot: response was sustained beyond end of treatment in 5 patients



CR, complete response; MRD, minimal residual disease; NE, not estimable; PD, progressive disease; PR, partial response.
The swimmer plot represents the safety run-in population, as assessed by independent review. Each bar represents one patient in the study.
Data cutoff: October 4, 2024. Median duration of follow-up: 37.2 months (range, 34.1-41.5).

References
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