INTRODUCTION
Patients with refractory or relapsed diffuse large B-cell lymphoma (DLBCL) typically have poor outcomes following standard treatment.1

Loncastuximab tesirine (loncastuximab tesirine-ipI; Lonca), an antibody-drug conjugate (ADC) comprising a humanized anti-CD19 monoclonal antibody conjugated to a pyrrolobenzodiazepine (PBD) dimer toxin, is approved in relapsed/refractory (R/R) DLBCL based on data from the phase 2 LOTIS-2 trial.1,2

Lonca is internalized by cells expressing CD19, the linker is cleaved, and the PBD dimer causes interstrand DNA crosslinks that lead to cell death (Figure 1).1,3

Preclinical evidence suggests that the addition of rituximab to anti-CD19 ADC therapy may result in prolonged tumor control.2

LOTIS-5 aims to evaluate Lonca + R (Lonca-R) vs. standard immunomodulatory of R + gemcitabine + oxaliplatin (R-GemOx) in patients with R/R DLBCL.

METHODS

STUDY DESIGN

This is a phase 3, randomized, open-label, two-part, two-arm, multicenter study of Lonca-R in patients with relapsed/refractory DLBCL (NCT04384484).

Table 1. Study objectives and endpoints

<table>
<thead>
<tr>
<th>Primary Objectives</th>
<th>Secondary Objectives</th>
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<tr>
<td>- Efficacy of Lonca-R vs. R-GemOx</td>
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<tr>
<td>- Progression-free survival (PFS)</td>
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<td>- Overall survival (OS)</td>
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<td>- Clinical response rate</td>
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<td>- Safety</td>
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OUTCOMES

The primary endpoint is progression-free survival by independent central review.

The key secondary end points include overall survival, overall response rate, safety, duration of response, pharmacokinetic parameters, and changes in patient-reported outcomes (Table 1).

Eligibility Criteria

The key inclusion criteria and exclusion criteria are shown in Table 2.

Study Assessments

The study assessments are shown in Table 3. Time-to-event endpoints will be assessed for the intent-to-treat population using a stratified log-rank test, and an interim futility analysis will be conducted after one-third of the expected progression-free survival (PFS) events have occurred.

STUDY STATUS

The study opened in September 2020.

The randomized part of the study commenced in January 2022, and recruitment is ongoing.

KEY MESSAGE

This phase 3, randomized, open-label, trial-in-progress evaluates Lonca in combination with rituximab versus standard immunomodulatory in patients with R/R DLBCL.

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References


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