Safety and Antitumor Activity Study Evaluating Loncastuximab Tesirine and Rituximab Versus Immunochemotherapy in Diffuse Large B-Cell Lymphoma

Yuliya Linhares¹, Mitul Gandhi², Michael Chung³, Jennifer Adeleye⁴, David Ungar⁴, Mehdi Hamadani⁵

¹Medical Oncology, Miami Cancer Institute, Baptist Health, Miami, FL, USA; ²Medical Oncology, Virginia Cancer Specialists, Gainesville, VA, USA; ³Hematology/Oncology, The Oncology Institute of Hope and Innovation, Downey, CA, USA; ⁴Clinical Development, ADC Therapeutics America, Inc., Murray Hill, NJ, USA; ⁵Division of Hematology and Oncology, Medical College of Wisconsin, Milwaukee, WI, USA

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7:00 am – 3:30 pm (Pacific Time)
**Introduction**

The prognosis of patients with DLBCL whose disease is refractory to initial chemotherapy (and are thus ineligible for ASCT) or relapse early after ASCT is extremely poor\(^1,2\)

The development of a more effective, less toxic salvage treatment for DLBCL remains an unmet need\(^2\)

Loncastuximab tesirine (Lonca) is an ADC comprising a humanized monoclonal anti-CD19 antibody conjugated to a pyrrolobenzodiazepine (PBD) dimer toxin, through a protease cleavable valine–alanine linker

Rituximab is an anti-CD20 monoclonal antibody used as a standard component of care for the treatment of DLBCL, either as monotherapy or in combination with chemotherapy

**Mechanism of action of Lonca**

In a Phase 2 study, Lonca demonstrated single-agent antitumor activity with manageable toxicity in patients with R/R DLBCL\(^3\)

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Rituximab is licensed for treatment of NHL but is being used in combination with an unlicensed drug (loncastuximab tesirine) in this study


ADC, antibody-drug conjugate; ASCT, autologous stem cell transplantation; DLBCL, diffuse large B-cell lymphoma; Lonca-R, loncastuximab tesirine plus rituximab; NHL, non-Hodgkin lymphoma; R-GemOx, rituximab/gemcitabine/oxaliplatin; R/R, relapsed/refractory.
Study Design

This Phase 3, randomized, open-label, two-part, two-arm, global study of Lonca-R versus standard immunochemotherapy in patients with R/R DLBCL (NCT04384484) is currently recruiting patients.

Part 1: non-randomized safety run-in

Lonca-R
Lonca 150 µg/kg +
R 375 mg/m²
Q3W × 2

Lonca-R
Lonca 75 µg/kg +
R 375 mg/m²
Q3W × 6

Target N=20

Part 2: randomized, two-arm study

Randomization
1:1

Lonca-R
Lonca 150 µg/kg +
R 375 mg/m²
Q3W × 2

Lonca-R
Lonca 75 µg/kg +
R 375 mg/m²
Q3W × 6

R-GemOx
R 375 mg/m² + Gem 1000 mg/m² +
Ox 100 mg/m²
Q2W × 8

Target N=330

DLBCL, diffuse large B-cell lymphoma; Lonca-R, loncastuximab tesirine plus rituximab; R-GemOx, rituximab/gemcitabine/oxaliplatin; Q2W, every 2 weeks; Q3W, every 3 weeks; R/R, relapsed/refractory.
Study Objectives and Endpoints

**Primary Objective**
Evaluate the efficacy of Lonca-R versus R-GemOx

**Primary Endpoint**
PFS\(^a\) (by independent central review)

**Secondary Objectives**
• Further efficacy evaluation
• Characterize the safety profile of Lonca-R
• Characterize the pharmacokinetics of Lonca-R
• Characterize the immunogenicity of Lonca-R
• Evaluate the impact of Lonca-R on PROs, and overall health status

**Secondary Endpoints**
• OS, ORR, CRR, and DoR
• Frequency and severity of AEs, and laboratory values
• Lonca PK parameters
• Anti-drug antibody titers to Lonca
• Changes in PROs from baseline

\(^a\)Defined as time between randomization and the first documentation of recurrence or progression, or death from any cause.

AE, adverse event; CRR, complete response rate; DoR, duration of response; Lonca-R, loncastuximab tesirine plus rituximab; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; PK, pharmacokinetics; PRO, patient-reported outcome; R-GemOx, rituximab/gemcitabine/oxaliplatin.
## Inclusion and Exclusion Criteria

### Key Inclusion Criteria

- Adults with a pathologic diagnosis of R/R DLBCL (WHO 2016 classification), or HGBCL, with MYC and BCL2 and/or BCL6 rearrangements
- R/R disease following at least one multiagent systemic treatment regimen
- Measurable disease (2014 Lugano Classification)
- Not a candidate for SCT based on performance status, advanced age, and/or significant medical comorbidities (as considered by the investigator)
- Patients who have received previous CD19-directed therapy must have a biopsy which shows CD19 expression after completion of the CD19-directed therapy
- ECOG performance status 0–2
- Adequate organ function

### Key Exclusion Criteria

- Previous treatment with Lonca or R-GemOx
- ASCT within 30 days prior to start of study drug
- Allogeneic SCT within 60 days prior to start of study drug
- Lymphoma with active CNS involvement, including leptomeningeal disease
- Serologic evidence of chronic HBV infection and unable or unwilling to receive standard prophylactic antiviral therapy or with detectable HBV viral load
- Serologic evidence of 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, radiotherapy, chemotherapy or other antineoplastic therapy within 14 days prior to start of study drug, unless approved by Sponsor

## Study Assessments

### Efficacy

#### Disease assessment
- Imaging (PET-CT)<sup>a</sup>
- Clinical examination for lymphoma

### Safety
- Adverse events
- ECOG performance status
- Hematology and chemistry
- Physical examination
- Pregnancy test (if applicable)
- Vital signs
- Weight
- 12-lead ECG

### PK and Immunogenicity
- PK of Lonca PBD-conjugated Ab, total Ab, and SG3199 free warhead
- ADA in blood

### Symptoms, PROs, and Overall Health
- EORTC QLQ-C30
- EQ-5D-5L
- LymS subscale of FACT-Lym
- GP5 item of FACT-Lym

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<sup>a</sup>Performed at 6 and 12 weeks after Cycle 1, Day 1, then every 12 weeks until end-of-treatment.

Current Status

Recruitment

This Phase 3, randomized, open-label, two-part, two-arm study of Lonca-R versus standard immunochemotherapy in patients with R/R DLBCL (NCT04384484) is currently recruiting patients:

- Global: North America and Europe
- Target N=20 for Part 1
- Target N=350 for Parts 1 and 2 combined

DLBCL, diffuse large B-cell lymphoma; Lonca-R, loncastuximab tesirine plus rituximab; R/R, relapsed/refractory.
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