



Rationale

- **Loncastuximab tesirine** (Lonca) is an antibody-drug conjugate (ADC) that has been designed to target and kill CD19-expressing malignant B cells
- **Glofitamab** is a CD20xCD3 T-cell engaging bispecific antibody that redirects T cells to eliminate malignant B cells
- Combining 2 agents with different mechanisms of action has the potential to have increased activity compared to either agent alone



Patients

Adults with **R/R B-NHL** (including DLBCL, HGBCL, and FL*) with ≥ 2 (part 1) or ≥ 1 (part 2) prior systemic treatments



Trial

LOTIS-7 (NCT04970901) is a **phase 1b** trial evaluating the safety/tolerability and antitumor activity of **Lonca in combination with other anticancer agents**

Arm E combines Lonca with a bispecific CD20-targeted CD3 T-cell engager



Status

Dose escalation for the **Lonca + glofitamab** arm is complete

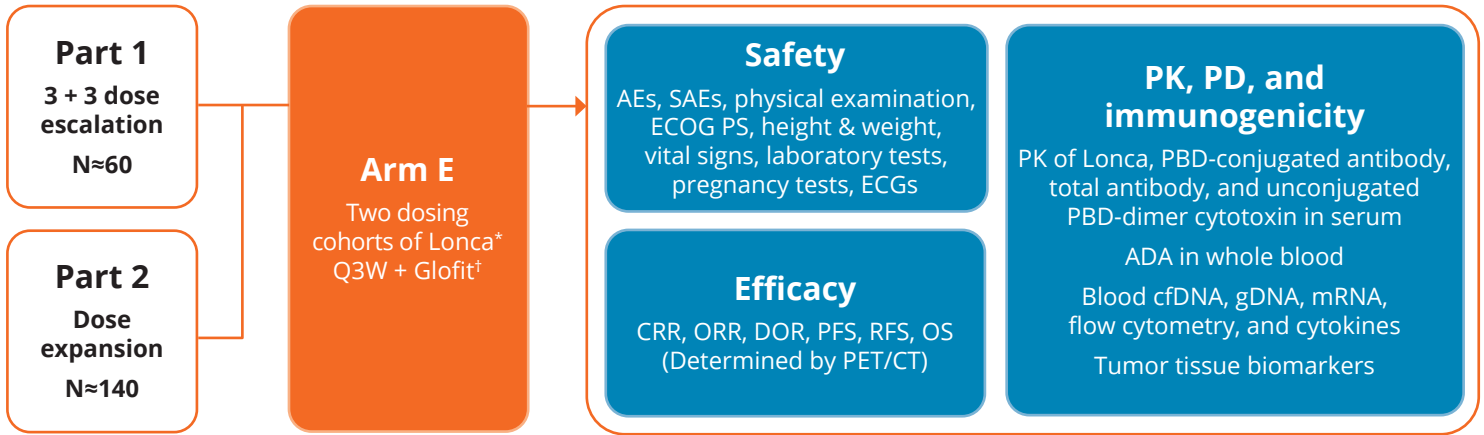
Enrollment continues in the **Lonca + glofitamab** arm for dose expansion in the 120- $\mu\text{g}/\text{kg}$ and 150- $\mu\text{g}/\text{kg}$ Lonca starting dose cohorts

Key Inclusion Criteria

- Age ≥ 18 years
- Pathologic diagnosis of R/R B-NHL (2016 WHO classification) with treatment failures/intolerance: DLBCL, HGBCL, FL, or MZL
- ≥ 2 prior systemic treatment regimens (part 1) or ≥ 1 systemic treatment regimens (part 2)
- Measurable disease (2014 Lugano classification)
- ECOG PS 0-2
- Adequate organ function based on laboratory parameters:
 - Absolute neutrophil count of $>1.5 \times 10^3 \mu\text{L}$
 - Platelet count $\geq 75 \times 10^3/\mu\text{L}$ without transfusion in the past 7 days
 - Hemoglobin $\geq 9 \text{ g/dL}$
 - ALT, AST, or GGT $<2.5 \times \text{ULN}$
 - Total bilirubin $<1.5 \times \text{ULN}$
 - Calculated CrCl $\geq 60 \text{ mL/min}$ (Cockcroft-Gault)

Key Exclusion Criteria (Arms E)

- Previously received study medication will impact arm assignment
- Lymphoma with active CNS involvement, history of CNS lymphoma or leptomeningeal infiltration, or current or history of CNS disease
- Clinically significant third space fluid accumulation (ascites or pleural effusion requiring drainage or associated with shortness of breath)
- Active acute graft-versus-host disease
- Posttransplant lymphoproliferative disorder
- History of hypersensitivity to a CD19 antibody resulting in treatment discontinuation or positive serum human ADA to a CD19 antibody
- History of Stevens-Johnson syndrome, toxic epidermal necrolysis, or macrophage activation syndrome/hemophagocytic lymphohistiocytosis
- History of confirmed progressive multifocal leukoencephalopathy
- Significant medical comorbidities
- Received autologous stem cell transplant within 100 days before study treatment
- Received allogeneic stem cell or solid organ transplant
- Known active infection; reactivation of a latent infection, whether bacterial, viral, fungal, mycobacterial, or other pathogens; or any major episode of infection requiring hospitalization or treatment with IV antibiotics within 4 weeks prior to C1D1
- Active or history of autoimmune disease or immune deficiency
- Prior treatment with CAR-T therapy within 100 days prior to C1D1; patients who are primary refractory[†] to CAR-T therapy



*Cohort 1 will receive Lonca 120 µg/kg for 2 cycles and Cohort 2 will receive Lonca 150 µg/kg for 2 cycles, then Lonca will be reduced to 75 µg/kg in both cohorts for remaining cycles for up to 8 cycles total or until disease progression. Lonca will be administered on D1 of each cycle, 1 hour before combination drugs, with the exception of Arm E C1, which will be administered on C1D2. †Obinutuzumab pretreatment on C1D1; IV Glofit 2.5 mg on C1D8, 10 mg on C1D15, and then 30 mg for C2-12 on D1.

ARM E DOSING^{1,2} LONCA + GLOFITAMAB

Arm E investigates the CD19-targeted ADC Lonca in combination with glofitamab, a bispecific antibody targeting CD20×CD3 in a 2:1 ratio.^{1,3,4} Treatment may continue up to 1 year or until disease progression

| | | Days | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | 19 | 20 | 21 |
|-------------|---------------------------------|------|---|---|---|---|---|---|---|---|---|----|----|----|----|----|----|----|----|----|----|----|----|
| Cycle 1 | Obin 1000 mg IV | ✓ | | | | | | | | | | | | | | | | | | | | | |
| | Lonca IV* | ★ | | | | | | | | | | | | | | | | | | | | | |
| | Glofit 2.5 mg IV ^{†,‡} | | | | | | | | | ✓ | | | | | | | | | | | | | |
| | Glofit 10 mg IV [‡] | | | | | | | | | | | | | | | | ✓ | | | | | | |
| Cycle 2 | Lonca IV* | ★ | | | | | | | | | | | | | | | | | | | | | |
| | Glofit 30 mg IV [‡] | ✓ | | | | | | | | | | | | | | | | | | | | | |
| Cycles 3-8 | Lonca IV* | ★ | | | | | | | | | | | | | | | | | | | | | |
| | Glofit 30 mg IV [§] | ✓ | | | | | | | | | | | | | | | | | | | | | |
| Cycles 9-12 | Glofit 30 mg IV [§] | ✓ | | | | | | | | | | | | | | | | | | | | | |

*Cohort 1 will receive Lonca 120 µg/kg for 2 cycles and Cohort 2 will receive Lonca 150 µg/kg for 2 cycles, then Lonca will be reduced to 75 µg/kg in both cohorts for remaining cycles for up to 8 cycles or until disease progression. Administer Lonca 1 to 1.5 hours before administration of Glofit. Administer dex (4 mg twice daily or equivalent), the day before, the day of, and the day after Lonca administration; †Administration of Glofit 2.5 mg IV on C1D8 requires 24 hours of hospitalization; ‡Administer dex (20 mg) at least 1 hour before administration of Glofit. Administer an antihistamine and an antipyretic at least 30 minutes before administration of Glofit; §In C3 and beyond, administer Glofit premedication in patients who experienced any grade cytokine release syndrome with the previous doses.

ADA, anti-drug antibody; ADC, antibody-drug conjugate; AE, adverse event; ALT, alanine transaminase; AST, aspartate aminotransferase; B-NHL, B-cell non-Hodgkin lymphoma; C, cycle; CAR-T, chimeric antigen receptor T-cell; cfDNA, circulating free DNA; CNS, central nervous system; CrCl, creatinine clearance; CRR, complete response rate; CT, computed tomography; D, day; dex, dexamethosone; DLBCL, diffuse large B-cell lymphoma; DOR, duration of response; ECG, electroencephalogram; ECOG, Eastern Cooperative Oncology Group; FL, follicular lymphoma; gDNA, genomic DNA; GGT, gamma-glutamyl transferase; Glofit, glofitamab; HGBCL, high-grade B-cell lymphoma; IV, intravenous; Lonca, loncastuximab tesirine-lpyl; MZL, marginal zone lymphoma; Obin, obinutuzumab; ORR, objective response rate; OS, overall survival; PBD, pyrrolbenzodiazepine; PD, pharmacodynamics; PET, positron emission tomography; PFS, progression-free survival; PK, pharmacokinetics; PS, performance status; Q3W, every 3 weeks; RFS, relapse-free survival; R/R, relapsed/refractory; SAE, serious adverse event; tFL, transformed follicular lymphoma; ULN, upper limit of normal; WHO, World Health Organization.

References

- Ayers EC, et al. Poster presented at: Society of Hematologic Oncology Annual Meeting (SOHO 2024); September 4-7, 2024; Houston, TX.
- ADC Therapeutics SA. Data on File.
- ZYNLONTA® (loncastuximab tesirine-lpyl). Full Prescribing Information. Murray Hill, NJ; ADC Therapeutics; 2026.
- González Barca E. *Front Immunol*. 2022;13:909008.