LOTIS-7: A study of loncastuximab tesirine in combination with other anticancer agents in patients with relapsed or refractory B-cell non-Hodgkin lymphoma

ADC THERAPEUTICS

Scan for more information

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-µg/kg and 150-µg/kg Lonca starting dose cohorts

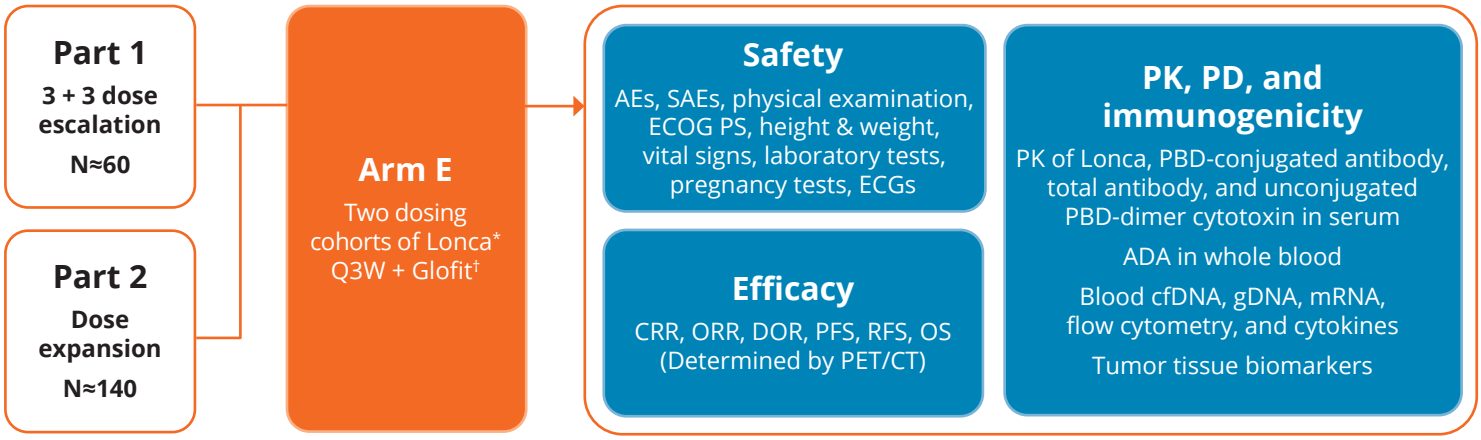
Key Inclusion Criteria

- Age ≥18 years
- Pathologic diagnosis of R/R B-NHL (2016 WHO classification) withtreatment 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 >1.5×10^3 µL
  - Platelet count ≥75×10^3/µL without transfusion in the past 7 days
  - Hemoglobin ≥9 g/dL
  - ALT, AST, or GGT <2.5× ULN
  - Total bilirubin <1.5× ULN
  - Calculated CrCl ≥60 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 allogenic 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

*Arm E, part 1 enrolled patients with DLBCL, HGBCL, MZL, and FL. Arm E, part 2 is enrolling patients with DLBCL not otherwise specified, HGBCL, and tFL. †Primary refractory is defined as patients who have progressive or persistent disease within 30 days of treatment.



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

ADC THERAPEUTICS