

Investigational Loncastuximab Tesirine-Ipyl – LOTIS-7 Dosing, Premedication Prophylaxis

The safety and efficacy of loncastuximab tesirine in combination with glofitamab has not been established, and this combination has not been approved by any regulatory agency. Loncastuximab tesirine is approved at 150 µg/kg for the first two cycles and 75 µg/kg for subsequent cycles for adult patients with relapsed or refractory large B-cell lymphoma after two or more lines of systemic therapy, including diffuse large B-cell lymphoma (DLBCL) not otherwise specified, DLBCL arising from low-grade lymphoma, and high-grade B-cell lymphoma.

Summary

- LOTIS-7 (NCT04970901) is a Phase 1b open-label study to evaluate the safety and anti-cancer activity of Loncastuximab tesirine (Lonca) in combination with other anti-cancer agents in patients with relapsed or refractory B-cell Non-Hodgkin Lymphoma (R/R B-NHL).²
 - The primary objective of this study is to characterize the safety and tolerability of Lonca in combination with glofitamab and to identify the maximum tolerated dose (MTD) and/or recommended dose for expansion (RDE) for the combination.
 - Key select secondary outcomes are overall response rate (ORR), duration of response (DOR), complete response rate (CRR), progression-free survival (PFS), relapse-free survival (RFS), and overall survival (OS).
- Patients will receive Lonca at 120 and 150 µg/kg (part 1 and 2) Q3W for a fixed duration of up to 8 cycles; Lonca doses 120 and 150 µg/kg were reduced to 75 µg/kg for cycles 3 and up.³
 - After pretreatment with obinutuzumab 1,000 mg on Cycle 1 Day 1, Lonca is given on Day 2. Glofitamab is then administered on Day 8 with step-up dosing in Cycle 1, followed by 30 mg every 3 weeks (Q3W) for up to 12 cycles.
- As of the Nov 17, 2025, data cutoff, 49 efficacy-evaluable 2L+ large B-cell Lymphoma patients (LBCL) treated with Loncastuximab tesirine (120 or 150 µg/kg) with ≥6 months follow-up were included. Eligible patients had R/R B-NHL, ECOG 0–2, measurable disease per Lugano 2014, and met regimen-specific prior therapy requirements (≥2 prior lines in Part 1; ≥1 prior line in Part 2). Patients with clinically significant third-space fluid accumulation were excluded. Prior ASCT or CAR-T (>100 days) was permitted.³
 - The grade ≥3 treatment emergent adverse events (TEAEs) occurring in >5% of patients included neutropenia (32.7%), increase in GGT (16.3%), anemia (10.2%), decrease in WBC (8.2%), generalized edema (8.2%), increase in ALT (8.2%), increase in AST (6.1%), and thrombocytopenia (6.1%).
- Per the LOTIS-7 study, premedication for loncastuximab tesirine includes dexamethasone (Dex) 4 mg or an equivalent, given either orally (PO) or intravenously (IV) twice daily, unless contraindicated. Dex should be administered the day before treatment, if

possible, on the day of treatment (at least two hours prior if it was not given the day before), and again the day after every treatment with lonca.¹

- Lonca should not be administered to patients with known hypersensitivity to any component of the drug product.
- When lonca and glofitamab are administered on the same day (Cycle 2 and beyond) Dex 20 mg (or equivalent) is used in place of other same-day Dex dosing.
 - Dex: 20 mg IV (complete at least 1 hour before glofitamab).
 - Antihistamine: diphenhydramine hydrochloride 50-100 mg (or equivalent) PO or IV.
 - Antipyretic/analgesic: paracetamol 500-1,000 mg at least 30 minutes before treatment.
- Glofit treatment is associated with a risk of cytokine release syndrome (CRS). Most CRS events occur during the first treatment cycle; however, CRS can recur in later cycles and is typically at lower grades.
- For patients who experience a Grade ≥ 2 infusion-related reaction, prophylactic premedication should be administered in subsequent cycles in accordance with the guidance below.¹
 - On Day 1 of each cycle, dexamethasone 20 mg should be given orally about 12 and 6 hours before starting loncastuximab tesirine. In addition, diphenhydramine hydrochloride 50 mg IV and ranitidine (or an equivalent agent) 50 mg IV should be given 30 minutes before the infusion.
 - Following Lonca treatment, Dex 4mg should be given orally twice daily for 2 days.
- Growth colony-stimulating factors (G-CSF) may be used per American Society of Clinical Oncology guidelines if a patient develops febrile neutropenia, but it is prohibited during cycle 1 of treatment.¹
- Anti-infective prophylaxis for viral (including SARS-CoV-2), fungal, bacterial, or pneumocystis infections is permitted and should be instituted per institutional practice or investigator preference based on individual patient risk factors.¹
 - Primary prophylaxis may start in Cycle 1 with PO acyclovir plus trimethoprim/sulfamethoxazole (or an equivalent alternative, such as dapsone in patients with an allergy).
 - Preferred prophylaxis is acyclovir 400 mg PO twice daily throughout treatment; valacyclovir 500 mg PO twice daily is an acceptable alternative.
- Please refer to **Table 1** below for detailed premedication for Lonca + Glofit in accordance with the LOTIS-7 clinical study.
- For more information regarding the LOTIS-7 Study please visit www.clinicaltrials.gov/study/NCT04970901

Treatment timepoint	Patients requiring premedication	Premedication (Arm E) *	Administration
Cycle 1 Day 1	All patients	<ol style="list-style-type: none"> 1. IV corticosteroid: Dex 20 mg 2. PO analgesic/antipyretic: acetaminophen/paracetamol 650-1,000 mg 3. Antihistamine: 50-100 mg diphenhydramine hydrochloride (or equivalent) orally or intravenously 4. Fluids 	Corticosteroid completed at least 1 hour prior to obinutuzumab infusion; other premedications completed at least 30 minutes prior to obinutuzumab administration. Patients should be well hydrated and given supplementary fluids as clinically indicated, according to institutional guidelines.
Cycle 1 Day 1	Patients at risk of tumor lysis syndrome (TLS) (e.g., bulky disease or renal impairment with creatinine clearance < 70 mL/min)	<ol style="list-style-type: none"> 1. Allopurinol or suitable alternative (e.g., rasburicase) with adequate hydration 	Administer 48-72 hours prior to study treatment
Cycle 1 Day 2	All patients	<ol style="list-style-type: none"> 1. Lonca premedication: Dex 4 mg PO or IV BID, or equivalent 	At least 2 hours prior to lonca administration when not given the day before; otherwise, any time prior to administration, and on the day after lonca
Cycle 1 Day 8 and Day 15; Cycle 2 Day 1; Cycle 3 Day 1	All patients	<ol style="list-style-type: none"> 1. IV corticosteroid: Dex 20 mg; 2. Antihistamine: 50-100 mg diphenhydramine hydrochloride or equivalent PO or IV 3. PO analgesic/antipyretic: acetaminophen/paracetamol 650-1,000 mg 4. Fluids; lonca-specific premeds on C2D1 and C3D1: Dex 4 mg PO or IV BID, or equivalent (unless contraindicated) 	Corticosteroid completed at least 1 hour prior to glofit administration; antihistamine and analgesic completed at least 30 minutes prior to glofit; patients should be well hydrated and given supplementary fluids as clinically indicated; **C2D1 and C3D1 lonca premeds given the day before lonca (if possible), the day of lonca, or the day after, with at least 2 hours prior to administration when not given the day before
All subsequent cycles, Day 1	All patients	<ol style="list-style-type: none"> 1. Antihistamine: 50-100 mg diphenhydramine 	Antihistamine and analgesic completed at least 30 minutes

		<p>hydrochloride or equivalent PO OR IV</p> <p>2. Oral analgesic/antipyretic: acetaminophen/paracetamol 650-1,000 mg</p> <p>3. Fluids; for cycles with lonca (Cycles 4–8): Dex 4 mg PO or IV BID, or equivalent (unless contraindicated)</p>	<p>prior to glofit; patients should be well hydrated and given supplementary fluids as clinically indicated; lonca premeds administered the day before lonca (if possible), the day of lonca, or the day after, with at least 2 hours prior to administration when not given the day before</p>
Any cycle, any day	<p>Patients who experienced any grade CRS with the previous dose</p>	<p>1. IV corticosteroid: Dex 20 mg</p>	<p>Complete at least 1 hour prior to glofit administration</p>

*Doses and agents may be adjusted per institutional guidelines and individual patient factors. ** Premedication of dexamethasone 20 mg will supersede other dexamethasone (or equivalent) to be administered on the same day.

References

¹Data on File. ADC Therapeutics LOTIS 7 Protocol. Accessed May 4, 2026

²ADCT Therapeutics SA. A study to evaluate the safety and anti-cancer activity of loncastuximab tesirine in combination with other anti-cancer agents in participants with relapsed or refractory B-cell non- Hodgkin lymphoma (LOTIS 7). ClinicalTrials.gov registration number: NCT04970901. Updated March 13, 2026. Accessed May 4, 2026. <https://clinicaltrials.gov/ct2/show/NCT04970901>

³Alderuccio JP, Okada C, et al. Initial Results From LOTIS-7: A Phase 1b Study of Loncastuximab Tesirine Plus Glofitamab in Patients With Relapsed/Refractory (R/R) Diffuse Large B-Cell Lymphoma (DLBCL) Oral Poster presented at the ICML June 17-21, 2025,

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