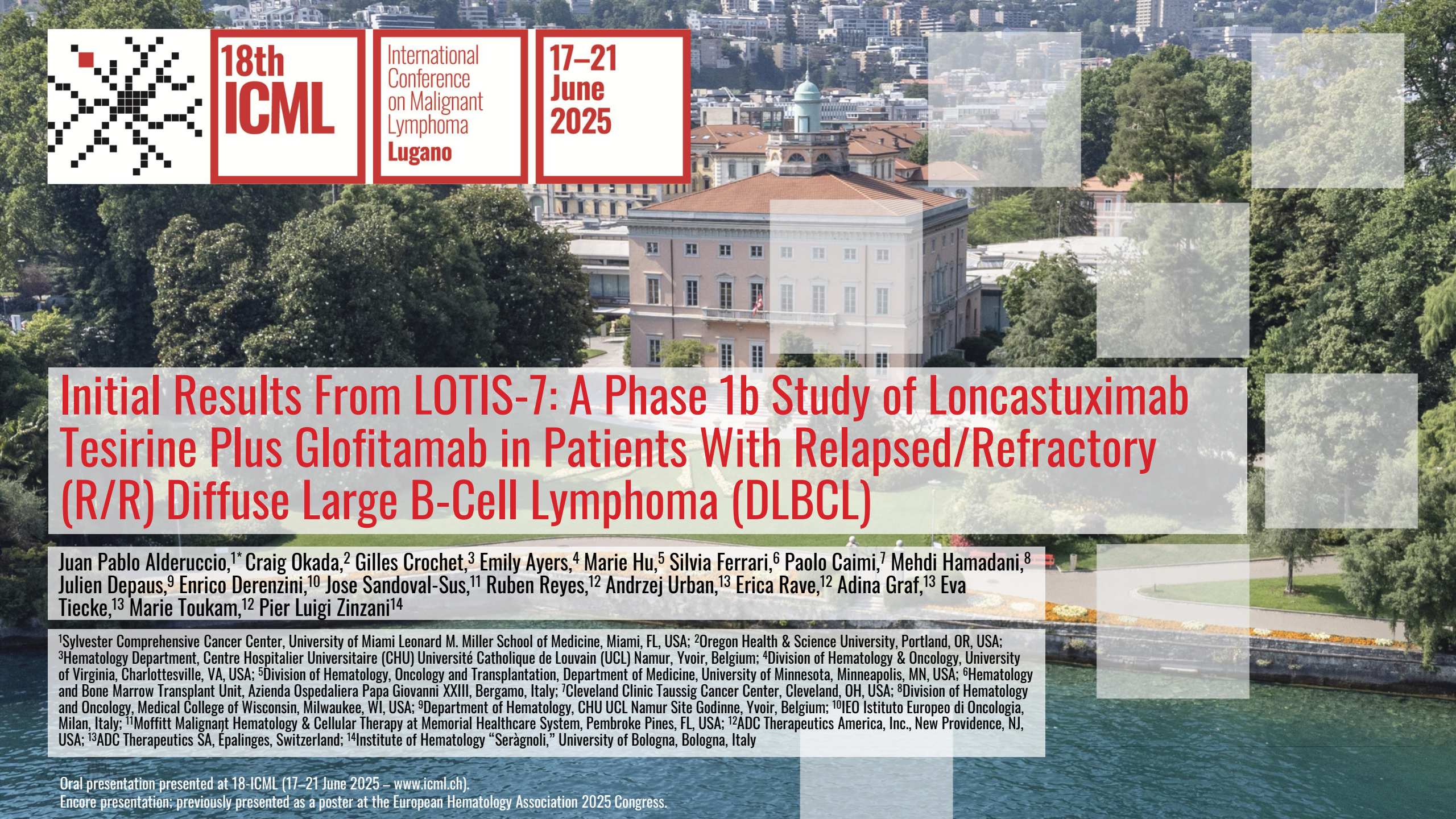

18th ICML
International Conference on Malignant Lymphoma
Lugano
17–21 June 2025

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)

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Oral presentation presented at 18-ICML (17–21 June 2025 – www.icml.ch).
Encore presentation; previously presented as a poster at the European Hematology Association 2025 Congress.

CONFLICT OF INTEREST DISCLOSURES

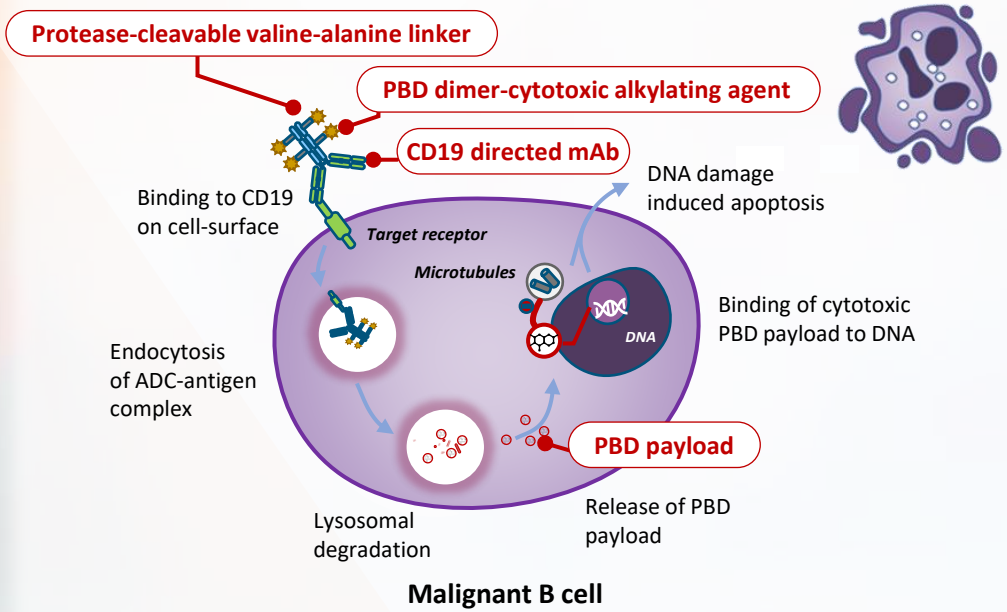
Juan P. Alderuccio

Consultant for AbbVie, ADC Therapeutics SA, Genentech, Genmab, Lilly, Novartis, and Regeneron; recipient of research funding from AbbVie, ADC Therapeutics SA, BeiGene, and Genmab; immediate family member has served on the advisory boards of Anheart, Fore, Rigel, and Servier; and speaker for Medscape.

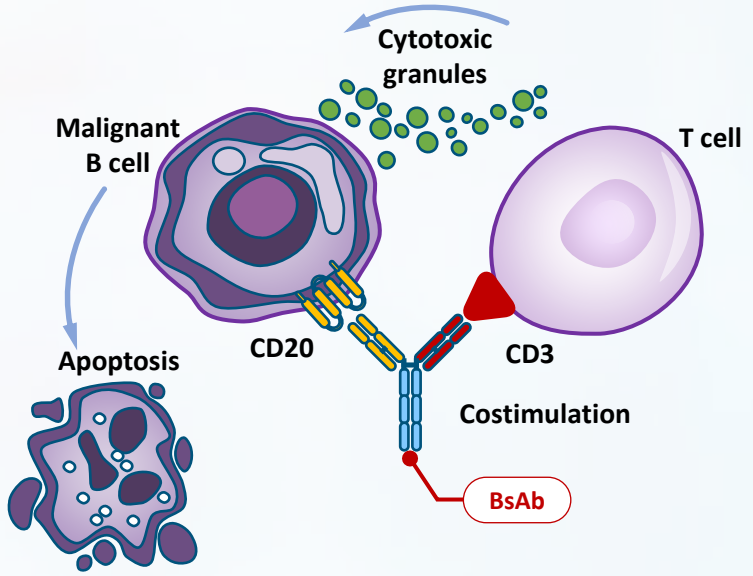
INTRODUCTION

- LOTIS-7 is a multinational (including US and EU), phase 1b, open-label, multi-arm trial evaluating loncastuximab tesirine (Lonca) in combination with other anticancer agents, including glofitamab (Glofit), in patients with R/R B-NHL
- This analysis evaluates Lonca (120 µg/kg and 150 µg/kg starting doses[a]) + Glofit in patients with 2L+ LBCL
- Lonca + Glofit is expected to have synergistic efficacy with minimal overlapping toxicities[1,2]

Loncastuximab tesirine (Anti-CD19 ADC)



Glofitamab (Anti-CD20/CD3 T-cell engaging BsAb)



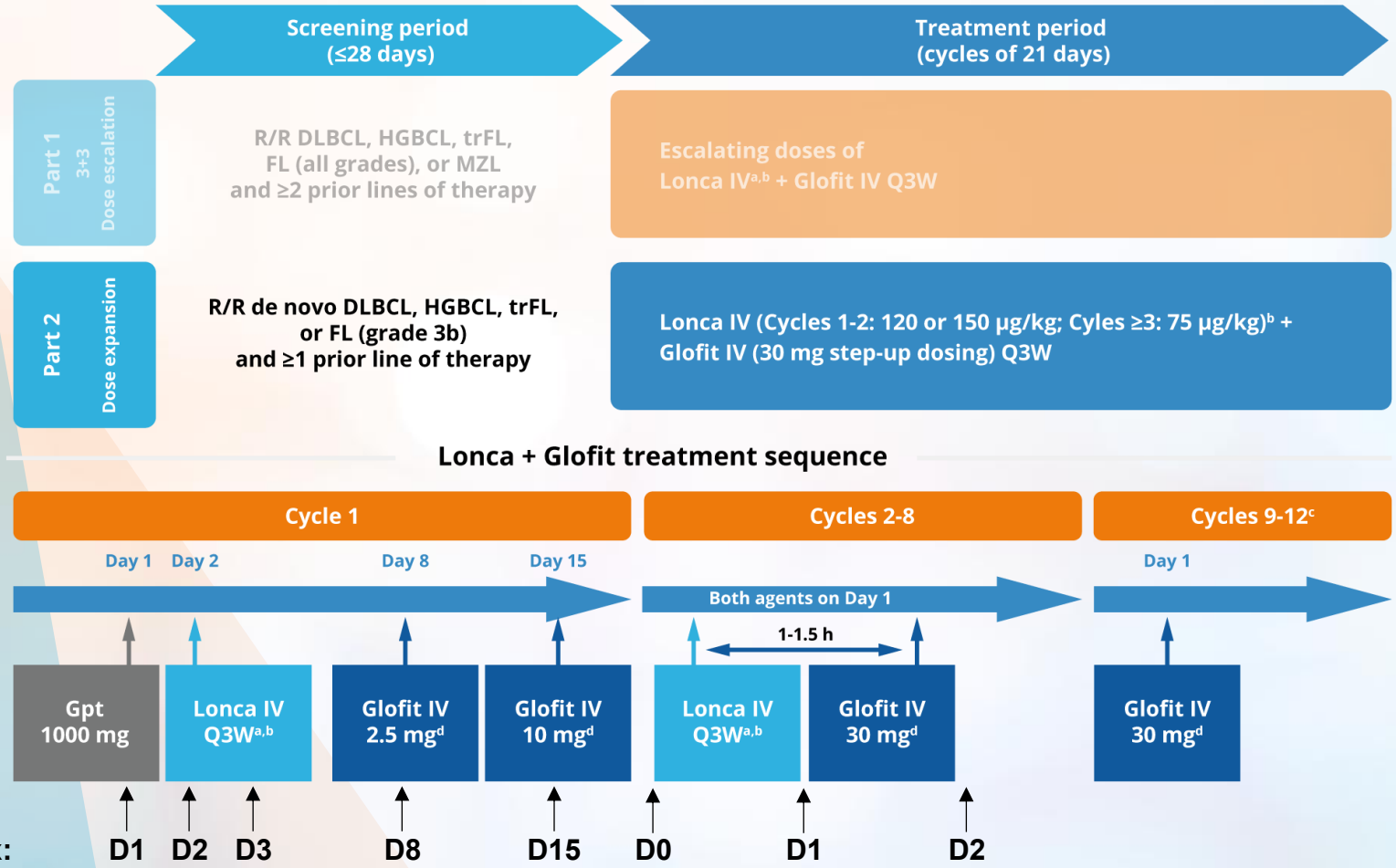
2L+, second line or later; 3L+, third line or later; ADC, antibody–drug conjugate; B-NHL, B-cell non-Hodgkin lymphoma; BsAb, bispecific antibody; DLBCL, diffuse large B-cell lymphoma; LBCL, large B-cell lymphoma; PBD, pyrrolobenzodiazepine; R/R, relapsed/refractory.
[a]When the starting dose of Lonca is 120 µg/kg or 150 µg/kg, the dose will be reduced to 75 µg/kg for Cycles ≥3.
1. Caimi PF, et al. Lancet Oncol. 2021;22(6):790-800. 2. Hutchings M, et al. J Clin Oncol. 2021;39(18):1959-1970.

OBJECTIVES

- **Primary endpoint:** Safety and tolerability, maximum tolerated dose (MTD) and/or recommended dose for expansion (RDE)
- **Secondary endpoints:** Efficacy outcomes (ORR, DOR, CR rate, PFS, RFS, and OS); PK and immunogenicity
- **Exploratory endpoints:** Glofit concentration in circulation; biomarker and PK correlations with clinical outcomes

CR, complete response; DOR, duration of response; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; PK, pharmacokinetics.

STUDY DESIGN & PATIENT POPULATION



Study population

- Patients with 3L+ R/R B-NHL (part 1) and 2L+ R/R LBCL (part 2)
- ECOG PS score of 0-2
- Prior autologous SCT (>100 days) or CAR-T therapy (>100 days) is allowed
- Measurable disease (per 2014 Lugano Classification)
- Excludes patients with clinically significant third-space fluid accumulation

Endpoints

- **Primary**: safety and tolerability; MTD and/or RDE
- **Secondary**: ORR, DOR, CR rate, PFS, RFS, and OS; PK and immunogenicity
- **Exploratory**: Glofit concentration in circulation; biomarker and PK correlations with clinical outcomes

2L+, second line or later; 3L+, third line or later; B-NHL, B-cell non-Hodgkin lymphoma; CAR-T, chimeric antigen receptor T cell; CR, complete response; CRS, cytokine release syndrome; D, day; Dex, dexamethasone; DLBCL, diffuse large B-cell lymphoma; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group Performance Status; FL, follicular lymphoma; Glofit, glofitamab; Gpt, obinutuzumab; HGBCL, high-grade B-cell lymphoma; IV, intravenous; Lonca, loncastuximab tesirine; MTD, maximum tolerated dose; MZL, marginal zone lymphoma; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; PK, pharmacokinetic; Q3W, every 3 weeks; RDE, recommended dose for expansion; RFS, relapse-free survival; R/R, relapsed or refractory; SCT, stem cell transplant; trFL, transformed follicular lymphoma.

[a]Dose level 1, 90 µg/kg; dose level 2, 120 µg/kg; and dose level 3, 150 µg/kg. [b]If the starting dose of Lonca is 120 µg/kg or 150 µg/kg, the dose will be reduced to 75 µg/kg for Cycles ≥3 per label. [c]Participants may continue Glofit up to 12 cycles and may continue lonca up to 8 cyles (or until disease progression, unacceptable toxicity, or other discontinuation criteria, whichever occurs first). The follow-up period is for ≤2 years from the end of treatment. [d]The first dose of Glofit on Cycle 1, Day 8 has a 24-hour mandatory hospitalization; subsequent doses require hospitalization if grade ≥2 CRS occurs.

PATIENT ENROLLMENT & ANALYSIS POPULATION

As of April 14, 2025, 47 patients with R/R B-NHL had received ≥1 dose of treatment at the Lonca 90 µg/kg, 120 µg/kg, or 150 µg/kg starting doses[a]

- Six patients who received Lonca 90 µg/kg or had another B-NHL histology (i.e., FL grades 1-3a or MZL) were excluded from the present analysis

- **Treated population**[b]: 41 patients with LBCL treated with Lonca 120 µg/kg or 150 µg/kg starting doses[a]
- **Efficacy population**[b]: 30 patients in the treated population who underwent ≥1 disease assessment

Data cutoff: April 14, 2025.
B-NHL, B-cell non-Hodgkin lymphoma; FL, follicular lymphoma; LBCL, large B-cell lymphoma; Lonca, loncastuximab tesirine; MZL, marginal zone lymphoma; R/R, relapsed/refractory.
[a]When the starting dose of Lonca is 120 µg/kg or 150 µg/kg, the dose will be reduced to 75 µg/kg for Cycles ≥3. [b]Populations as defined for this presentation.

PATIENT BASELINE CHARACTERISTICS

TREATED POPULATION (N=41)

	Glofit + Lonca, 120 µg/kg[a] (n=20)	Glofit + Lonca, 150 µg/kg[a] (n=21)	All dose levels (N=41)
Age, median (range), y	70 (50-82)	74 (26-85)	71 (26-85)
Male sex, n (%)	11 (55.0)	12 (57.1)	23 (56.1)
ECOG PS score, n (%)			
0	9 (45.0)	14 (66.7)	23 (56.1)
1	10 (50.0)	7 (33.3)	17 (41.5)
2	1 (5.0)	0	1 (2.4)
Ann Arbor disease stage, n (%)			
Stage I/II	3 (15.0)	3 (14.3)	6 (14.6)
Stage III/IV	17 (85.0)	18 (85.7)	35 (85.4)
IPI score, n (%)			
0-2	9 (45.0)	10 (46.7)	19 (46.3)
3-5	11 (55.0)	11 (52.4)	22 (53.7)
Bulky disease, n (%)	2 (10.0)	2 (9.5)	4 (9.8)
LDH levels high, n (%)	11 (55.0)	10 (47.6)	21 (51.2)
LBCL histology, n (%)			
de novo DLBCL	13 (65.0)	17 (81.0)	30 (73.2)
HGBCL	4 (20.0)	2 (9.5)	6 (14.6)
trFL	2 (10.0)	2 (9.5)	4 (9.8)
FL grade 3b	1 (5.0)	0	1 (2.4)

	Glofit + Lonca, 120 µg/kg[a] (n=20)	Glofit + Lonca, 150 µg/kg[a] (n=21)	All dose levels (N=41)
DLBCL subtype, n (%)			
GCB	10 (50.0)	11 (52.4)	21 (51.2)
non-GCB	5 (25.0)	8 (38.1)	13 (31.7)
Double or triple hit, n (%)	3 (15.0)	5 (23.8)	8 (19.5)
Number of prior LOT			
Median (range)	2 (1-4)	2 (1-5)	2 (1-5)
1, n (%)	10 (50.0)	10 (47.6)	20 (48.8)
≥2, n (%)	10 (50.0)	11 (52.4)	21 (51.2)
Refractory status, n (%)			
Refractory to primary therapy	8 (40.0)	13 (61.9)	21 (51.2)
Refractory to last prior therapy	7 (35.0)	13 (61.9)	20 (48.8)
Prior stem cell transplant, n (%)	3 (15.0)	1 (4.8)	4 (9.8)
Prior CAR-T therapy, n (%)	4 (20.0)	4 (19.0)	8 (19.5)

Data cutoff: April 14, 2025.

CAR-T, chimeric antigen receptor T cell; DLBCL, diffuse large B-cell lymphoma; ECOG PS, Eastern Cooperative Oncology Group Performance Status; FL, follicular lymphoma; HGBCL, high-grade B-cell lymphoma; IPI, International Prognostic Index; LBCL, large B-cell lymphoma; LDH, lactate dehydrogenase; Lonca, loncastuximab tesirine; LOT, lines of therapy; trFL, transformed follicular lymphoma.

[a]When the starting dose of Lonca is 120 µg/kg or 150 µg/kg, the dose will be reduced to 75 µg/kg for Cycles ≥3.

SAFETY OUTCOMES
TREATED POPULATION (N=41)

	120 µg/kg[b] n=20	150 µg/kg[b] n=21	All n = 41
Grade 3/4 TEAEs (> 5% of patients)[a]	**11 (55%)**	**12 (57.1%)**	**23 (56.1%)**
Neutropenia	4 (20%)	6 (28.6%)	10 (24.4%)
Anemia	1 (5%)	3 (14.3%)	4 (9.8%)
AST increased	2 (10%)	1 (4.8%)	3 (7.3%)
GGT increase	1 (5%)	2 (9.5%)	3 (7.3%)
Thrombocytopenia	2 (10%)	1 (4.8%)	3 (7.3%)
Grade 3/4 AESI (all patients)[a]			
Febrile neutropenia	0	1 (4.8%)	1 (2.4%)
Thrombocytopenia	2 (10%)	1 (4.8%)	3 (7.3%)
GGT increase	1 (5%)	2 (9.5%)	3 (7.3%)
Generalized oedema	1 (5%)	1 (4.8%)	2 (4.9%)
Rash	1 (5%)	0	1 (2.4%)
Photosensitivity reaction	0	1 (4.8%)	1 (2.4%)
Sepsis	1 (5%)	0	1 (2.4%)
Upper respiratory infection	1 (5%)	0	1 (2.4%)
Pneumonia	1 (5%)	0	1 (2.4%)
Serious TEAE	**11 (55%)**	**9 (42.9%)**	**20 (48.8%)**
No Grade 5 TEAEs occurred			

[a]As per Investigator reported adverse events. [b]When the starting dose of Lonca is 120 µg/kg or 150 µg/kg, the dose will be reduced to 75 µg/kg for Cycles ≥3.
TEAE = treatment emergent adverse event; AESI = adverse event of special interest | Data cutoff: 14 Apr 2025. Data extracted from live clinical database. Data is subject to change.

SAFETY SUMMARY: TEAES LEADING TO DRUG DISCONTINUATION
TREATED POPULATION (N=41)

Patients with TEAEs leading to study drug discontinuation[a]	120 µg/kg[b] n=20	150 µg/kg[b] n=21	All n = 41
TEAE leading to loncastuximab discontinuation only	**1 (5%)**	**2 (9.5%)**	**3 (7.3%)**
Pericardial effusion	1 (5%)	0	1 (2.4%)
Generalized oedema and GGT increased	0	1 (4.8%)	1 (2.4%)
Pleural effusion and erythema	0	1 (4.8%)	1 (2.4%)
TEAE leading to glofitamab discontinuation only	**0**	**3 (14.3%)**	**3 (7.3%)**
ICANS	0	1 (4.8%)	1 (2.4%)
Polyneuropathy	0	1 (4.8%)	1 (2.4%)
Febrile Neutropenia	0	1 (4.8%)	1 (2.4%)

Neutropenia was the most common TEAE leading to dose delay of Lonca (12.2%) and Glofit (17.1%); there was only 1 patient who had a dose reduction of Lonca

[a]As per Investigator reported adverse events. [b]When the starting dose of Lonca is 120 µg/kg or 150 µg/kg, the dose will be reduced to 75 µg/kg for Cycles ≥3.
TEAE = treatment emergent adverse event; AESI = adverse event of special interest
Data cutoff: 14 Apr 2025. Data extracted from live clinical database. Data is subject to change.

SAFETY SUMMARY: CRS/ICANS PROFILE & MANAGEMENT

TREATED POPULATION (N=41)

	120 µg/kg[b] n=20	150 µg/kg[b] n=21	All n = 41
Cytokine Release Syndrome[a]			
Any grade	11 (55%)	5 (23.8%)	16 (39.0%)
Grade 1	7 (35%)	5 (23.8%)	12 (29.3%)
Grade 2	3 (15%)	0	3 (7.3%)
Grade 3	1 (5%)	0	1 (2.4%)
Grade 4/5	0	0	0
ICANS[a]			
Any grade	2 (10%)	1 (4.8%)	3 (7.3%)
Grade 1	1 (5%)	0	1 (2.4%)
Grade 2	1 (5%)	1 (4.8%)	2 (4.9%)
Grade ≥ 3	0	0	0

Any-grade CRS was less frequent at the Lonca 150 µg/kg starting dose[b] (23.8%) than at 120 µg/kg starting dose[b] (55.0%)

- Grade 1 and 2 CRS cases managed with tocilizumab, corticosteroids, acetaminophen, and/or fluid bolus, without ICU admittance or pressor support
- Grade 3 CRS case managed with tocilizumab, acetaminophen, dexamethasone, norepinephrine. ICU admittance

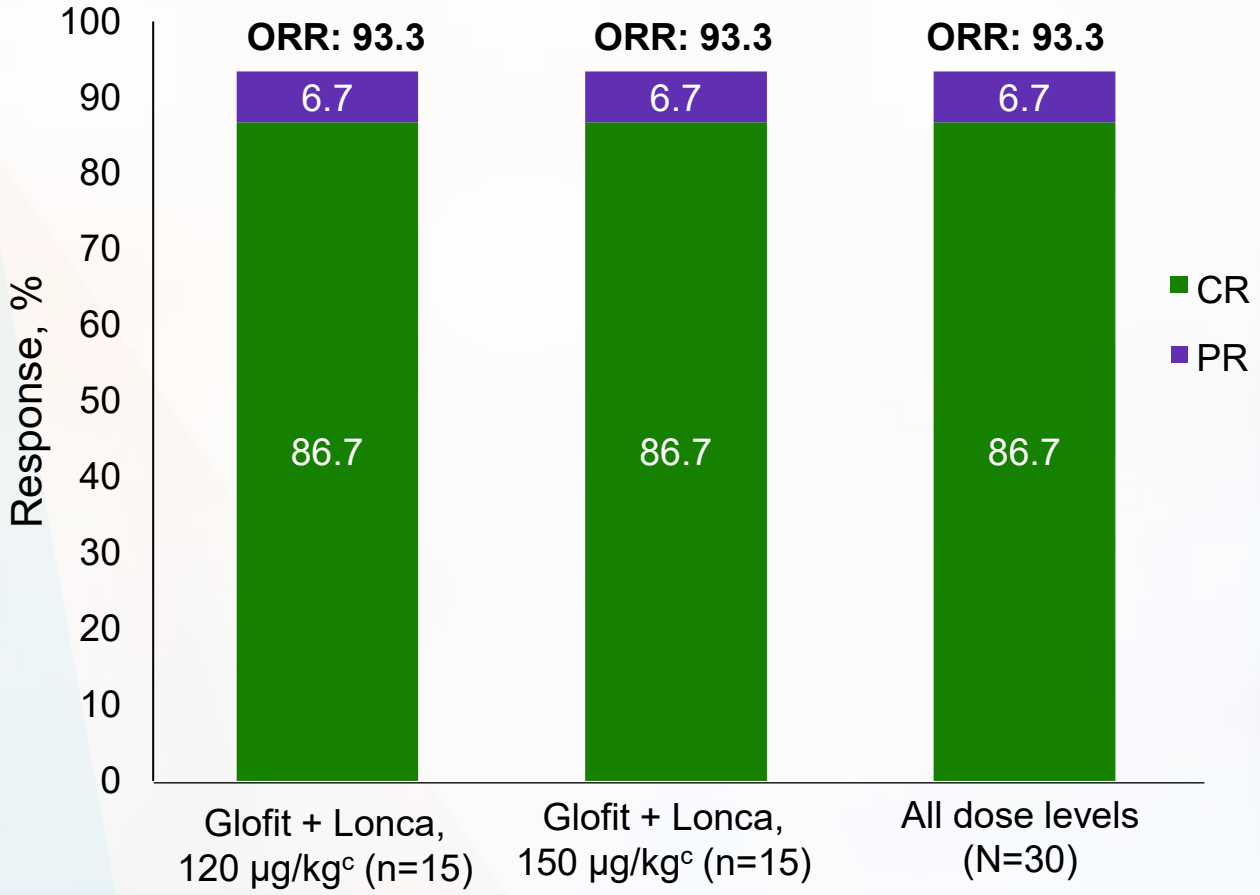
- All patients with ICANS had complete resolution of symptoms
  - Two patients resumed treatment and ultimately achieved a CR
  - One patient elected to discontinue treatment
- ICANS managed primarily with corticosteroids

[a]Number of patients who experienced at least 1 event per ASTCT Consensus Grading for Cytokine Release Syndrome and Neurologic Toxicity Associated with Immune Effector Cells; worst grade reported if applicable
[b]When the starting dose of Lonca is 120 µg/kg or 150 µg/kg, the dose will be reduced to 75 µg/kg for Cycles ≥3.
Data Cutoff 14 Apr 2025. Data extracted from live clinical database. Data is subject to change.

BEST OVERALL RESPONSE & DURATION OF RESPONSE

EFFICACY EVALUABLE POPULATION (N=30)[a]

Best overall response[b]



Duration of response

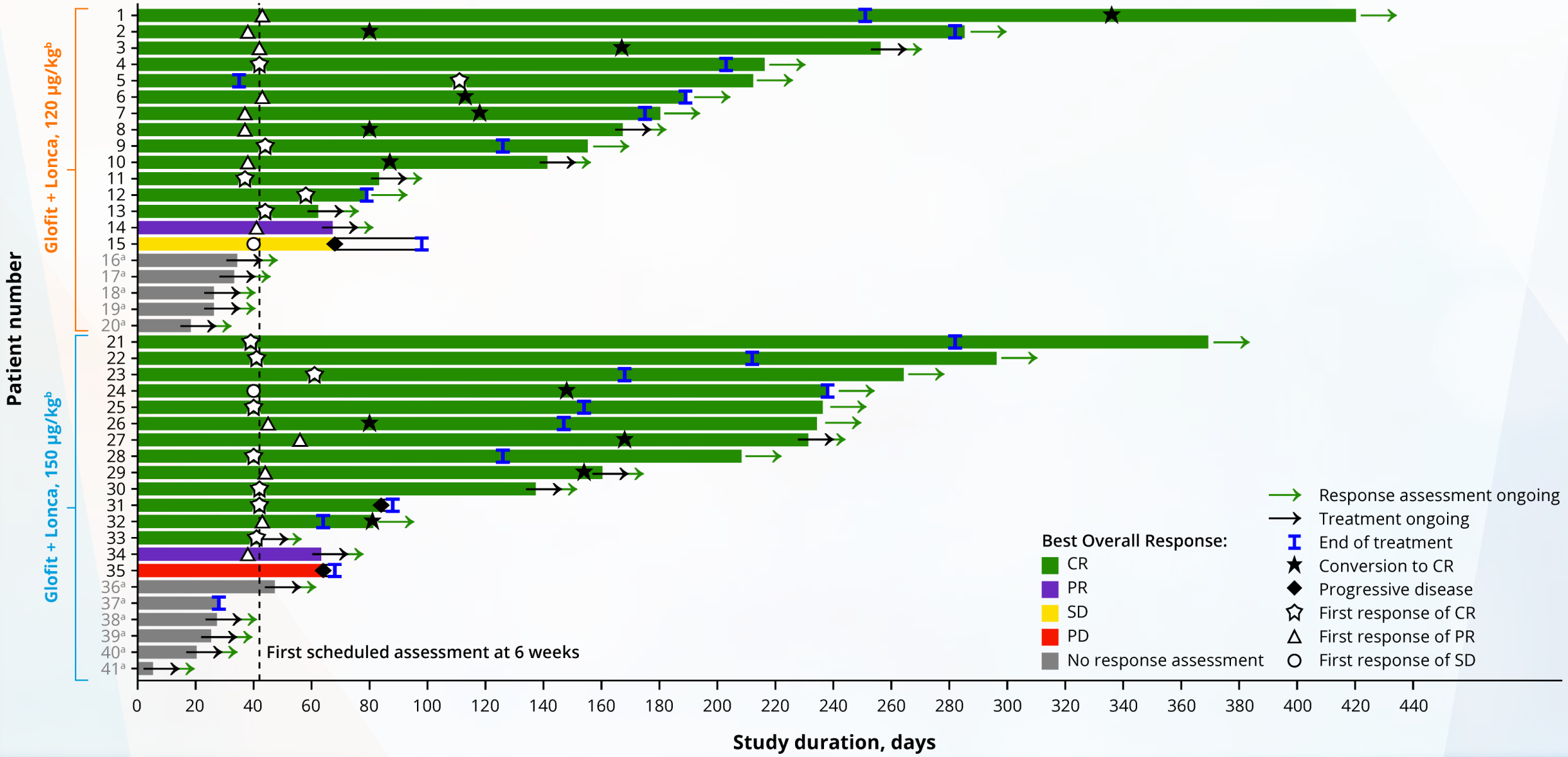
Characteristic, n (%)	Glofit + Lonca, 120 µg/kg[c] (n=15)	Glofit + Lonca, 150 µg/kg[c] (n=15)	All dose levels (N=30)
DOR[d] Median	(n=14) NE	(n=14) NE	(n=28) NE
Time to first response (CR or PR) Median, days	(n=14) 42.0	(n=14) 42.0	(n=28) 42.0
Time to first CR Median, days	(n=13) 80.0	(n=13) 42.0	(n=26) 70.5

Data cutoff: April 14, 2025.

CR, complete response; DOR, duration of response; Glofit, glofitamab; Lonca, loncastuximab tesirine; NE, not estimable; ORR, overall response rate; PR, partial response.

[a]The efficacy evaluable population (N=30) included all patients who received ≥1 dose of the study drug with a valid baseline and ≥1 valid postbaseline disease assessment. Patients who did not have a postbaseline assessment owing to early clinical progression or death were also included. [b]Percentages do not add up to total due to rounding. [c]When the starting dose of Lonca is 120 µg/kg or 150 µg/kg, the dose will be reduced to 75 µg/kg for Cycles ≥3. [d]In the efficacy evaluable population, the DOR and probability of maintaining an event-free response were evaluated in responders (n=28), including all patients who had a best response of CR or PR.

EFFICACY OVER TIME (N=41)



Data cutoff: April 14, 2025.
Each bar represents 1 patient in the study. Response was determined by an independent reviewer.
CR, complete response; Glofit, glofitamab; Lonca, loncastuximab tesirine; PD, progressive disease; PR, partial response; SD, stable disease.
[a]Patients were not yet efficacy evaluable because they had not reached the 6-week assessment (n=10) or had withdrawn before any assessment (Patient 39).[b]When the starting dose of Lonca is 120 µg/kg or 150 µg/kg, the dose will be reduced to 75 µg/kg for Cycles ≥3.

PHARMACOKINETICS & BIOMARKER OUTCOMES

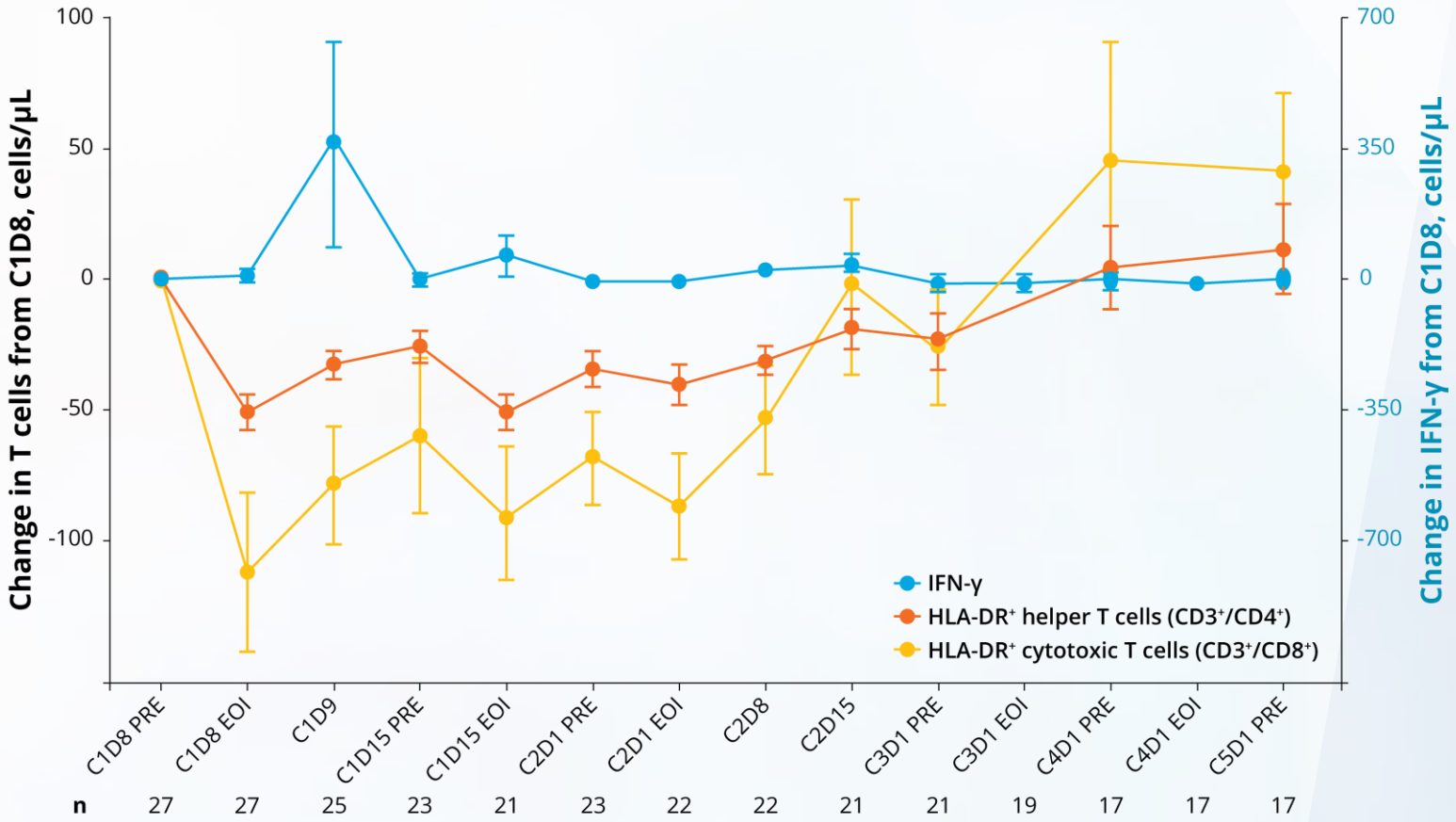
Pharmacokinetics

- Lonca exposure showed a dose-dependent increase during the first 2 cycles
- There was low immunogenicity with no cases of postdose Lonca antidrug antibodies

Biomarker

- Lonca + Glofit produced a similar $CD4^+/CD8^+$ T-cell margination and activation pattern as previously reported for Glofit monotherapy[1]
- Immune activation was evidenced by a transient increase of IFN-γ and an increase in monocytes and NK cells

Patterns of helper T cells, cytotoxic T cells, and IFN-γ



Data cutoff: April 14, 2025.

C, cycle; D, day; EOI, end of infusion; Glofit, glofitamab; HLA-DR, human leukocyte antigen – DR isotype; Lonca, loncastuximab tesirine; IL-6, interleukin-6; IFN-γ, interferon gamma; PRE, pretreatment.

1. Bröske A-M, et al. *Blood Adv*. 2022;6(3):1025-1037.

CONCLUSIONS

- In this multinational (US and EU), phase 1b trial, loncastuximab tesirine + glofitamab demonstrated a manageable safety profile and early clinical efficacy in patients with 2L+ LBCL
  - The ORR was 93.3% (28/30), and the CR rate was 86.7% (26/30)
    - For most patients who have ended treatment, response was sustained beyond the end of treatment
  - The median time to first response (CR or PR) was 42.0 days across doses
    - Median time to first CR was 42 days in the Lonca 150 µg/kg starting dose[a] and 80 days in the 120µg/kg starting dose[a] group
  - No grade 5 TEAEs occurred, and rates of CRS and ICANS were low
    - Grade 3 CRS occurred in 1 patient (2.4%; 120 µg/kg starting dose[a] group); no grade 4 CRS was observed
    - No grade ≥3 ICANS events were observed
- Based on the shorter time to CR and lower rates of CRS in the Lonca 150 µg/kg starting dose[a] group versus the 120 µg/kg starting dose[a] group, enrollment is expanding in the Lonca 150 µg/kg starting dose[a] group to include additional patients

CR, complete response; CRS, cytokine-release syndrome; DLBCL, diffuse large B-cell lymphoma; Glofit, glofitamab; ICANS, immune-effector cell–associated neurotoxicity syndrome; LBCL, large B-cell lymphoma; Lonca, loncastuximab tesirine; ORR, overall response rate; PR, partial response; R/R, relapsed/refractory; TEAE, treatment-emergent adverse event.

[a]When the starting dose of Lonca is 120 µg/kg or 150 µg/kg, the dose will be reduced to 75 µg/kg for Cycles ≥3.

THANK YOU

- The authors would like to thank all the participating patients and their families, study sites, study co-investigators, and research coordinators.
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