and non-relapse mortality (NRM) did not significantly differ between the two therapies (Figure 1). At one and two years, PFS was 67.1% and 60.9% after CAR T versus 73.1% and 62.6% after auto-HSCT ($p = 0.064$), respectively; OS was 82.6% and 72.5% after CAR T versus 87.1% and 79.3% after auto-HSCT ($p = 0.14$), respectively; and NRM was 2.6% and 2.6% after CAR T versus 4.8% and 5.5% after auto-HSCT ($p = 0.248$), respectively.
In a subgroup analysis, outcomes for axi-cel recipients were comparable to those of auto-HSCT patients, with no significant differences in RI, PFS, OS, or NRM.
Conclusions: Auto-HSCT remains a valid treatment option for selected fit, transplant-eligible LBCL patients achieving CR after salvage therapy. While improving access to CAR T-cell therapy should remain a priority, discussing the possibility of auto-HSCT in this specific subset of patients seems reasonable.

Keywords: cellular therapies; aggressive B-cell non-Hodgkin lymphoma; stem cell transplant

No potential sources of conflict of interest.

78 | 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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Introduction: Loncastuximab tesirine (Lonca), a CD19-targeted, antibody–drug conjugate, and glofitamab (Glofit), a CD20×CD3 bispecific engager, are FDA/EMA-approved for R/R DLBCL as ≥ 3rd line therapy. LOTIS-7 (NCT04970901), an open-label, multicenter, phase 1b trial, evaluates Lonca+Glofit in R/R DLBCL. Eligible patients (pts) have histologically confirmed R/R B-NHL (DLBCL, FL, and MZL) and ≥ 1 prior systemic therapy. Primary objective is to characterize safety/tolerability of Lonca+Glofit and identify maximum tolerated/recommended expansion dose. Secondary objectives evaluate antitumor effects, pharmacokinetics (PK), and anti-drug antibodies (ADAs). Exploratory objective investigates correlations between tumor tissue/biomarkers/PK and clinical activity.

Methods: LOTIS-7 evaluated Lonca at 90, 120, and 150 μg/kg (part 1, dose escalation) and 120 or 150 μg/kg (part 2, dose expansion) Q3W for a fixed duration ≤ 8 cycles; doses 120 and 150 μg/kg were reduced to 75 μg/kg for cycles ≥ 3 per label. Glofit was dosed 30 mg Q3W with step-up dosing ≤ 12 cycles. PK of Lonca and its analytes were assessed using parameters from a non-compartmental analysis. ADAs were evaluated with a tiered strategy. Circulating immune cells/cytokines were assessed longitudinally. Immune phenotypes were analyzed by flow cytometry, and plasma cytokines by multiplex immunoassay.

Results: As of 17Jan2025, 31 pts received ≥ 1 Lonca dose. Median age was 73; 45.2% had DLBCL, 16.1% HGBCL, 61.3% received ≥ 2 prior therapies, and 19.4% had prior CAR-T therapy. A subset was refractory to primary (45.2%) and/or last (61.3%) therapy. Most common TEAE grade (Gr) ≥ 3 was neutropenia (32.3%). Gr 1/2 instances of CRS (29.0%/9.7%) and ICANS (0%/6.5%) were observed, but no Gr ≥ 3. Gr 3/4 TEAEs of interest included generalized edema, pericardial effusion, photosensitivity reaction, rash, sepsis, and pneumonia (each 3.2%). In the efficacy evaluable population ORR was 95.5% (21/22), CRR was 90.9% (20/22), and median DOR was not reached (Table 1). Of responders ($n = 21$), 20 remained in response (CR). Lonca+Glofit versus Lonca showed comparable exposure (AUC_{last}) but lower maximum concentration (C_{max}), with moderate to high PK variability (cycles 1/2). Only 4.7% of pts had ADAs. As of 4Oct2024, T-cell margination was appreciable, circulating activated $CD4^+$ and $CD8^+$ T cells increased during treatment. Amount of circulating monocytes and NK cells were also modulated and showed a trend of increase over time. Cytokine profiles indicated immune activation; when present, IL-6 induction was relatively modest in most pts.

Table 1. Best overall response and duration of response

Efficacy measures	120 μg/kg	150 μg/kg	Total
Best overall response[a]	(n=11)	(n=11)	(n=22)
ORR (CR+PR), n (%) [95% CI]	10 (90.9) [58.7-99.8]	11 (100.0) [71.5-100]	21 (95.5) [77.2-99.9]
CR*, n % [95% CI]	10 (90.9) [58.7-99.8]	10 (90.9) [58.7-99.8]	20 (90.9) [70.8-98.9]
PR, n (%)	0	1(9.1)	1(4.5)
SD, n (%)	1 (9.1)	0 (0)	1 (4.5)
PD, n (%)	0 (0)	0 (0)	0 (0)
Duration of response[b]	(n=10)	(n=11)	(n=21)
Event, n (%)	0 (0)	1 (9.1)	1 (4.8)
Median	NE	NE	NE
Probability to maintain event free for 6 months (95% CI)	100 (100-100)	87.5 (38.7-98.1)	92.9 (59.1-99.0)
Probability to maintain event free for 12 months (95% CI)	100 (100-100)	87.5 (38.7-98.1)	92.9 (59.1-99.0)

CR, complete response; NE, not estimable; ORR, overall response rate; PD, progressive disease; PR, partial response, SD, stable disease.

*A total of 4 pts (2 each at 120 μg/kg and 150 μg/kg) had their first CR assessment within 3 weeks (1 treatment cycle) after the data cut (17Jan2025) and are included as CRs in the table.

[a]The efficacy evaluable population (n=22) included all patients who received ≥1 dose of study drug with a valid baseline and ≥1 valid postbaseline disease assessment. Patients who do not have a postbaseline assessment owing to early clinical progression or death were also included.

[b]In the efficacy population, duration of response and probability to maintain event free was evaluated in responders (n=21), including all patients who had a best response of PR or CR.

Conclusions: Lonca+Glofit in R/R B-NHL showed a manageable safety profile consistent with each drug and encouraging efficacy in heavily pretreated aggressive lymphoma pts. Lonca+Glofit induced T-cell margination, and sustained circulating $CD4^+$ and $CD8^+$ T-cell activation was noted. Results support that Lonca complements Glofit's mechanism and provides additive efficacy. Updated data will be presented.

Research funding declaration: ADC Therapeutics SA and Sobi; medical writing: Citrus Health Group.

Encore Abstract: EHA 2025

Keywords: aggressive B-cell non-Hodgkin lymphoma; molecular targeted therapies; combination therapies

Potential sources of conflict of interest:

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Consultant or advisory role: Consultant: AbbVie, ADC Therapeutics SA, Genentech, Genmab, Lilly, Novartis, and Regeneron.

Other remuneration: Research funding: AbbVie, ADC Therapeutics SA, BeiGene, and Genmab. Immediate family member has served on the advisory boards: Anheart, Fore, Rigel, and Servier. Speaker: Medscape.

C. Okada

Other remuneration: Research funding: ADC Therapeutics SA, Genentech, Genmab A/S, Ono Pharmaceutical, and Pfizer.

G. Crochet

Other remuneration: Honorary, consultancy, or travel grant: AbbVie, Gilead, Roche, and Sobi.

E. C. Ayers

Consultant or advisory role: Consultancy or advisory role: AbbVie, ADC Therapeutics SA, and Genentech.

Other remuneration: Research funding: AbbVie and Loxo Oncology/Lilly.

P. F. Caimi

Other remuneration: Advisory committees: ADC Therapeutics SA, Autolus, BMS, Genentech, Genmab, Novartis, and Synthekine.

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Consultant or advisory role: Consultant: AbGenomics, ADC Therapeutics SA, Celgene Corporation, Incyte Corporation, Janssen R&D, Omeros, Pharmacyclics, TeneoBio, and Verastem. Speakers' bureau: AstraZeneca, BeiGene, and Sanofi Genzyme.

Other remuneration: Research support: Astellas Pharma, Spectrum Pharmaceuticals, and Takeda.

J. Depaus

Consultant or advisory role: Consultancy or advisory role: Janssen/J&J Innovative Medicine, Novartis AG, and Takeda Pharmaceutical Company Limited.

E. Derenzini

Consultant or advisory role: Advisory board: AbbVie, AstraZeneca, BeiGene, and Roche.

Other remuneration: Research funding: ADC Therapeutics SA and Takeda.

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79 | OUTCOME OF AUTOLOGOUS AND ALLOGENIC HCT IN BURKITT LYMPHOMA: AN EBMT REGISTRY ANALYSIS

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Introduction: Hematopoietic stem cell transplantation (HCT), either autologous (auto-HCT) or allogeneic (allo-HCT), is generally not performed as first-line consolidation in Burkitt lymphoma (BL). Relapsed or refractory (R/R) BL has a poor prognosis, often demonstrating resistance to salvage therapy. In general, Auto-HCT is applied to deepen remission or as a bridge to allo-HCT, with the latter recommended for second or later complete remission (CR ≥ 2). However, existing data on the role of HCT in BL are limited and not up-to-date.

Methods: Patients (pts) meeting the following criteria in the EBMT registry were included: Age ≥ 18y, diagnosis of BL, and history of auto- or allo-HCT from 2000 to 2022 in 1st (CR1/PR1) or 2nd (CR2/ PR2) remission or with no response. To improve comparability, a propensity score-matched analysis was conducted based on performance status, age, and year of transplantation.

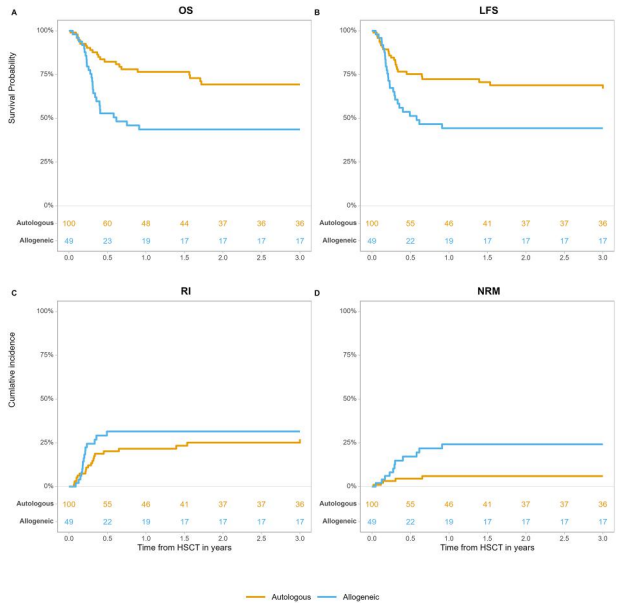
Results: 1200 pts were included, 958 with auto-HCT (med. 42y, 71% male, 30% Karnofsky index (KI) < 90, med. time between diagnosis and HCT 7.0 m) and 242 with allo-HCT (med. 37.6 y, 71% male, 44% KI < 90, med. time between diagnosis and HCT 9.4 m). Median follow up was 5y.

HCT as consolidation in CR1/PR1 resulted in 1y-OS for allo/auto of 63.7%/82.2%, relapse incidence (RI) for allo/auto of 25%/19.9%, and non-relapse mortality (NRM) for allo/auto of 14.3%/2.7%. Inferiority of allo-HCT in CR1/PR1 was validated by propensity-score analysis of 54 allo-HCT and 161 pair-matched pts with auto-HCT: OS HR: 2.61 (95% CI: 1.5–4.53; $p = 0.001$); LFS HR: 2.21 (95% CI: 1.32–3.69; $p = 0.003$); NRM HR: 4.1 (95% CI: 1.81–9.3; $p = 0.001$).

HCT in CR2/PR2 resulted in 1y-OS for allo/auto of 42.1%/76.4%, RI for allo/auto of 38.1%/25.6%, and NRM for allo/auto of 24.4%/5.7%. Propensity-score analysis of 49 allo-HCT and 100 pair-matched pts with auto-HCT confirmed inferiority of allo-HCT for CR2/PR2 for OS HR: 2.01 (95% CI: 1.11–3.65; $p = 0.021$), NRM HR: 4.31 (95% CI: 1.59–11.65; $p = 0.004$) and by trend for LFS HR: 1.69 (95% CI: 0.94–3.03; $p = 0.081$) (Figure). In non-responders no sign, difference was observed in the pair-matched analysis.

Conclusion: This registry analysis of HCT in BL supports less toxic auto-HCT rather than allo-HCT, if indicated in CR1/PR1, but in particularly in chemosensitive 2nd remission (CR2/PR2), if an optimal autologous stem cell product is available. This register analysis has several limitations including incomplete baseline data for viral status, leukemic & CNS-manifestations or type of frontline or salvage treatment, however due to its size and also the lack of published data of HCT in BL, it could be of help.

Figure: Propensity-score comparison of Allo- versus Auto-HCT at CR2/PR2: (A) 2y-OS allo/auto: 43.6%/69.3%; HR: 2.01 (95% CI: 1.11–3.65; $p = 0.021$), (B) 2y-LFS: 44.3%/68.9%; HR: 1.69 (95% CI: 0.94–3.03; $p = 0.081$), (C) 2y-RI: 31.5%/25.1%; HR: 1.11 (95% CI: 0.54–2.27; $p = 0.783$), (D) 2y-NRM: 24.2%/6%; HR: 4.31 (95% CI: 1.59–11.65; $p = 0.004$).



Keyword: aggressive B-cell non-Hodgkin lymphoma

No potential sources of conflict of interest.

SESSION 14: BIOLOGY OF FOLLICULAR LYMPHOMA

80 | WHOLE GENOME SEQUENCING OF SERIAL FL BIOPSIES FROM 96 PATIENTS WITH FOLLICULAR LYMPHOMA REVEAL TREATMENT-SPECIFIC PATTERNS OF TUMOUR EVOLUTION

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