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Safety and Efficacy of Polatuzumab Vedotin plus Glofitamab as bridging therapy prior to Talicabtagene autoleucel for relapsed/ refractory B-cell lymphoma

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Introduction

- Effective bridging therapy (BT) is critical to control disease while awaiting CAR-T infusion in relapsed/refractory (R/R) B-cell lymphomas (BCL).
- Traditional BT options offer limited disease control.
- Polatuzumab vedotin (Pola) and Glofitamab (Glofit), both active in R/R DLBCL, may offer synergistic benefit when combined.
- Early-phase data suggest Pola-Glofit is safe and efficacious (Hutchings M et al., ASH 2024).

Aim

To evaluate the safety and efficacy of using Pola-Glofit as bridging therapy in R/R BCL patients undergoing anti-CD19 CAR-T cell therapy.

Method

- Study type: Retrospective, single-center
- Inclusion: Patients with R/R BCL, aged ≥15 years, who received Pola-Glofit as BT prior to Talicabtagene autoleucel (Tali-cel) infusion.
- Treatment regimen:
  Cycle 1: Obinutuzumab 1000 mg or Rituximab 375 mg/m² on Day 1; Polatuzumab vedotin 1.8 mg/kg on Day 2; Glofitamab 2.5 mg on Day 8 and 10 mg on Day 15 of a 21-day cycle.

  Subsequent cycles (Cycle ≥2): Polatuzumab 1.8 mg/kg plus Glofitamab 10 mg administered on Day 1 of each 21-day cycle.
- Conditioning chemotherapy: Flu-Cy over 3 days prior to CAR-T infusion.
- CAR-T therapy: Single infusion of Tali-cel at a target dose of ≥5 × 10^6 cells/kg.
- Maintenance therapy post-CAR-T infusion was permitted.
- Outcome assessments: Overall response rate (ORR), complete remission (CR), toxicity profile, cytokine release syndrome (CRS), immune effector cell-associated neurotoxicity syndrome (ICANS), progression-free survival (PFS), and overall survival (OS).

Results

At the time of data abstraction (January 30, 2025), 43 patients underwent leukapheresis and 14 received Pola+Glofit as BT. Here in, we present the updated results of these patients.

Table 1. Baseline demographic and patient characteristics

Characteristic	All patients N=14
Median age, years	55
(range)	(21-72)
Female, %	57%
Diagnosis, n (%)	
DLBCL	9 (64%)
PMBCL	3 (21%)
tFL	1 (7%)
HG B-NHL	1 (7%)
Prior lines of therapy, median	2
(range)	(1-5)
Bulky disease, %	50%
BT cycles, median	1
(range)	(1-3)
Vein-to-vein time in days, median	59
(range)	(40-118)

Table 2. Efficacy analysis post-BT and CAR T-cell therapy

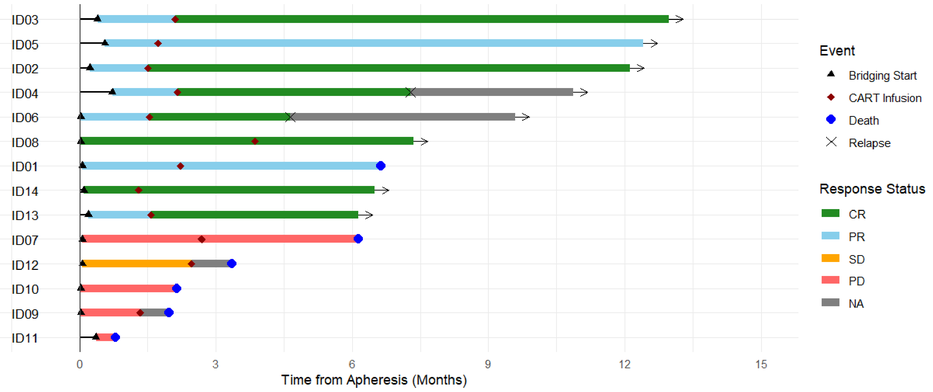
Response assessment, n (%)	Post Pola-Glofit (N=14)	Post Tali-cel (N=12)
Overall response rate	9 (64%)	9 (75%)
Complete response (CR)	2 (14%)	7 (58%)
Partial response (PR)	7 (50%)	2 (17%)
Stable disease (SD)	1 (7%)	0
Progressive disease (PD)	4 (29%)	1 (8%)
Not available (NA)	-	2 (14%)

Safety analysis post BT - CRS occurred in 36% (Gr 1: 29%, Gr 2: 7%) with no neurological events. All managed with tocilizumab; no ICU admissions or treatment-related deaths. Two deaths due to PD prior to receiving CAR T-cell therapy.

Table 3. Safety analysis post Tali-cel

Toxicity assessment, n (%)	Post Tali-cel (N=12)
Cytokine release syndrome, gr 3-4	1 (8%)
IEC-HS	3 (25%)
ICANS, grade 1-2	1 (8%)
Cytopenia, grade 3-4	12 (100%)
Hypogammaglobulinemia	6 (50%)

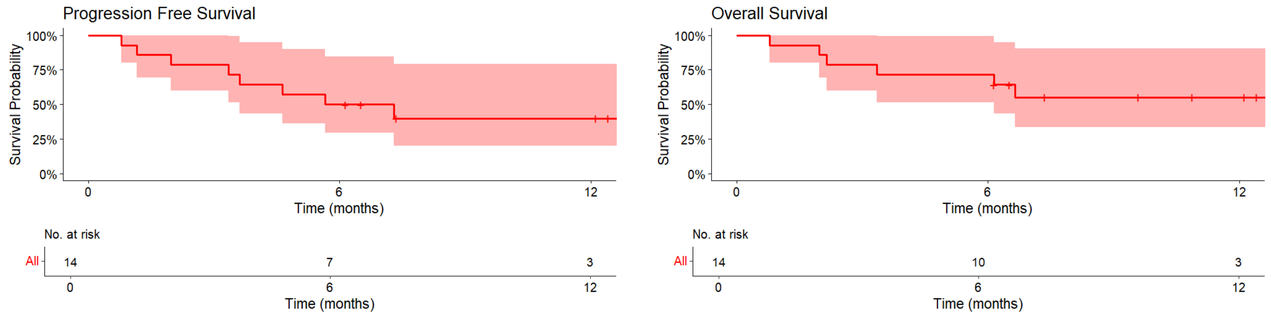
Figure 1. Pola-Glofit Bridging Cohort: Longitudinal Response, Relapse, and Survival



Response overview:

- 10 out of 12 patients who received Tali-cel infusion underwent day-28 response assessment.
- Two patients died (1 due to sepsis, 1 due to sepsis with co-existing ICANS).
- After a median follow-up of 10.8 months, 6 out of 9 responders remain disease free with ongoing B-cell aplasia.
- None of the patients who had progression post BT achieved any response post CAR-T infusion.

Figure 2. Kaplan Meier curves showing Progression free survival and Overall Survival



Survival analysis	Median (95% CI)	12-month (95% CI)
Progression free survival	6.5 months (3.6-NR)	40% (95%CI; 20-79)
Overall survival	NR (6.1 months-NR)	55% (95%CI; 34-90)

Conclusions

- Pola+Glofit as bridging therapy in R/R BCL demonstrated high response rates, even after a single cycle, with sustained responses following Tali-cel infusion.
- The combination showed favourable safety profile with manageable toxicity.

References

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