Comparison of Bispecific T-Cell Engager Antibodies and CAR-T Therapies for Patients with Relapsed/Refractory Diffuse Large B-Cell Lymphoma: A Systematic Review and Pooled Survival Analysis

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Background and Aims

- Diffuse large B-cell lymphoma (DLBCL) is the most common subtype of non-Hodgkin lymphoma.
- Chimeric antigen receptor T-cell (CAR-T) therapies, including axicabtagene ciloleucel (axi-cel), lisocabtagene maraleucel (liso-cel), and tisagenlecleucel (tisa-cel), as well as bispecific T-cell engager antibodies (TCEAbs) such as glofitamab, epcoritamab, and odronextamab are approved for relapsed or refractory (r/r) DLBCL.
- CAR-T therapies offer durable remission but is limited by cost, toxicity, and manufacturing time, whereas TCEAbs are off-the-shelf with favorable safety.
- **This study aims to synthesize evidence from clinical trials and real-world data to compare the outcomes of TCEAbs and CAR-T therapies in r/r DLBCL patients.**

***Table 1**. Comparison of CAR-T therapies and TCEAbs.*

Feature	CAR-T therapies	TCEAbs
Cost	High	Lower than CAR-T
Safety	High CRS and neurotoxicity	Favorable safety
Administration	Personalized cell therapy	Off-the-shelf
Efficacy	Potential durable remission	Effective; long-term data limited

Methods

- This systematic review and pooled survival analysis evaluated the efficacy of TCEAbs and CAR-T therapies in patients with r/r DLBCL.
- Eligible studies published up to May 29, 2025, were identified from PubMed and Embase. Inclusion criteria required patients with r/r DLBCL who had received at least two prior lines of systemic therapy.
- Kaplan-Meier curves for overall survival (OS) and progression-free survival (PFS) were extracted and reconstructed as individual patient data to perform pooled survival analyses by treatment type.
- Reconstructed survival curves were analyzed using standard statistical methods to allow indirect comparisons across studies.

Results

- Nine studies including 1,445 patients met the inclusion criteria, comprising two retrospective cohort study and seven clinical trials.
- The analysis revealed substantial heterogeneity across studies. The between-study variance (τ^2) was 0.31, indicating notable differences in true effect sizes. Approximately 88.8% of the total variation was due to real differences between studies (I^2 = 88.8%), and the heterogeneity was confirmed as high (H = 2.99), suggesting that variability in treatment effects cannot be attributed to chance alone.
- Complete response (CR) rates and overall response rates (ORR) for each therapy are summarized in **Table 2**. Axi-cel showed the highest CR (58.4%) and ORR (81.0%), followed by liso-cel (CR 56.7%, ORR 75.4%), tisa-cel (CR 41.4%, ORR 61.6%), epcoritamab (CR 40.0%, ORR 61.7%), glofitamab (CR 39.0%, ORR 52.0%), and odronextamab (CR 31.5%, ORR 52.0%).

***Table 2**. CR rates and ORR across clinical trials of TCEAbs and CAR-T therapies in r/r DLBCL.*

	Glofitamab	Epcoritamab	Odronextamab	Axi-cel	Tisa-cel	Liso-cel
CR rates	39.0%	40.0%	31.5%	58.4%	41.1%	56.7%
ORR	52.0%	61.7%	52.0%	81.0%	61.6%	75.4%

- Across the six therapies, liso-cel demonstrated the highest 2-year OS (53.5%) and PFS (42.4%), followed closely by axi-cel with OS of 52.4% and PFS of 40.7%. However, the survival curves for liso-cel showed a steeper decline beyond two years, whereas axi-cel maintained a more stable long-term survival. Other therapies demonstrated lower survival rates at two years (OS: 31.7–44.3%; PFS: 20.8–26.7%) **(Figures 1-2)**.
- Cox proportional hazards analysis using liso-cel as the reference showed that axi-cel had a comparable risk of death (HR 0.96, 95% CI 0.75–1.22). Epcoritamab had a modestly higher risk that was marginally significant (HR 1.29, 95% CI 1.00–1.66), whereas glofitamab, tisa-cel, and odronextamab had even greater risks (HR 1.49–1.78) **(Figure 3)**.

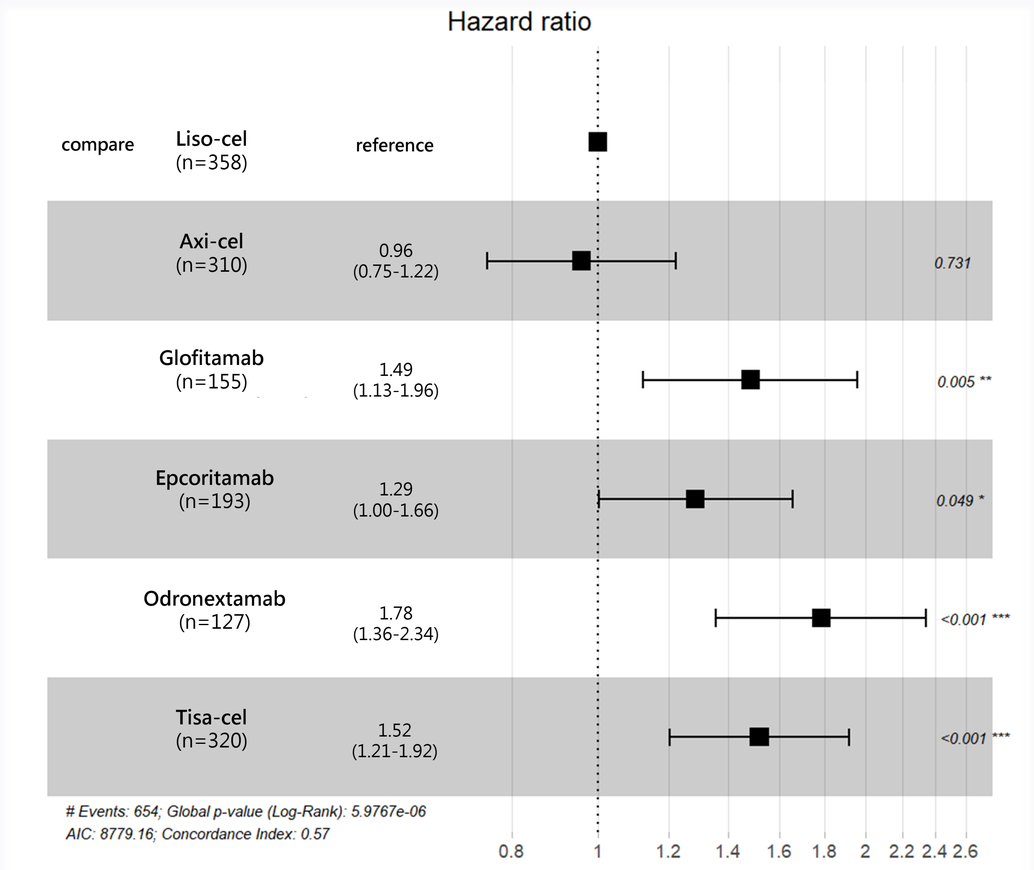

***Figure 3**. Hazard ratios for OS.*

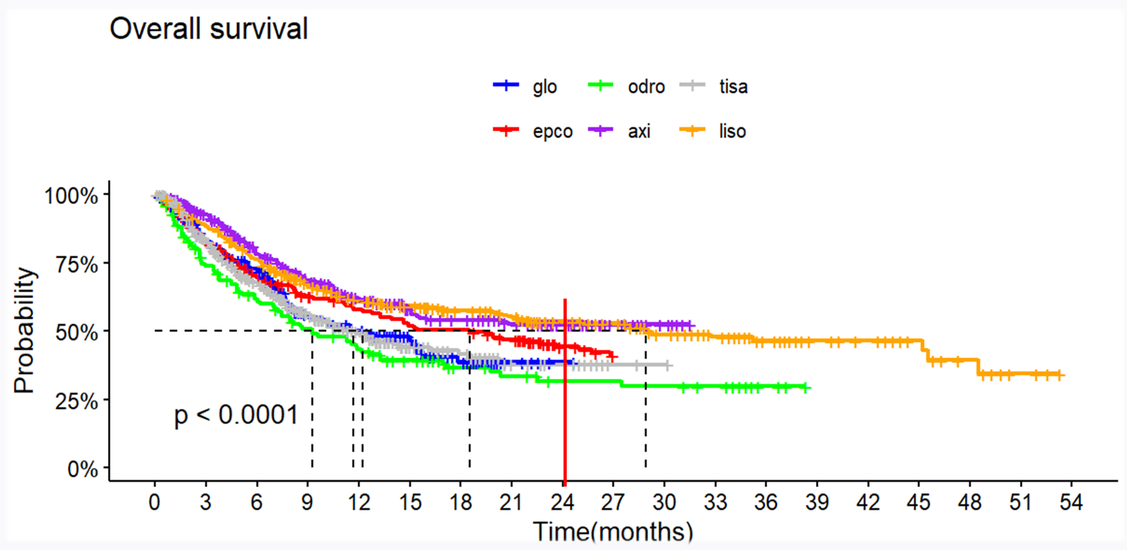

***Figure 1**. Kaplan–Meier curves for OS with CAR-T and TCEAbs.*

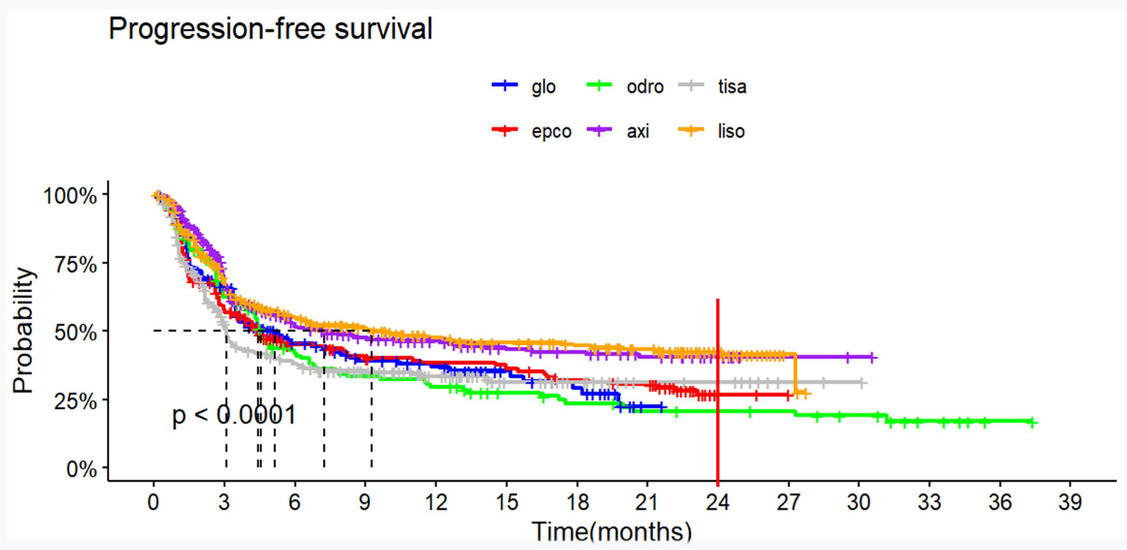

***Figure 2**. Kaplan–Meier curves for PFS with CAR-T and TCEAbs.*

Conclusions

- This comprehensive synthesis demonstrates that axi-cel showed the highest CR and ORR, followed by liso-cel, tisa-cel, epcoritamab, glofitamab, and odronextamab.
- Liso-cel and axi-cel achieved the most favorable 2-year OS and PFS, with comparable mortality risks (HR 0.96, 95% CI 0.75–1.22). Glofitamab, tisa-cel, and odronextamab were associated with higher mortality risks (HR 1.49–1.78) compared to liso-cel.
- Given the substantially higher cost of CAR-T therapies, further economic evaluations are warranted to assess cost-effectiveness compared with TCEAbs in real-world clinical practice.

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