COMPARATIVE EFFICACY AND SAFETY OF APPROVED THERAPIES IN ≥3L RELAPSED/REFRACTORY LARGE B-CELL LYMPHOMA: A BAYESIAN NETWORK META-ANALYSIS

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INTRODUCTION

Multiple novel agents are approved for ≥3L relapsed/refractory large B-cell lymphoma, including CAR-T cell products (axi-cel, liso-cel, tisa-cel), bispecific antibodies (epcoritamab, glofitamab, mosunetuzumab), antibody-drug conjugates (pola-BR, loncastuximab tesirine), and others (tafasitamab + lenalidomide, selinexor). No head-to-head trials exist. We performed a Bayesian network meta-analysis to rank these agents on complete response (CR) rate and safety.

AIM

To rank approved ≥3L LBCL therapies, via Bayesian network meta-analysis, on:

- Complete response (CR) rate
- Grade ≥3 cytokine release syndrome (CRS)
- Grade ≥3 neurotoxicity

— across CAR-T, bispecific antibody, ADC, and other agent classes.

METHOD

- Systematic searches of MEDLINE, Embase, Cochrane CENTRAL, and ASH/ASCO/EHA proceedings through March 2026 identified prospective trials
- 9 of 10 studies lacked a control arm — used an arm-based parametrization with synthetic BR comparators anchored to the GO29365 BR CR rate (17.5%)
- Bayesian random-effects model (binomial likelihood, logit link; 4 chains × 50,000 iterations, 20,000 burn-in)
- Convergence confirmed by Gelman-Rubin $\hat{R} < 1.05$
- Rankings derived from SUCRA (surface under the cumulative ranking curve); transitivity checked across effect modifiers
- Grade ≥3 CRS/neurotoxicity pooled descriptively (occur only with T cell–engaging agents)

CONCLUSIONS

CAR-T therapies ranked highest for CR rate but with greater toxicity and selection bias.

- Among bispecific antibodies, epcoritamab ranked most favorable for combined efficacy and safety (SUCRA 58.3% vs 56.1% glofitamab, 47.8% mosunetuzumab)
- Near-disconnected, star-topology network with predominantly single-arm data — results carry very low certainty (CINeMA) and warrant cautious interpretation

Time-to-event analyses (PFS/OS) are needed to complement response-rate rankings.

RESULTS

Ten studies (1,258 patients; 11 nodes) were included ($\hat{R}$max=1.04; τ=1.08 — substantial between-study heterogeneity).

CR ranking: Axi-cel ranked first for CR (SUCRA 75.5%; P[rank 1]=29.7%), followed by liso-cel (72.5%), epcoritamab (58.3%), tafasitamab + lenalidomide (58.1%), and pola-BR (57.4%). No pairwise comparison reached significance (e.g., axi-cel vs BR: OR 6.09, 95% CrI 0.16–207.7) — wide intervals expected given indirect comparisons across single-arm data.

Safety: CAR-T CR rates were derived from manufactured-to-treat populations — 22–31% of enrolled patients never received infusion — inflating CR relative to off-the-shelf agents. Pooled grade ≥3 CRS was 12% with CAR-T vs 3% with bispecific antibodies; neurotoxicity was 17% vs 2%, respectively. Sensitivity analyses excluding mosunetuzumab and L-MIND produced similar rankings.

Figure 1&2 and Table 1 for full rankings →

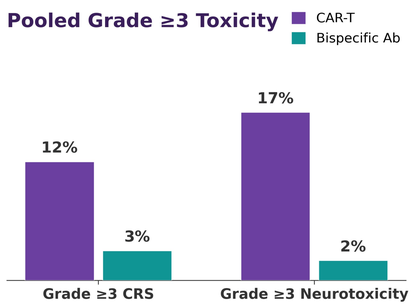
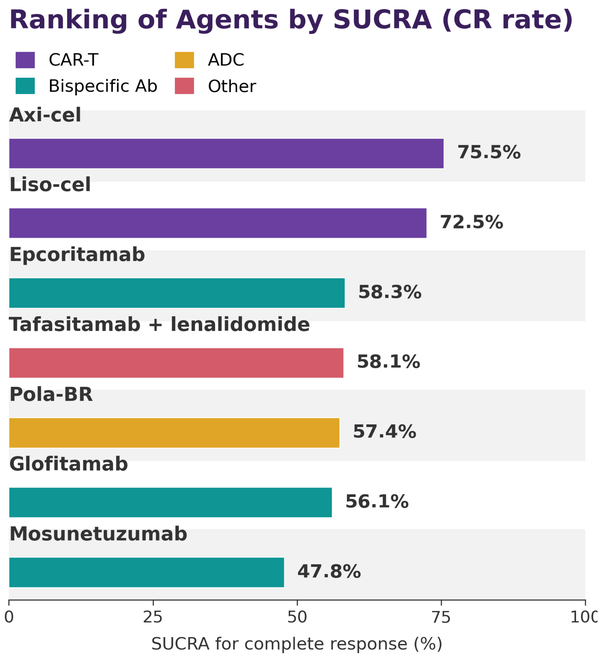


Figure 1. and 2. SUCRA rankings for complete response by agent class, and pooled grade ≥3 CRS/neurotoxicity for CAR-T vs bispecific antibodies.



SUCRA not individually reported for tisa-cel, loncastuximab tesirine, selinexor, or the synthetic BR comparator.

Table 1. All 11 network nodes by drug class. NR = SUCRA not individually reported.

Class	Agent	SUCRA (CR)	Grade ≥3 CRS / Neurotox	Notes
CAR-T	**Axi-cel**	75.5%	12% / 17%	Ranked 1st overall; P(rank 1)=29.7%
CAR-T	**Liso-cel**	72.5%	12% / 17%	—
CAR-T	**Tisa-cel**	NR	12% / 17%	—
Bispecific Ab	**Epcoritamab**	58.3%	3% / 2%	Most favorable bispecific (efficacy + safety)
Bispecific Ab	**Glofitamab**	56.1%	3% / 2%	—
Bispecific Ab	**Mosunetuzumab**	47.8%	3% / 2%	—
ADC	**Pola-BR**	57.4%	—	—
ADC	**Loncastuximab tesirine**	NR	—	—
Other	**Tafasitamab + lenalidomide**	58.1%	—	L-MIND trial
Other	**Selinexor**	NR	—	—
Comparator	**BR (synthetic)**	Ref. (17.5% CR anchor)	—	GO29365 anchor