Therapeutic Strategies After CAR-T Failure in B-Cell Malignancies: A Systematic Review and Network Meta-Analysis

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INTRODUCTION / BACKGROUND

- CAR-T therapy has transformed treatment outcomes in relapsed/refractory B-cell malignancies.
- However, **40% to 60%** of patients eventually relapse or develop resistance.
- Optimal management after CAR-T failure remains undefined.

OBJECTIVE

To evaluate the comparative efficacy and safety of emerging salvage therapeutic strategies following CAR-T relapse in B-cell malignancies using a systematic review and network meta-analysis.

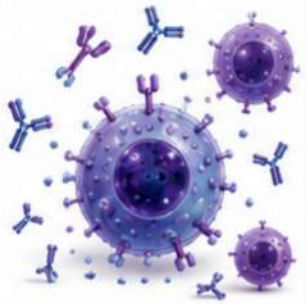
METHODS

Systematic search of PubMed, Embase, Scopus, and Cochrane Library

Studies evaluating post-CAR-T salvage therapies in B-cell malignancies

Bayesian network meta-analysis performed using Stata 18

Primary end points: CR, OS, and PFS
Safety outcomes: CRS and neurotoxicity



RESULTS

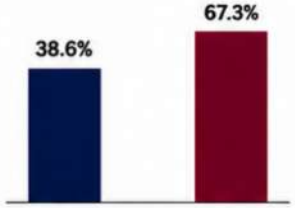
37 STUDIES
4,892 PATIENTS

PATIENT POPULATION

- Relapsed/refractory DLBCL, mantle cell lymphoma, follicular lymphoma, and B-ALL
- Median age range: 49–67 years
- Male predominance in most cohorts (58.4%)

EFFICACY OUTCOMES

Response Rates



Sequential CAR-T in B-ALL

MRD-negative remission
96.0%
(95% CI, 90.4–98.8)

12-month PFS
54.2%
(95% CI, 46.3–61.8)

Overall Survival (12-month OS)

Allogeneic Hematopoietic Cell Transplantation
70.3%
(95% CI, 63.1–77.5)

Conventional Salvage Chemotherapy
34.1%
(95% CI, 27.2–41.9)

SAFETY OUTCOMES

Grade ≥3 Cytokine Release Syndrome (CRS)

Grade ≥3 Neurotoxicity

Hematologic Toxicity
40.0%
(95% CI, 25.0–55.0)
in high-risk DLBCL cohorts

NETWORK META-ANALYSIS FRAMEWORK

KEY TAKEAWAY

A multimodal approach incorporating bispecific antibodies and/or sequential CAR-T followed by consolidative allogeneic transplantation offers the

CONCLUSION

Bispecific antibodies and allogeneic transplantation emerged as the **most effective** post-CAR-T salvage strategies in B-cell malignancies.

Sequential targeted immunotherapy followed by consolidative transplantation demonstrated the **most favorable survival outcomes.**

These findings provide a **clinically actionable framework** for therapeutic sequencing after CAR-T relapse in an area lacking standardized management guidelines.