Clinical Outcomes, Challenges, and Outcomes of Indigenous CD19-Directed CAR T-Cell Therapy for Relapsed/Refractory Diffuse Large B-Cell Lymphoma in India: A Systematic Review

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Introduction

Relapsed/refractory diffuse large B-cell lymphoma (R/R DLBCL) remains a major treatment hurdle in low- and middle-income countries, where high costs and limited infrastructure restrict access to commercial CAR-T cell therapies. Over the past few years, India has introduced multiple indigenous CD19-directed CAR-T platforms. This review synthesizes available evidence from early Indian studies to evaluate clinical outcomes, toxicity profiles, and feasibility of these therapies.

Aim

To systematically synthesize early Indian evidence on indigenously developed CD19-directed CAR-T therapy for relapsed/refractory DLBCL by evaluating clinical efficacy (ORR/CR), safety (CRS/ICANS), operational feasibility (turnaround/follow-up), and cost using peer-reviewed studies and conference abstracts.

Objectives

Primary: Quantify early clinical activity and operational feasibility of indigenous CD19-directed CAR-T for relapsed/refractory DLBCL in India by estimating pooled ORR/CR at first post-infusion assessment and summarizing manufacture/vein-to-vein turnaround across included trials and conference reports.

Secondary:
• Safety: Characterize CRS and ICANS incidence with grade distribution; report grade ≥3 AEs, ICU admission, HLH-like syndromes, treatment-related mortality; summarize use of tocilizumab and steroids.
• Economics: Quantify per-infusion cost of indigenous CAR-T and contextualize against contemporary international programs and note delivery setting (outpatient vs inpatient) when specified.
• Durability (when available): Summarize short-term response durability and any reported PFS/OS landmarks (e.g., 3-6 months).
• Heterogeneity of effect: Explore differences by platform/manufacturing (vector, cell dose), treatment context (bridging, lymphodepletion), disease features (lines of therapy, high-risk biology)

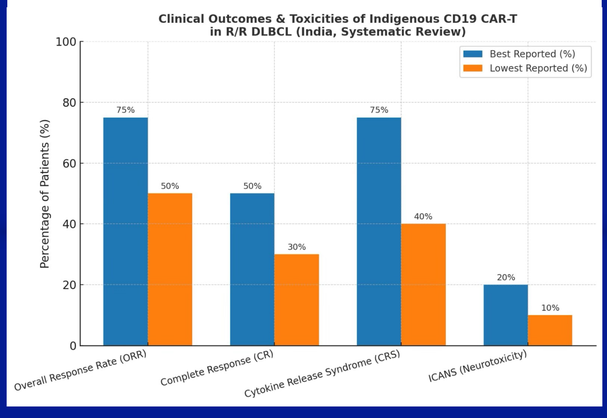
• Implementation metrics: Document manufacturing success/release rates, operational delays, and bottlenecks (apheresis failures, OOS/OOT release criteria).
• Evidence synthesis/quality: Assess risk of bias; where feasible, pool effects (random effects proportions for ORR/CR; HRs for time-to-event when reported) with sensitivity analyses (e.g., excluding abstract only or short follow-up); otherwise provide a structured narrative synthesis.

Methods

We systematically reviewed peer-reviewed publications and conference abstracts reporting outcomes of Indian patients with R/R DLBCL treated with CD19-targeted CAR-T cells. Four studies were included - two clinical trials and two abstract publications. Data on efficacy, outcome and adverse events were extracted and summarized.

Results

A total of 62 patients with R/R DLBCL received CD19 CAR-T therapy across four studies. Median age ranged from 44 to 52 years, and most had received ≥2 prior therapies. Overall response rates (ORR) ranged from 50% to 75%, with complete response (CR) rates between 30% and 50%. Cytokine release syndrome (CRS) occurred in 40%-75%, mostly Grade 1-2, with only one case of Grade ≥3 CRS and one fatal CRS event. Immune effector cell-associated neurotoxicity syndrome (ICANS) occurred in up to 20%; Grade ≥3 ICANS was rare (2 cases). One ICU admission and one HLH-like syndrome were reported. Tocilizumab and steroids were used in most CRS cases. Median turnaround time ranged from 11 to 42 days, and follow-up durations ranged from 146 to 174 days. The median cost per infusion was USD 12,700-35,105, significantly lower than international standards. Limitations included small sample sizes and short follow-up.



Conclusion

These early data from India point to promising clinical activity and acceptable toxicity with indigenously developed CAR-T therapies in R/R DLBCL. The promising outcomes and lower costs suggest these approaches may offer a viable and scalable alternative for LMICs like India. Further long-term studies are needed to confirm durability of response and survival benefits.

References

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SOHO2025