Efficacy of CAR T-Cell Therapy in Relapsed or Refractory Follicular Lymphoma: A Systematic Review and Meta-Analysis

Mohammed Zuber, Shaimaa Elshafie, Lorenzo Villa Zapata
Department of Clinical and Administrative Pharmacy, College of Pharmacy, University of Georgia

CO146

UNIVERSITY OF GEORGIA College of Pharmacy

Background

- Follicular lymphoma (FL) accounts for ~20% of non-Hodgkin lymphomas and is typically indolent but incurable[1]
- Relapsed or refractory FL remains a **major clinical challenge**[2]
- Patients with relapsed/refractory FL often have limited durable treatment options after ≥2 prior lines of therapy[2]
- CAR T-cell therapy is a novel immunotherapy that reprograms T-cells to target CD19-positive lymphoma cells[2]
- Clinical trials show promising outcomes, but **evidence varies across studies**[3,4]
- Long-term outcomes such as **durability of remission and late relapse patterns** are not consistently reported
- A comprehensive synthesis of efficacy outcomes is needed to guide **clinical and policy decision-making**

Objective

- To evaluate the efficacy of CAR T-cell therapy in relapsed/refractory FL
- Outcomes assessed:
  - ✓ Overall Response Rate (ORR);
  - ✓ Complete Response (CR);
  - ✓ Overall Survival (OS);
  - ✓ Progression-Free Survival (PFS)

Methods

- **Study Design:** Systematic review and meta-analysis
- **Data Sources:** PubMed, Embase, ClinicalTrials.gov, conference abstracts of ASH, ASCO & ESMO (last 2 years)
- **Eligibility Criteria:** Adults with relapsed/refractory FL; Studies evaluating the efficacy of CAR T-cell therapy
- **Study Selection and Data Extraction:**
  - ✓ Two reviewers independently screened studies using Rayyan. Relevant data were extracted in Microsoft Excel
- **Risk of Bias:**
  - ✓ ROBINS-I (non-randomized studies)
- **Statistical Analysis:**
  - ✓ Random- effects models (DerSimonian–Laird)
  - ✓ Pooled proportions with 95% CIs
  - ✓ Heterogeneity assessed using I²

Results

Figure 1. Forest Plot for Overall Response Rate Outcome

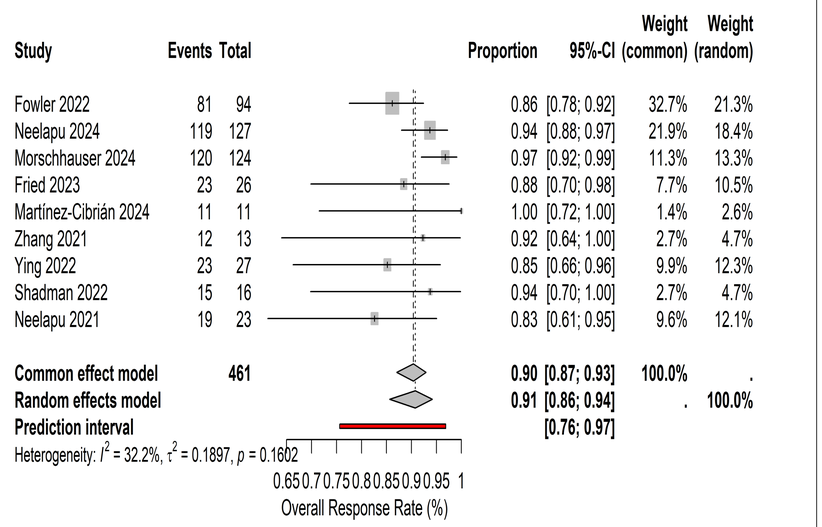
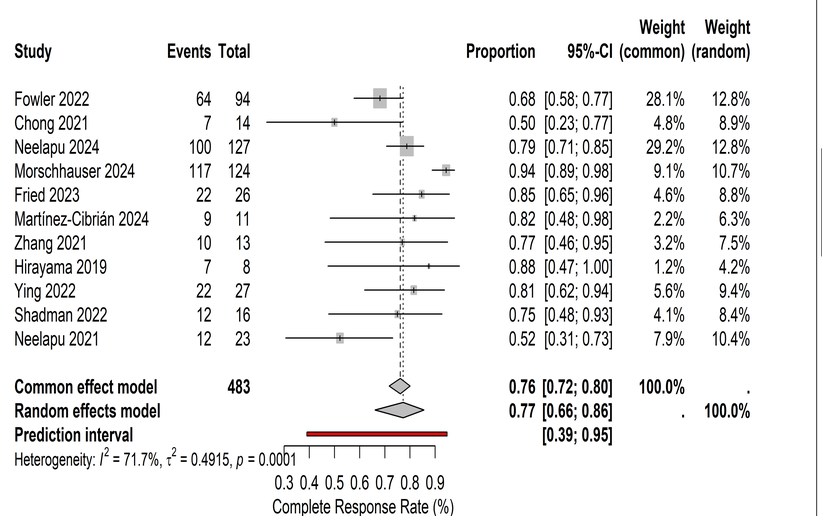


Figure 2. Forest Plot for Complete Response Outcome



- A total of 6,020 records were identified, of which 4,787 remained after duplicate removal; 217 full-text articles were assessed for eligibility, and 11 single-arm trials (27 reports) were included in the final analysis.
- **Study Characteristics**
  - ✓ All studies were single-arm CAR-T trials
  - ✓ Sample size ranged from 8 to 130 patients
  - ✓ CAR-T products: tisagenlecleucel, axicabtagene ciloleucel, lisocabtagene maraleucel, other investigational CAR T-cell therapies
- **Efficacy outcomes:**
  - ✓ ORR ranged from 82.6% to 100%
  - ✓ CR rates frequently ≥ 75%
  - ✓ Median PFS is often not reached
  - ✓ 12-month PFS: 43%–85%
  - ✓ 12-month OS: up to 95%
- **Meta-analysis:**
  - ✓ Pooled ORR- 91% (95% CI: 86%–94%); I² = 32%
  - ✓ Pooled CR: 77% (95% CI: 66%–86%); I² = 71.7%
  - ✓ 1-Year OS-rate 89% (95% CI: 67%–97%); I² = 83%
  - ✓ 1-Year PFS rate 62% (95% CI: 44%–77%); I² = 84.5%
- **Risk of bias assessment**
  - ✓ Nine single-arm trials were assessed, of which four had a moderate risk of bias, and three had a high risk, with key concerns including confounding, selection bias, and reporting bias.

Conclusion

- CAR-T therapy demonstrates **high efficacy** in relapsed/refractory FL
- Pooled ORR: 91%, CR: 77%
- Strong short-term survival outcomes observed
- Future research should focus on:
  - ✓ Long-term outcomes
  - ✓ Real-world effectiveness
  - ✓ Comparative value vs emerging therapies

References

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4. Tisagenlecleucel in Adult Relapsed or Refractory Follicular Lymphoma.New England Journal of Medicine. 2022;386:1967–1977.