EARLY MORTALITY FOLLOWING CAR-T THERAPY IN HEMATOLOGIC MALIGNANCIES: A POPULATION-LEVEL STUDY

7,604 patients
46 studies

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BACKGROUND

- CAR-T therapy has transformed outcomes in relapsed/refractory hematologic malignancies, producing durable remissions in heavily pretreated patients.
- As relapse outcomes improve, non-relapse mortality (NRM) has emerged as an increasingly important limitation to long-term therapeutic benefit.
- Although cytokine release syndrome (CRS) and immune effector cell-associated neurotoxicity syndrome (ICANS) receive substantial clinical attention, accumulating real-world evidence suggests that infection, prolonged cytopenias, impaired immune reconstitution, and other delayed complications may account for a greater proportion of treatment-related deaths.

OBJECTIVE

- Evaluate the incidence, timing, causes and clinical/access determinants of early mortality and overall NRM after CAR-T therapy across hematologic malignancies.

DESIGN AND DATA SOURCES

SEER Medicare | CIBMTR | DESCART-T | NRD | Global Meta-analyses

- Population: >7600 adult and pediatric patients across 46 trials and real-world studies: Lymphoma, MM, ALL

CLINICAL FRAMEWORK

WHY INFECTION PERSISTS AFTER INFUSION

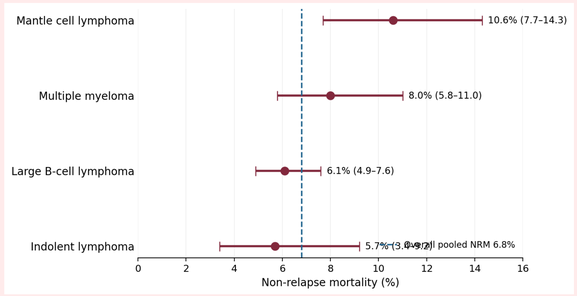
CAR-T infusion → Prolonged cytopenias → B-cell / plasma-cell aplasia → Immune dysfunction → INFECTION

CLINICAL FRAMEWORK

Risk stratification (CAR-HEMATOTOX) | Antimicrobial prophylaxis | Longitudinal infection surveillance | Immune reconstitution monitoring

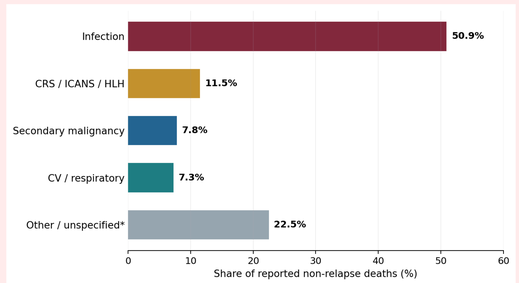
RESULTS: NRM VARIES BY DISEASE

Disease-level pooled estimates with 95% confidence intervals



6.8% Pooled NRM | 10.6% Highest: MCL | 8.0% Multiple myeloma

RESULTS: WHAT DRIVES NON-RELAPSE DEATH?



*"Other/unspecified" is the residual share calculated from reported categories shown here; it is not a separately reported pooled category.

Infection accounted for ~4.4× the share of NRM deaths attributed to CAR-T–specific acute toxicities (50.9% vs 11.5%).

EARLY MORTALITY & HEALTHCARE BURDEN

Older adults experienced more AKI, cardiovascular events, prolonged hospitalization and readmissions across real-world datasets.

30 DAY MORTALITY
5.0–6.7%

Late NRM increasingly includes infection and secondary malignancy.

ACCESS IS PART OF THE OUTCOME

+37.6%
potential increase in CAR-T use

Modeling suggests that reducing travel distance in poor-access U.S. states to the level of better-access states could increase CAR-T utilization from 6.6% to 9.1%.

Geographic and socioeconomic barriers may therefore blunt population-level survival gains.

DISCUSSION & CLINICAL IMPLICATIONS

The toxicity landscape after CAR-T is shifting.

- Acute immune toxicities remain clinically important, but they account for a minority of NRM deaths compared with infection.
- Disease biology, prior therapy, cytopenias, and delayed immune reconstitution likely create sustained vulnerability beyond the initial infusion window.
- Survivorship programs should extend beyond CRS/ICANS monitoring to structured infection prevention, immune recovery assessment, and rapid evaluation of febrile illness.
- Decentralized/shared-care models may improve access while preserving specialized toxicity oversight.

LIMITATIONS & CONCLUSION

Limitations

- Heterogeneous definitions, follow-up, products, indications, and reporting across registries/trials; pooled estimates do not establish causality.

Conclusion

- Infections, not CRS/ICANS, are the leading preventable contributor to NRM after CAR-T. Risk-adapted prophylaxis, longitudinal surveillance, and equitable access should be central to CAR-T survivorship.

REFERENCES

- Key references: Cordas dos Santos DM et al. Nature Medicine. 2024; systematic review/meta-analysis of 7,604 patients. | Muthukrishnan S et al. Blood Advances. 2025; SEER–Medicare CAR-T access analysis. | Data shown are limited to values supported by the submitted abstract and these source publications.