Real-World Insights into Cytokine Release Syndrome Following CAR-T Therapy: A Nationwide Inpatient Analysis by Malignancy Subtype

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Introduction

- **Cytokine release syndrome (CRS)** remains one of the most frequent and clinically significant toxicities associated with **chimeric antigen receptor T-cell (CAR-T) therapy**.
- CRS results from widespread **immune activation** and elevated **cytokine levels**, producing a spectrum of manifestations from mild flu-like symptoms to **life-threatening organ dysfunction**.
- While **clinical trial data** provide important insight into CRS incidence, grading, and management strategies, evidence from **real-world practice** remains limited.
- **Trends and outcomes stratified by underlying hematologic malignancy** are particularly under characterized, highlighting the need for **comprehensive population-level analyses**.

Methods

- We performed a **retrospective cohort analysis** using the **National Inpatient Sample (NIS), 2019–2021**.
- Hospitalizations involving **cytokine release syndrome (CRS) after CAR-T therapy** were identified.
- Patients were **stratified by hematologic malignancy subtype**:
- **Diffuse large B-cell lymphoma (DLBCL)**
- **Multiple myeloma (MM)**
- **Acute lymphoblastic leukemia (ALL)**
- **Follicular lymphoma**
- **Mantle cell lymphoma**
- **Others** (including PMBCL, Burkitt lymphoma, CLL, AML, and additional lymphoid malignancies)
- **Demographic characteristics**, **in-hospital mortality**, **length of stay (LOS)**, **hospitalization costs**, and **toxicity profiles** were compared across subgroups.

Results

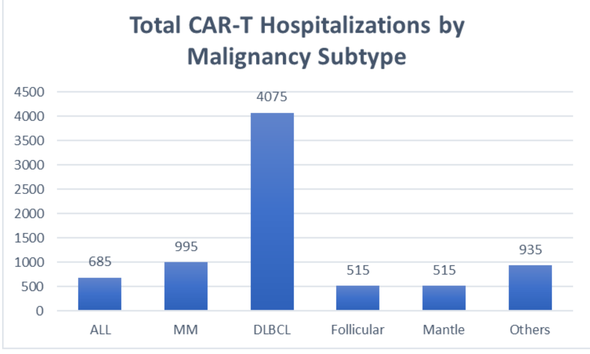


Figure 1. Distribution of CAR-T hospitalizations by malignancy subtype. Diffuse large B-cell lymphoma (DLBCL) accounted for the majority of admissions, followed by multiple myeloma (MM) and acute lymphoblastic leukemia (ALL).

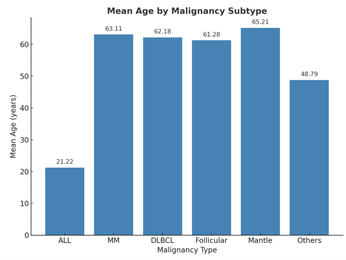


Figure 2. Mean patient age at CAR-T hospitalization by malignancy subtype. Patients with acute lymphoblastic leukemia (ALL) were youngest (21.2 years), while those with mantle cell lymphoma were oldest (65.2 years). Other malignancies clustered around ages 61–63 years.

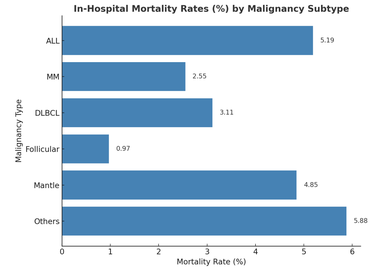


Figure 3. In-hospital mortality rates following CAR-T hospitalization by malignancy subtype. Mortality was highest among "other" malignancies (5.9%) and ALL (5.2%), followed by mantle cell lymphoma (4.9%), while DLBCL, MM, and follicular lymphoma had lower rates.

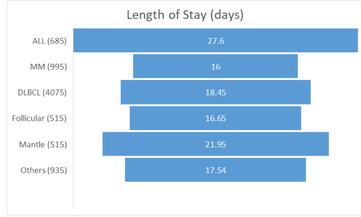
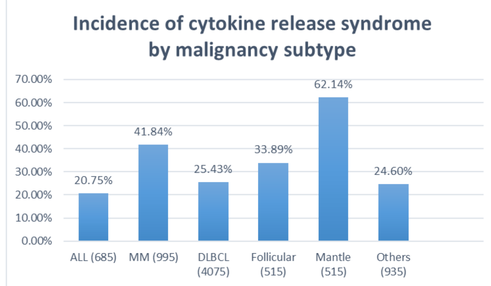
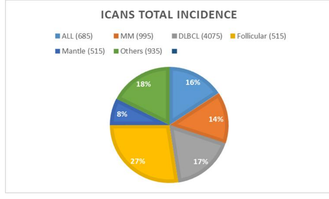
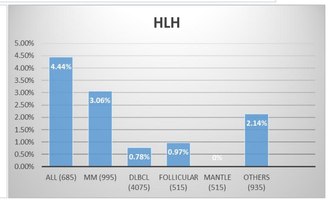


Figure 4. Median length of stay by malignancy subtype. Hospitalization was longest for ALL (27.6 days) and mantle cell lymphoma (22.0 days), compared with shorter stays for MM, follicular lymphoma, and others.







Figures 5,6,7:Incidence of CAR-T–related toxicities (CRS, ICANS, and HLH) across malignancy subtypes

Conclusion

- *This national analysis reveals **marked variation in CRS outcomes** across malignancy subtypes, with **ALL and mantle cell lymphoma showing the highest toxicity and resource use**. These findings underscore the need for **disease-specific risk stratification**, **tailored supportive care**, and **expanded caregiver and housing support** to reduce disparities and ensure **equitable CAR-T access**.*

Acknowledgements and Author Information

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