Inpatient Outcomes of Cytokine Release Syndrome and ICANS Among CAR-T Hospitalizations in the United States: 2022–2023

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INTRODUCTION

- CAR T-cell therapy has reshaped the treatment of relapsed/refractory hematologic malignancies.
- Cytokine release syndrome (CRS) and immune effector cell-associated neurotoxicity syndrome (ICANS) remain its predominant short-term toxicities.
- Severity-stratified outcome data come largely from registration trials and single-center series, where populations are more selected and closely monitored than in routine care.
- National data linking toxicity grade with in-hospital mortality, length of stay and resource use are limited.

AIM & METHODS

To quantify in-hospital mortality, length of stay and total charges across CRS and ICANS severity strata in a nationally representative sample of CAR T-cell hospitalizations.

- **Design.** Retrospective analysis of the HCUP National Inpatient Sample, 2022–2023.
- **Cohort.** Adult hospitalizations with a CAR T-cell administration code.
- **Exposure.** CRS (D89.831–D89.839) and ICANS (G92.00–G92.05) categorized as no recorded code, low (grade 1–2), high (grade 3–5) or unspecified.
- **Outcomes.** In-hospital mortality, length of stay (LOS), total inpatient charges.
- **Analysis.** Discharge weights for national estimates; Pearson χ^2 for mortality; one-way ANOVA for LOS and charges; independent-samples t-test for Elixhauser score.

RESULTS

10,310
weighted CAR T-cell discharges
2022–2023, HCUP NIS

59.7%
with grade-specific CRS coded
Grade 3–5: 3.7% of all discharges

20.9%
with grade-specific ICANS coded
Grade 3–5: 9.1% of all discharges

99.8%
delivered at urban teaching hospitals
CAR-T inpatient care was highly concentrated

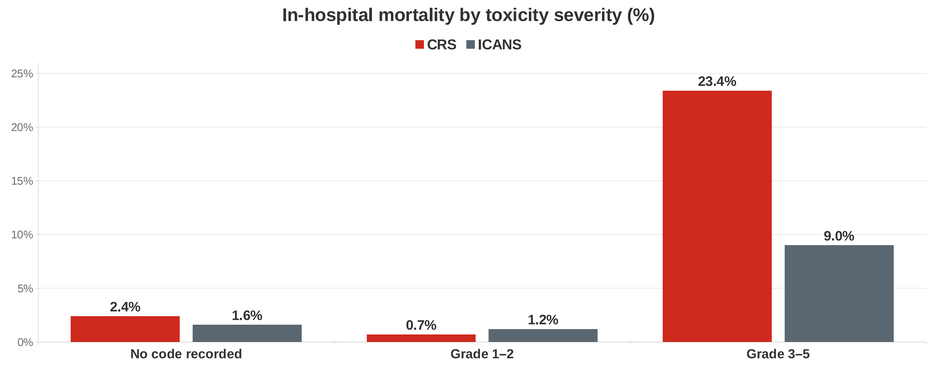
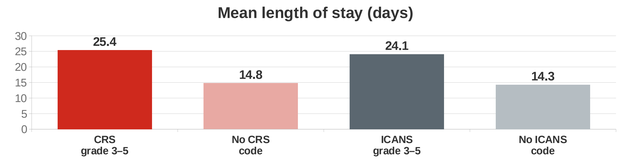
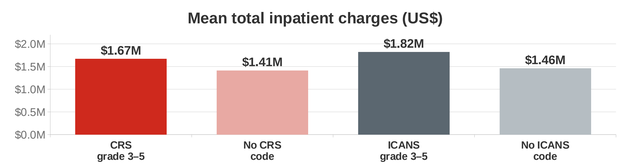


Figure 1. Weighted in-hospital mortality across CRS and ICANS severity strata (Pearson χ^2 = 840.9 for CRS and 213.4 for ICANS; both P < 0.001). Hospitalizations coded with unspecified-grade toxicity are not shown.

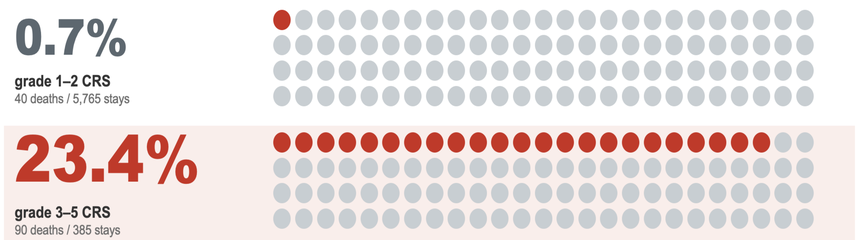




Figures 2–3. Mean LOS was ≈10 days longer with grade 3–5 toxicity than with no recorded toxicity code (overall ANOVA F = 234.2, P < 0.001). Mean charges: $1,668,113 vs $1,413,869 (CRS); $1,820,637 vs $1,458,915 (ICANS).

Comorbidity burden. Elixhauser score 1.87 in survivors vs 2.13 in decedents (mean difference −0.26; 95% CI −0.47 to −0.05; P = 0.015).

Nearly 1 in 4 hospitalizations with grade 3–5 CRS ended in death



Each field = 100 hospitalizations; one marker shown for grade 1–2, which is under one death per 100. χ^2 = 840.9, P < 0.001. ICANS: 9.0% vs 1.2%, χ^2 = 213.4, P < 0.001.

CONCLUSIONS

- High-grade CRS and ICANS were uncommon but were associated with a high-mortality, high-resource inpatient profile after CAR T-cell therapy.
- Mortality was markedly higher with grade 3–5 toxicity than with grade 1–2 toxicity or no recorded toxicity code.
- Grade 3–5 toxicity was associated with ≈10-day longer mean LOS and ≈$250,000–$360,000 higher mean charges versus no recorded toxicity code.
- Decedents had modestly higher Elixhauser comorbidity burden (2.13 vs 1.87; P = 0.015).
- Findings support severity-stratified risk assessment, early recognition and proactive management of CAR T-cell toxicities.

LIMITATIONS

- Toxicity severity was based on discharge coding rather than clinically adjudicated grading; unspecified-grade codes were present.
- The NIS counts hospitalizations, not unique patients; this analysis did not stratify outcomes by CAR T-cell product or underlying malignancy.
- Charges reflect billed amounts, not costs or reimbursement.
- Analyses are cross-sectional and unadjusted; associations cannot establish temporality or causality.

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REFERENCES

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