Real-World Claims Analysis of Toxicity Burden and Inpatient Length of Stay After CAR-T Cell Therapy

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Introduction

Chimeric antigen receptor T-cell (CAR-T) therapy is frequently complicated by cytokine release syndrome (CRS) and immune effector cell-associated neurotoxicity syndrome (ICANS), which significantly impact healthcare utilization[1].

As CAR-T administration scales, claims-based estimates of toxicity patterns and hospitalization burden are essential for resource planning.

Objectives

To characterize the incidence and severity of CRS and ICANS and evaluate inpatient length of stay (LOS) across six CAR-T products within an administrative healthcare claims cohort.

Methods

A retrospective cohort study was conducted using de-identified U.S. medical and pharmacy claims from the PurpleLab® CLEAR database (January 1, 2019 through September 30, 2024). Adult patients with hematologic malignancies and at least one claim for an FDA-approved CAR-T product (cilta-cel, ide-cel, axi-cel, brexu-cel, liso-cel, or tisa-cel) were included (N=881).

The index date was defined as the date of CAR-T administration; a twelve month pre-index continuous enrollment period was required to establish baseline clinical history. CRS and ICANS were identified via ICD-10-CM codes, with severity classified using administrative grade codes where available. Inpatient length of stay (LOS) was evaluated for admissions occurring within 45 days post-index with a duration of at least two days (per CMS two-midnight criteria)[2].

Differences in LOS across products were assessed using the Kruskal-Wallis test. Severity grade distributions were compared using Fisher's exact test (or the Chi-square test, depending on cell counts). All statistical analyses were performed using R (v4.5.1).

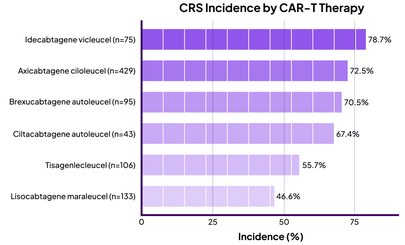
Results

Of the 881 patients included, CRS was identified in 514 (58.3%) and ICANS in 102 (11.6%) (Figure 1). Among patients with coded severity, events were predominantly Grade 1–2. Higher grade events (at least Grade 3) were infrequent (Figure 2).

There were no statistically significant differences in severity grade distributions across products for CRS (p=0.54) or ICANS (p=0.85). Inpatient stays of at least 2 days were observed in 413 patients (46.9%). Median LOS varied significantly by product, ranging from 8.5 to 11.5 days (Kruskal-Wallis p=0.036) (Figure 3, Table 1).

However, when categorized by complication type, median LOS did not differ significantly: 10 days (no complications), 11 days (CRS only), 11 days (ICANS only), and 12 days (both CRS and ICANS; Kruskal-Wallis p=0.742) (Figure 4, Table 2)

Figure 1. Bar Charts: CRS and ICANS Incidence by CAR-T Therapy



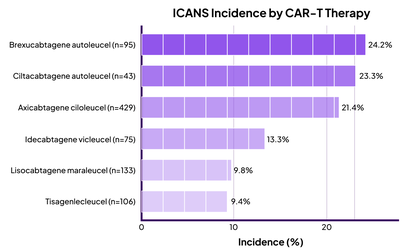
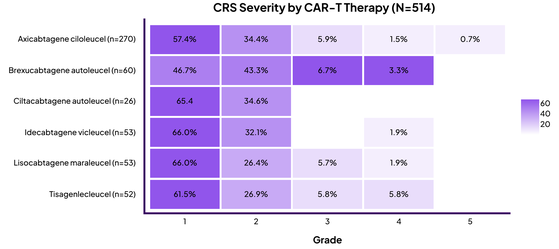


Figure 2.Heatmap CRS and ICANS Severity by CAR-T Therapy



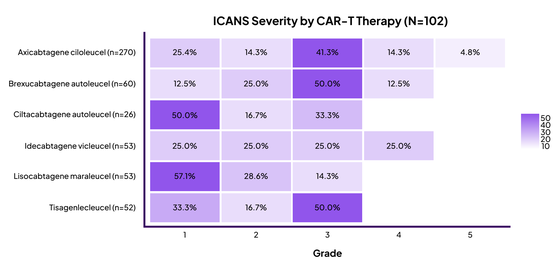


Figure 3.Violin/Boxplot: Length of Stay by CAR-T Therapy

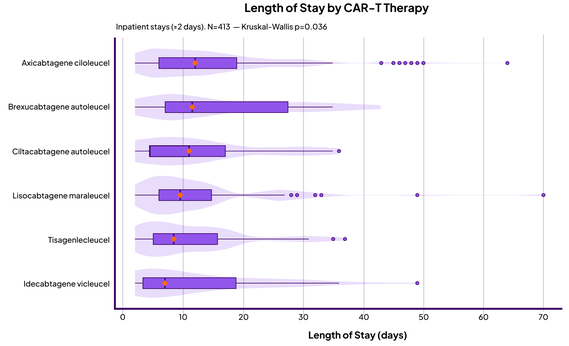


Figure 4.Violin/Boxplot: Length of Stay by CAR-T Therapy

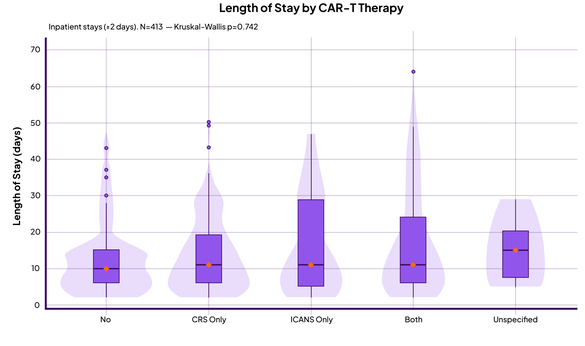


Table 1.LOS Summary by CAR-T Ingredient

Length of Stay by CAR-T Ingredient

Ingredient	N	Median (IQR)	Mean (IQR)	SD
Axicabtagene ciloleucel	23	11 (4.5–17)	11 (4.5–17)	10.8
Brexucabtagene autoleucel	34	7 (3.25–18.75)	7 (3.25–18.75)	11.6
Ciltacabtagene autoleucel	218	12 (6–19)	12 (6–19)	11.2
Lisocabtagene maraleucel	42	42 11.5 (7–27.5)	42 11.5 (7–27.5)	12.1
Tisagenlecleucel	50	9.5 (6–14.75)	9.5 (6–14.75)	12.8
Idecabtagene vicleucel	46	8.5 (5–15.75)	8.5 (5–15.75)	9.8

Table 2.LOS Summary by Complication Type

Length of Stay by CAR-T Ingredient

Complication	N	Median (IQR)	Mean	SD
No	90	10 (6–5)	13.0	11.2
CRS Only	229	11 (6–19)	13.5	9.8
ICANS Only	37	11 (5–29)	16.0	13.5
Both	51	12 (6–24)	17.0	15.2
Unspecified	6	15 (7.5–20.25)	15.2	9.8

Conclusions

In this real-world cohort study of adults receiving CAR-T therapy, coded CRS was common (58.3%), while ICANS was less frequent (11.6%). When severity was graded, CRS was predominantly low grade. High grade CRS or ICANS events were uncommon. While severity grade distributions did not differ significantly across products, inpatient LOS varied significantly by CAR-T product (p=0.036). Patients experiencing both CRS and ICANS exhibited longer LOS, though these differences did not reach statistical significance (p=0.742). These findings support refining monitoring protocols of CAR-T toxicity and inpatient resource use as administration expands across care settings.

Limitations

This analysis may be affected by temporal changes in CAR-T toxicity management, coding practices, and availability of grade ICD-10-CM codes. Also, CRS and ICANS severity was inferred from diagnosis codes. LOS analyses were restricted to inpatient stays lasting at least two days and therefore may not capture the full resource burden of outpatient monitoring, observation care, or short admissions. Product comparisons were limited by small subgroup sizes, particularly for ICANS and high grade events. Because CAR-T products are used in different disease states, and in different treatment lines, unadjusted product comparisons should not be interpreted as causal estimates of product safety.

References

1. Nishihori T, Chen L, Wagner B, et al. Beyond the trial: Real-world CRS, icans, and healthcare burden of CAR T-cell therapy across US oncology practices. Blood. 2025;146(Supplement 1):6263–6263. doi:10.1182/blood-2025-6263
2. Fact Sheet: Two-Midnight Rule. Published online July 1, 2015. https://www.cms.gov/newsroom/fact-sheets/fact-sheet-two-midnight-rule