Early Toxicities and Economic Burden of CAR-T Therapy in the United States: A Retrospective Cohort Study of ICANS and CRS Using Optum Data

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Background

- CAR-T therapy is an FDA-approved adoptive cellular immunotherapy for patients with relapsed or refractory hematologic malignancies.
- Approved U.S. CAR-T therapies target two antigens: CD19 (tisagenlecleucel, axicabtagene ciloleucel, brexucabtagene autoleucel, lisocabtagene maraleucel) and BCMA (idecabtagene vicleucel, ciltacabtagene autoleucel).
- Despite substantial clinical benefit, CAR-T therapy is associated with early immune-mediated toxicities, most notably CRS and ICANS.
- CRS and ICANS severity is graded using ASTCT criteria, which guide management and impact and influence care setting, healthcare resource utilization (HCRU), and economic burden.

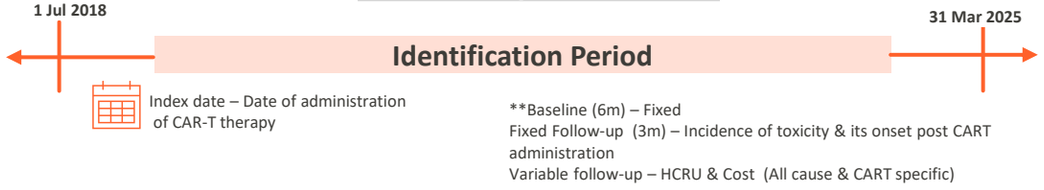
Objective

- To assess the incidence, severity, onset timing, and economic burden of CAR-T–related toxicities, including CRS and ICANS, in U.S. CAR-T therapy recipients

Methodology

Optum® Market Clarity (EHR + Claims)

Retrospective cohort study



Inclusion criteria

- ≥2 medical claims 30 days apart with ICD 10 codes for LBCL, MM, FL, MCL, ALL in study period
- ≥1 pharmacy or medical claim for CAR-T therapy in identification period
- Continuous enrolment for 06 months pre-index and 03 months post-index
- Patients aged ≥18 years

Exclusion criteria

- Patients with ≥1 medical claim of BMT and HSCT and missing demographics

Abbreviations: Chimeric antigen receptor T-cell (CAR-T) , Cytokine Release Syndrome (CRS), Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS), Large B-cell lymphoma (LBCL), multiple myeloma (MM), follicular lymphoma (FL), mantle cell lymphoma (MCL), acute lymphoblastic leukemia (ALL), ASTCT (American Society for Transplantation and Cellular Therapy) , BMT (Bone Marrow Transplant), HSCT (Hematopoietic Stem Cell Transplantation), IP (Inpatient), OP (Outpatient), ER (Emergency Room), Rx (Pharmacy)

Results

- In a CAR-T cohort of 1,722 patients, CD19-directed therapies (73%) were associated with earlier onset and greater severity of CRS and ICANS, including more frequent Grade ≥3 events, whereas BCMA-directed therapies demonstrated higher rates of any-grade CRS but a lower burden of severe toxicities.
- Mean onset of immune-mediated toxicities CRS preceding ICANS and earlier onset observed for CD19 directed therapies compared with BCMA directed therapies (CRS: 3.06 vs 4.05 days; ICANS: 4.59 vs 8.83 days). (Table 1, Figure 3.1 & 3.2)
- While CART drug costs averaged $250,000, toxicity management added a meaningful incremental cost ($80,507), with comparable spending across inpatient and outpatient toxicity care settings, underscoring the economic impact of toxicity management. (Table 2)

Table 1. CRS & ICANS Incidence & Severity

Toxicity	Target Antigen	Any Grade	Grade 1+2	Grade≥3	Mean Onset (days)
CRS	CD-19 (n=1,256)	50%	45%	6%	3.06
	BCMA (n=466)	68%	65%	2%	4.05
ICANS	CD-19 (n=1,256)	22%	13%	9%	4.59
	BCMA (n=466)	11%	9%	2%	8.83

Table 2. Healthcare Cost Utilization

Total Cost	Mean
CART Drug Cost	$250,000
Toxicity Associated Cost	$80,507
Place of Administration (CART)	
Inpatient Toxicity Cost	*$70,571*
Outpatient Toxicity Cost	*$65,215*

Figure 3.1. CRS Onset (Kaplan Meier)

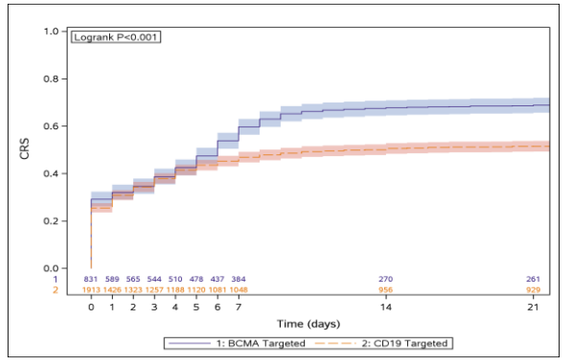
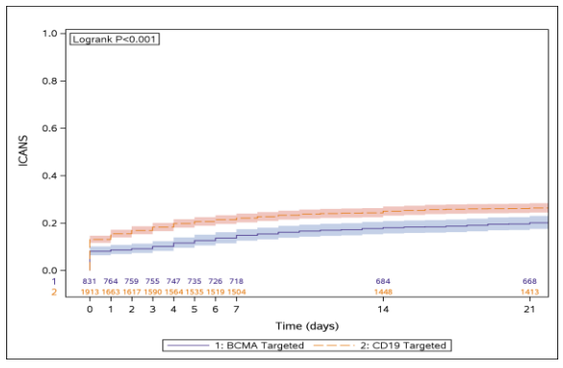


Figure 3.2. ICANS Onset (Kaplan Meier)



Conclusions

- CD19-directed CAR-T therapies were associated with earlier onset and greater severity of immune-mediated toxicities compared with BCMA-directed therapies.
- Toxicity-related costs were comparable across inpatient and outpatient settings, suggesting that toxicity management imposes a meaningful economic burden regardless of site of care and emphasizing the need for efficient resource planning across both settings.

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