Cardiovascular Adverse Events Among Cancer Patients Receiving Chimeric Antigen Receptor-T cell Therapy

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Introduction

- Chimeric antigen receptor T-cell (CAR-T) therapy has revolutionized the treatment of advanced cancers.
- While immune-related side effects such as ICANS and CRS are well recognized and supported by standardized management guidelines, data on cardiovascular adverse events (CAE) in real-world settings remain limited.
- We aimed to estimate the incidence and pattern of CAE events following CART exposure, from a large EMR-based TrinetX database

Methods

- **Data source: TrinetX Research data**
  - Comprising of data for over 142 million patients from 103 health care organizations
- **Inclusion criteria**
  - Administration of CART therapy at age ≥18 years, during 2017-2024
  - Procedure codes were used to identify administration of any of the six approved CART products: Tisagenlecleucel, Axicabtagene (Axicel), Idecabtagene (Idecel), Brexucabtagene, Lisocabtagene, and Ciltacabtagene.
  - CAE events after CART administration were identified using ICD codes for either of the following: acute myocardial infarction, unstable angina, heart failure, acute pericarditis, cardiomyopathy, pericardial effusion, or cardiac arrest. CRS and ICANS data were also extracted.
- **Exclusion criteria**
  - Patients with a preexisting cardiac diagnosis i.e. any of the ICD codes for CAE, falling before their CART date.
  - Missing/unknown data
- Descriptive statistics were performed using StataCorp. (2025).

Results

- **Cohort**: 1,932 patients identified; 514 excluded due to prior CAE.
- **Demographics**: Final cohort: 1,418 patients.
- 60.8% male (n=863); 80.1% White (n=1,136). *Age distribution*:
  - <65 years(47.3%, n= 671/1418),
  - 65–75 years (36.2%, n=514),
  - ≥75 years (16.4%, n=233).
- **CAR T Products**: 1,764 infusions; Axicel (46%, n=811), Idecel (15%, n=265) (Fig 1).
- **CAE Incidence**: 13%(n=182/1418)
  - *Types*:
    - Most common CAE: heart failure 5.3% (n=75/1418), and pericardial effusion 4.8% (n=68) (Fig 2).
  - *Duration between CART administration and CAEs*:
    - <1 month: 4.9% (n=70)
    - 2–6 months: 3.6% (n=51)
    - >6 months: 4.3% (n=61

- **CRS (Cytokine Release Syndrome)**
Occurred in **52%** of patients (735/1418)
Associated with ↑ **risk of CAE Odds Ratio:** 1.4 (95% CI: 1.03–1.95)

- **ICANS (Neurotoxicity)**
Seen in **20%** of patients (288/1418)
Associated with ↑ **risk of CAE Odds Ratio:** 1.8 (95% CI: 1.3–2.6)

- **Mortality**
24% of patients died (346/1418)
Death rate **among patients with CAE**: **46%** (84/182)
Death rate without CAE: **21%** (262/1236)
Development of CAE associated with ↑ **risk of death Odds Ratio:** 3.2 (95% CI: 2.3–4.4), **p < 0.0001**

Figure1: Types of CART therapy used

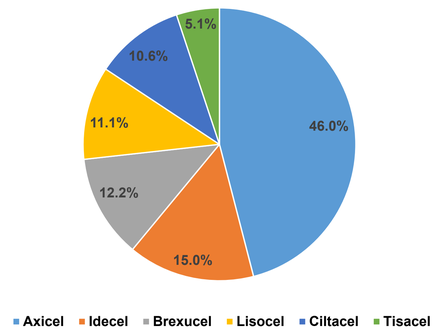
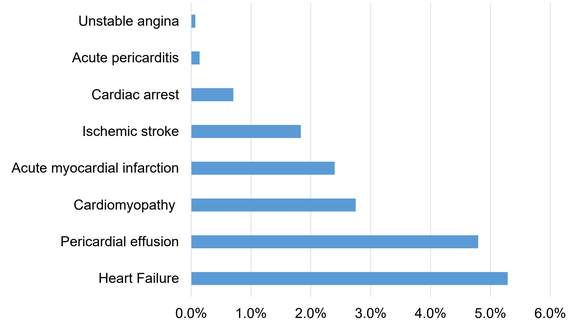


Figure 2 Type of cardiac adverse events



Summary

CAE occurred in **13%** of CAR-T recipients, with 5% events within the first month. **CRS and ICANS** significantly **increased CAE** risk, and **CAE was strongly associated with higher mortality**.

Conclusion

- CAEs represent a clinically significant complication in patients receiving CAR-T therapy.
- The association between CAE and inflammatory syndromes (CRS and ICANS), suggests a pathophysiologic link warranting further investigation.
- The observed increased risk of mortality among patients experiencing CAE underscores the need for vigilant cardiovascular monitoring and integrative toxicity management strategies.

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