Risk of Secondary Acute Myeloid Leukemia Following CAR-T Therapy in Multiple Myeloma

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BACKGROUND

Chimeric antigen receptor T-cell (CAR-T) therapy has transformed the treatment landscape for relapsed/refractory multiple myeloma (MM), with anti-BCMA agents idecabtagene vicleucel and ciltacabtagene autoleucel now in clinical use. Real-world data on secondary neoplasm risk in MM patients not receiving CAR-T therapy remain limited.

METHODS

Datasource: TriNetX US Collaborative Network.

Population: adults with MM (ICD-10 C90.0) diagnosed on or after 1 January 2010, free of myelodysplastic syndromes at baseline.

Analysis: 1:1 propensity score matching on age, sex, race, and comorbidities. Risk ratios, odds ratios, and Kaplan-Meier survival analyses with Cox proportional hazards models.

Outcomes: secondary AML over 3 years, overall mortality, neutropenia, thrombocytopenia, and anemia.

STUDY POPULATION

1,703
MM patients who received CAR-T (Cohort 1)

→ **1,613**
matchedCAR-T patients

131,157
MM patientsnever treated with CAR-T (Cohort 2)

→ **1,613**
matched controls

1:1 propensity score matching produced balanced cohorts of **1,613 patients each**, matched on age, sex, race, and comorbidities.

RESULTS

10.6% **vs 20.3%**
Secondary AML at 3 years
RR 0.52 (0.44–0.62); P<0.001

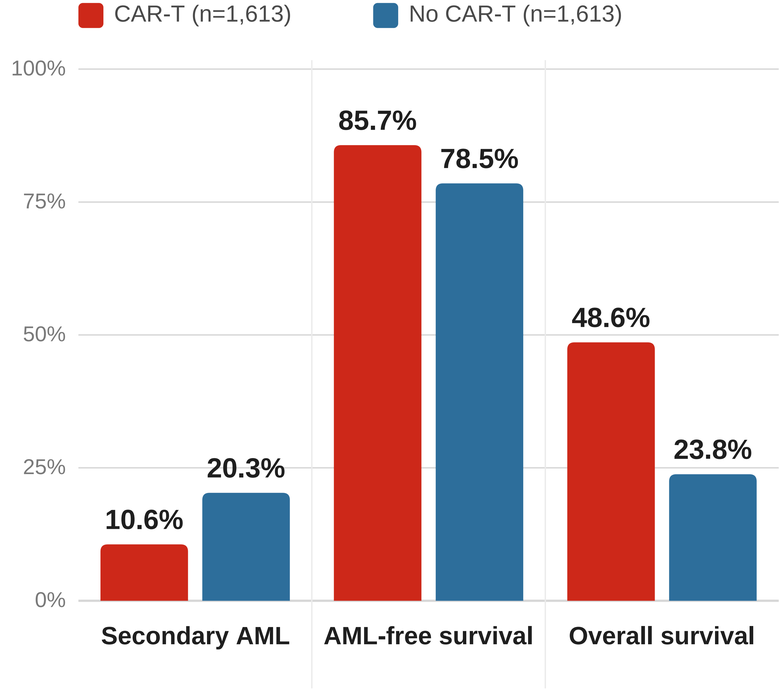
85.7% **vs 78.5%**
AML-free survival at 3 years
HR 0.48 (0.40–0.58); P<0.001

48.6% **vs 23.8%**
Overall survival probability
HR 0.79 (0.69–0.91); P=0.001

3.23×
Hazard of neutropenia with CAR-T
RR 2.11; P<0.001

Outcomes in matched cohorts

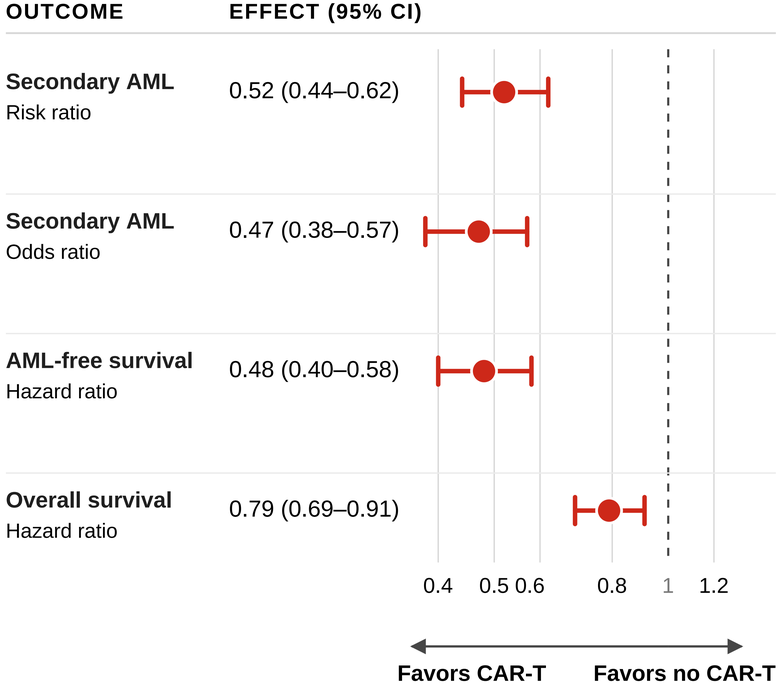
CAR-T–treatedvsCAR-T–naïveMMpatients(n=1,613 each)



Secondary AML and AML-free survival P<0.001; overall survival P=0.001. Estimates from the 1:1 propensity-score–matched cohorts.

Effect estimates for CAR-T therapy

Point estimate with 95% confidence interval



Log scale; reference line at 1.0. All estimates P<0.001 except overall survival (P=0.001). Estimates below 1.0 favor CAR-T therapy.

CONCLUSIONS

In this matched real-world analysis, CAR-T therapy for multiple myeloma was associated with a **significant overall survival benefit** and a **lower observed risk of secondary AML** at 3 years.

However, the **increase in cytopenias** underscores the ongoing hematologic burden of CAR-T therapy, which warrants vigilant post-treatment monitoring.

KEY TAKEAWAYS

- Secondary AML was **roughly half as frequent** in CAR-T–treated patients over 3 years (10.6% vs 20.3%).
- Both AML-free survival and overall survival **favored CAR-T therapy**.
- Neutropenia, thrombocytopenia, and anemia were all **significantly more common** after CAR-T.
- Findings support **structured hematologic surveillance** after CAR-T rather than concern for excess early leukemogenesis.

Hematologic toxicity

CAR-T–treatedvsCAR-T–naïve MM patients; all comparisons P<0.001

Outcome	Risk ratio	Hazard ratio	Direction
Neutropenia	2.11	3.23	▲ Higher with CAR-T
Thrombocytopenia	1.42	1.93	▲ Higher with CAR-T
Anemia	1.15	1.51	▲ Higher with CAR-T

WHAT THIS MEANS IN PRACTICE

Patients undergoing CAR-T therapy for multiple myeloma should have vigilant post-treatment hematologic monitoring, including repeated counts for neutropenia, thrombocytopenia, and anemia.

LIMITATIONS

Retrospective analysisof de-identified electronic health record data; outcomes rely on diagnostic coding, and residual confounding by indication, line of therapy, and survival bias cannot be excluded.

ABBREVIATIONS & KEYWORDS

AML acute myeloid leukemia**, BCMA** B-cell maturation antigen, **CAR-T** chimeric antigen receptor T-cell · **HR** hazard ratio · **MDS** myelodysplastic syndromes · **MM** multiple myeloma · **OR** odds ratio · **RR** risk ratio

Keywords: multiple myeloma, CAR-T therapy, secondary acute myeloid leukemia, idecabtagene vicleucel, ciltacabtagene autoleucel

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