Second Primary Malignancies After CAR-T Versus Stem Cell Transplantation in Multiple Myeloma

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INTRODUCTION AND AIM

- Improved survival following SCT and CAR-T therapy has made second primary malignancies (SPMs) an important concern in multiple myeloma survivorship.
- CAR-T therapy may introduce additional risk through lymphodepletion and prolonged immune dysfunction, with recent FDA labeling highlighting rare secondary T-cell malignancies.
- Real-world comparisons of SPM risk after SCT with versus without CAR-T remain limited. We compared the incidence of secondary malignancies in patients with MM treated with SCT with or without CAR-T therapy.

METHODS

- Retrospective cohort study using the TriNetX Research USA network.
- Two cohorts were constructed: **MM–SCT–No CAR-T:** Patients with MM who underwent SCT without CAR-T therapy and **MM–SCT–CAR-T:** Patients with MM who received both SCT and CAR-T therapy.
- Patients with non-MM malignancies before the index date were excluded. Index date: Date of SCT for the MM–SCT–No CAR-T cohort and Date of CAR-T administration for the MM–SCT–CAR-T cohort
- Propensity-score matching was used to balance baseline characteristics. Primary outcome: Incident secondary neoplasm. Outcomes were assessed beginning one day after the index date.

CONCLUSIONS

- Patients receiving CAR-T after SCT had a higher incidence of secondary malignancies than patients receiving SCT without CAR-T.
- Secondary malignancy risk should be considered in long-term survivorship planning after CAR-T therapy.
- Post–CAR-T care should emphasize: Extended clinical follow-up, guideline-directed cancer screening and prompt evaluation and treatment of suspected malignancies
- Further studies are needed to identify therapy-specific and patient-level risk factors and determine the appropriate intensity and duration of surveillance.

RESULTS

- After propensity-score matching, **239 patients** were included in each cohort.
- Baseline characteristics were balanced.
- Median follow-up: MM–SCT–No CAR-T: **390 days** and MM–SCT–CAR-T: **328 days**
- Secondary neoplasms occurred in: MM–SCT–No CAR-T: **13 patients;** MM–SCT–CAR-T: **61 patients;** Risk difference: **–0.226** (95% CI, −0.293 to −0.160); OR: **0.149** (95% CI, 0.079–0.281)
- Hazard ratio for SPM: **0.137** (95% CI, 0.074–0.255)
- Survival probability at the end of follow-up: MM–SCT–No CAR-T: **57.59%;** MM–SCT–CAR-T: **49.24%**

Characteristic	MM-SCT-No CAR-T (N=239)	MM with both SCT and CAR-T (N=239)	Standard difference
Age at Index	64.0 +/- 8.8 (n=239)	63.9 +/- 9.3 (n=239)	0.017
Female	104 (43.5%)	97 (40.6%)	0.059
Male	135 (56.5%)	142 (59.4%)	0.059
Black or African American	34 (14.2%)	29 (12.1%)	0.062
White	192 (80.3%)	187 (78.2%)	0.052
Hispanic or Latino	10 (4.2%)	10 (4.2%)	<0.001
Asian	10 (4.2%)	10 (4.2%)	<0.001
Tobacco use	10 (4.2%)	10 (4.2%)	<0.001
Alcohol related disorders	10 (4.2%)	10 (4.2%)	<0.001

Baseline characteristics of the two cohorts after matching.

CONTACT INFORMATION

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