Evaluating the Influence of Chimeric Antigen Receptor T-cell Therapy on Fracture Risk of Patients with Multiple Myeloma

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INTRODUCTION:

Patients with relapsed or refractory multiple myeloma may be eligible for a new treatment utilizing chimeric antigen receptor T-cells (CAR-T). Often, these patients will have a high burden of skeletal disease and may be at risk for pathologic fracture. However, little is known about the effect of CAR-T therapy on a patient's fracture risk. The purpose of the present study is to evaluate the effect of CAR-T therapy on fracture risk in multiple myeloma patients.

METHODS:

A prospective, consecutive cohort of multiple myeloma patients undergoing treatment with CAR-T therapy were reviewed retrospectively. Patients were required to have a PET-CT prior to CAR-T infusion and at least one PET-CT surveillance imaging 90 days following treatment. The minimum follow-up for surviving patients was set at 3 months. The primary outcome measure was fracture risk as characterized by a modified Mirel's criteria. The secondary outcome measure was change in lesion avidity, measured as standardized uptake value (SUV) units, on PET-CT. Descriptive statistics with univariate methods were performed and survival was investigated by Kaplan Meier method.

RESULTS:

We identified 139 patients who underwent CAR-T for multiple myeloma. The mean age was 64.4 years. 58 patients were female (41.7%) and the mean follow up for surviving patients was 9.5 months (3-28 months). There were 71 patients (51.4%) who had a discrete long bone lesion. Overall, 37 patients (27.8%) were characterized as being "at risk" for fracture prior to infusion. After CAR-T infusion, at latest follow up, only 3 patients (2.5%) were identified as being at risk (p=0.004). Most of the improvement in Mirel scoring was seen with resolution of the bone lesions and improvement in pain. The mean PET-CT SUV between at risk patients and patients at low risk was significantly different prior to infusion (8.2 vs 4.6, p=0.03). However, there was no difference in PET-CT SUV identified between these two groups after CAR-T therapy (5.7 vs 4.0 p=0.43). 2 fractures occurred in the post-transfusion period. 33 patients (23.7%) died of disease after CAR-T therapy at a mean of 6.6 months. There was no association between pre-infusion fracture risk and disease specific survival.

DISCUSSION AND CONCLUSION:

Our findings suggest that CAR-T therapy, when used to treat relapsed or refractory multiple myeloma, is associated with reduced fracture risk due to lesion resolution.

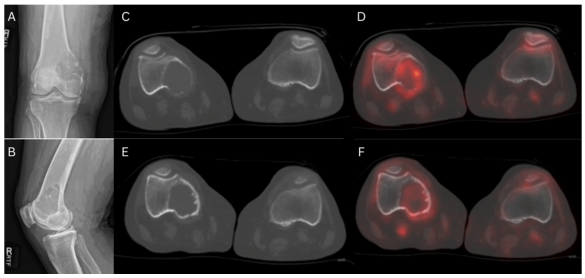

Table 1. Modified Mirel's criteria. The sum of each score is used to determine the Mirel's score for a given lesion. Scores < 9 are considered "low risk" for fracture while scores ≥ 9 are considered "high risk" for fracture, indicating for prophylactic fixation of the extremity. A score of 0 was added so that all patients in the study could be assigned a Mirel's score.

Score	0	1	2	3
Site	No primary lesion or diffuse subcentimeter lesions	Upper limb	Lower limb	Peritrochanteric
Pain	No primary lesion or no pain in primary or diffuse lesions	Mild	Moderate	Functional
Lesion nature	No primary lesion	Blastic	Mixed	Lytic
Size (relative to bone diameter)	No primary lesion or diffuse subcentimeter lesions	<1/3	1/3 to 2/3	>2/3