An Endothelial Activation and Stress Index (EASIX) Based Predictive Model for Neurotoxicity and Cytokine Release Syndrome (CRS) After B-Cell Maturation Antigen (BCMA)- Directed Chimeric Antigen Receptor (CAR) T-Cell Therapy for Relapsed/Refractory Multiple Myeloma (RRMM)

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Introduction

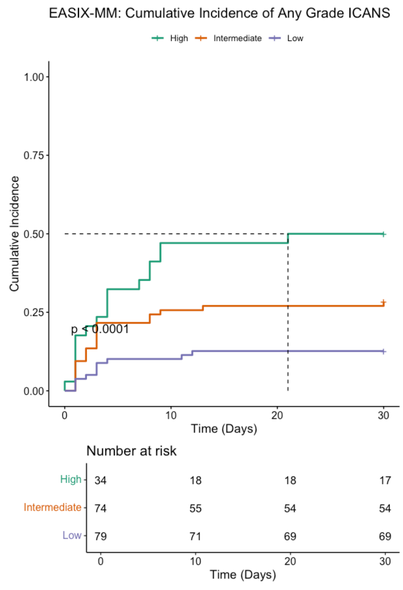
- The EASIX score is a validated predictor of survival post-allogeneic stem cell transplantation, reflecting endothelial dysfunction.
- Modified EASIX scores (EASIX-F, EASIX-FC, mEASIX, sEASIX) have shown predictive value for cytokine release syndrome (CRS) and immune effector cell-associated neurotoxicity syndrome (ICANS) in CAR T-cell therapy for conditions like B-acute lymphoblastic leukemia and diffuse large B-cell lymphoma.
- Despite these findings, there is limited evidence on the utility of EASIX scores for patients with relapsed/refractory multiple myeloma (RRMM) undergoing BCMA-directed CAR T therapy.
- This study aims to create an RRMM-specific EASIX-based model to predict the risk of CRS and ICANS following BCMA-directed CAR T treatment.

Methods

- Multi-center retrospective study of patients with RRMM who received SOC CAR T between May 1, 2021, and January 31, 2024
- We first assessed the utility of EASIX, mEASIX, sEASIX, EASIX-F, and EASIX-FC, in predicting CRS and ICANS within 30 days post CART
- We then developed a multivariable predictive model for RRMM
- Variables with a p value <0.1 on univariate analysis were included in the multivariable model. We employed backward elimination to arrive at the final predictive model.

Results

- A total of 193 patients were included
- Median of 6 prior lines
- 60% received ide-cel, 40% received cilta-cel
- 26% had active EMD, 13% had received a prior BCMA directed therapy



Parameter	HR for any grade ICANS (95% CI)	P value	Assigned score
EASIX Q4 (High)	2.02 (1.10-3.71)	0.023	1
ECOG PS ≥ 2	1.99 (0.98-4.02)	0.054	1
FISH: High risk	1.84 (1.02-2.03)	0.04	1
Low risk	Reference	Reference	0
Intermediate risk	2.47 (1.16-5.26)	<0.001	1
High risk	4.91 (2.24-10.74)	0.018	≥2

Summary

- EASIX-MM is a novel RRMM specific prediction model that predicts risk of ICANS, PFS, and OS after CAR T for RRMM. This model provides a practical tool for identifying high-risk patients, enabling tailored care and improved outcomes in RRMM CAR T therapy