Navigating the Toxicity Landscape of BCMA-Directed CAR T-Cell Therapies in Multiple Myeloma: A Systematic Review of CAR T-Cell Therapies

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Introduction

B-cell maturation antigen (BCMA)-directed chimeric antigen receptor (CAR) T-cell therapies are approved for relapsed/refractory multiple myeloma (RRMM). Among FDA-approved products, idecabtagene vicleucel (ide-cel) and ciltacabtagene autoleucel (cilta-cel) demonstrate efficacy but differ in toxicity profiles, necessitating comparative evaluation.[1,2]

Methods

A systematic literature search was conducted across PubMed, Embase, Scopus, Cochrane, and Web of Science. Of 112 identified studies, 92 met inclusion criteria (35 clinical trials, 27 retrospective analyses, 18 meta-analyses, 12 observational studies). Data on toxicity, cellular kinetics, and efficacy outcomes were extracted and analyzed using R software.[3,4,5,6]

Results

CRS occurred earlier with ide-cel (median 1–2 days) versus cilta-cel (median 7 days), warranting prompt intervention despite similar severity.[1,2] ICANS rates were comparable (18% vs. 20.6%), though cilta-cel was associated with delayed Parkinsonian-like neurotoxicity.[4] Severe infections were more frequent with cilta-cel (33% vs. 23%).[5] Hematologic toxicities were similar. Cilta-cel demonstrated superior efficacy, with higher overall survival (72% vs. 60%) and longer progression-free survival (12.2 vs. 8.6 months), potentially related to prolonged CAR T-cell persistence.[1,2,5] A delayed CAR T-cell peak expansion paralleled cilta-cel's toxicity timeline.[3]

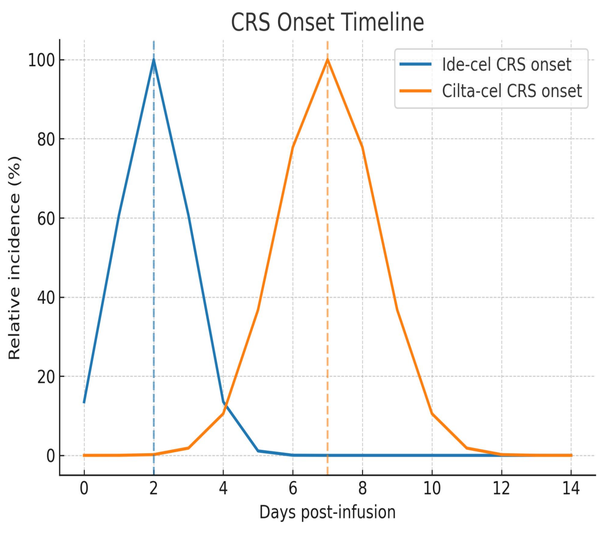


Figure 1. CRS Onset Timeline.
Cytokine release syndrome (CRS) occurred earlier with ide-cel (median 1–2 days) compared to cilta-cel (median 7 days), requiring earlier monitoring and intervention despite similar severity.

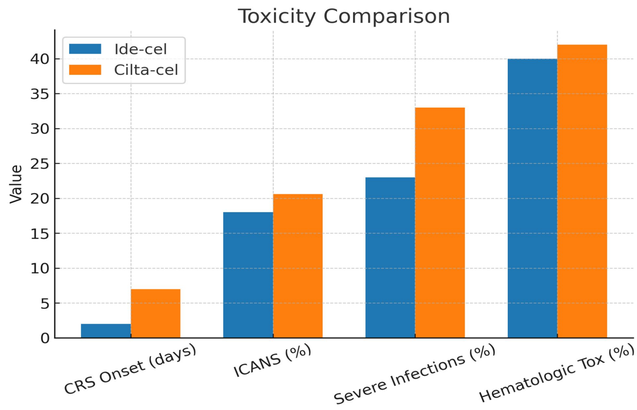


Figure 2. Toxicity Comparison.
Rates of ICANS were comparable between ide-cel (18%) and cilta-cel (20.6%). Cilta-cel was associated with more severe infections (33% vs. 23%). Hematologic toxicities were similar between the two therapies.

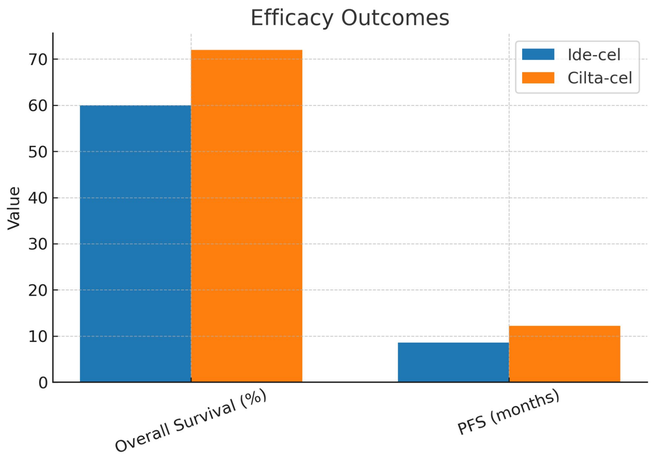


Figure 3. Survival Outcomes.
Cilta-cel demonstrated superior efficacy with higher overall survival (72% vs. 60%) and longer progression-free survival (12.2 vs. 8.6 months), potentially linked to prolonged CAR T-cell persistence.

Conclusion

Cilta-cel offers improved survival but carries greater risks of delayed CRS and neurotoxicity. Ide-cel requires vigilant early monitoring for CRS. Treatment should be individualized, balancing efficacy with toxicity in RRMM.

References

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