Comparative Efficacy and Safety of BCMA-Targeted CAR T-Cell Therapies and Bispecific Antibodies in Relapsed/Refractory Multiple Myeloma: A Comprehensive Review of Clinical Outcomes and Adverse Events

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Introduction

Targeted immunotherapies have transformed the treatment landscape of relapsed and refractory multiple myeloma (RRMM), a setting in which patients frequently exhibit resistance to proteasome inhibitors, immunomodulatory and alkylating agents.

Aim

To systematically compare the efficacy and safety of BCMA-targeted CAR T-cell therapies and bispecific antibodies in patients with relapsed/refractory multiple myeloma, using data from pivotal clinical trials and real-world studies, in order to clarify their relative clinical benefits, adverse event profiles, and implications for individualized treatment strategies.

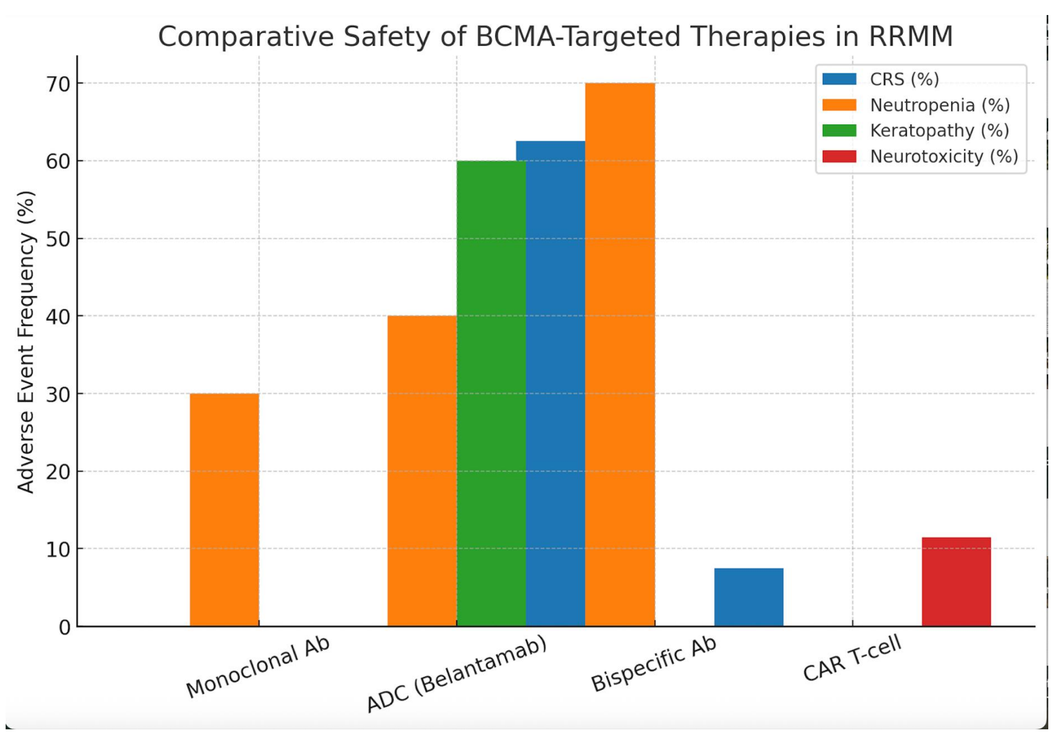
Objectives

1. To evaluate and compare efficacy outcomes .
2. To summarize and contrast safety profiles of these immunotherapies
3. To contextualize the clinical role of CAR T-cell therapies versus bispecific antibodies in RRMM

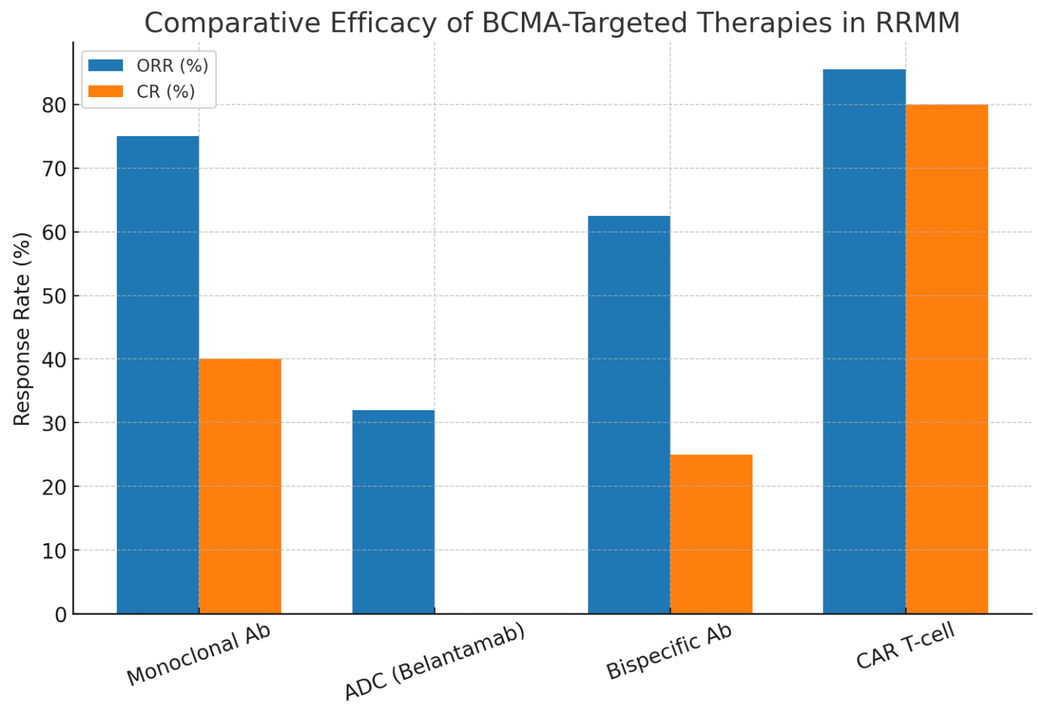
Methods

In this narrative review of pivotal phase I–III trials and real-world cohorts published through mid-2024, we evaluated key efficacy endpoints that included overall response rate (ORR), complete response (CR) rate, progression-free survival (PFS), and duration of response (DOR)—alongside safety profiles of monoclonal antibodies, antibody–drug conjugates (ADCs), bispecific T-cell engagers (BiTEs), and chimeric antigen receptor (CAR) T-cell therapies

Results



Monoclonal antibodies: Anti-CD38 antibodies daratumumab and isatuximab, when added to standard regimens, achieved ORRs of 60–90%, median PFS of 11–22 months, and CR rates up to 40%, with infusion reactions (15–50%), neutropenia (20–40%), and infections representing the most common adverse events.



Antibody drug conjugates: The anti-BCMA ADC belantamab mafodotin yielded an ORR of approximately 32% in heavily pretreated cohorts, with a median DOR of 11 months, although ocular keratopathy (>60%) and thrombocytopenia (35–45%) necessitated rigorous monitoring.

Bispecific antibodies: The BCMA×CD3 bispecifics such as teclistamab demonstrated ORRs of 60–65% and CR rates of 20–30%, with cytokine release syndrome in 55–70% (predominantly grade 1–2), alongside frequent neutropenia (70%) and hypogammaglobulinemia.

CAR T-cell therapies: Idecabtagene vicleucel and ciltacabtagene autoleucel produced ORRs of 73–98% and stringent complete response rates up to 80%, with median PFS beyond 18 months in select cohorts, although grade ≥3 cytokine release syndrome (5–10%), neurotoxicity (3–20%), and prolonged cytopenias remain important safety considerations.

Summary

Targeted immunotherapies have shown strong response rates and lasting remissions in patients with relapsed or refractory multiple myeloma; however, their unique benefits and side effects highlight the need for personalized treatment plans, careful monitoring, as well as continued research to manage side effects and address treatment resistance.

Discussion

BCMA-targeted therapies have expanded options in relapsed/refractory multiple myeloma, with CAR T-cells showing the most durable responses but limited by toxicity and access. Bispecific antibodies and monoclonal antibodies offer effective, more feasible alternatives, while ADCs remain constrained by ocular and hematologic toxicity. Ongoing studies are needed to refine sequencing and optimize real-world use.

References

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