Treatment Discontinuation and Dose Modifications Associated with Bispecific Antibody Therapy in Relapsed/Refractory Multiple Myeloma: A Systematic Review and Meta-Analysis

Rithika Manjunatha Reddy, MD[1]; Kala Seetharaman, MD[2]

1 Department of Hematology and Oncology, Saint Vincent Hospital, Worcester, Massachusetts, USA | 2 Department of Internal Medicine, Saint Vincent Hospital, Worcester, Massachusetts, USA

Saint Vincent Hospital

Worcester, Massachusetts, USA

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1 Context

Bispecific antibodies targeting BCMA, GPRC5D, and FcRH5 have demonstrated high response rates in relapsed/refractory multiple myeloma (RRMM); however, treatment discontinuation and dose modification due to toxicity and infection may limit sustained benefit. The incidence and drivers of these events remain incompletely characterized. As bispecific antibody use expands beyond clinical trials into routine practice, understanding these risks is critical for optimizing long-term treatment adherence and patient safety.

2 Objective

To quantify the incidence and determinants of treatment discontinuation and dose modification in patients with RRMM receiving bispecific antibody therapy. Secondary aims included characterizing the adverse events driving these interruptions and identifying differences by antibody target.

3 Design

A systematic review and meta-analysis was performed according to PRISMA guidelines. PubMed, Embase, Web of Science, and Cochrane Library databases were searched from 2019 to March 2026. Random-effects models pooled proportions (95% CIs) of discontinuation and dose modification, with heterogeneity assessed using I^2 and subgroup analyses by antibody target, agent, and study phase.

4 Setting

Multicenter phase I/II trials and real-world cohorts from international academic centers, spanning a broad range of practice settings consistent with real-world bispecific antibody use.

5 Participants

Twenty-five eligible studies encompassing 3,834 patients with heavily pretreated RRMM (median five prior lines) who received BCMA-, GPRC5D-, or FcRH5-directed bispecific antibodies — a high-risk population representative of contemporary RRMM practice.

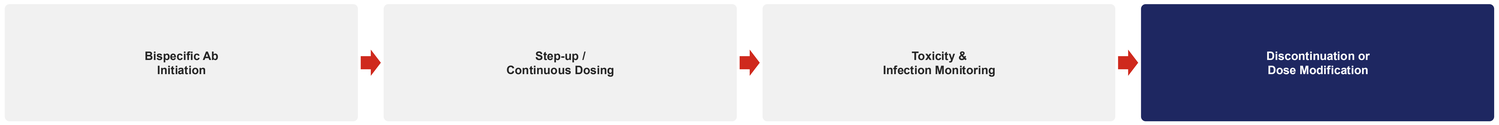
6 Interventions

Monotherapy and combination bispecific antibody regimens, administered via step-up or continuous dosing schedules, reflecting the diversity of dosing approaches across BCMA-, GPRC5D-, and FcRH5-directed programs.

7 Main Outcome Measures

Treatment discontinuation and dose modification rates, stratified by cause — including infection, hematologic toxicity, cytokine release syndrome, and other treatment-related adverse events.

Results



27%

pooled treatment discontinuation rate (95% CI 23–31)

42%

experienced dose modification or interruption (95% CI 36–49)

11%

discontinued specifically due to adverse events (95% CI 8–15)

- **Across 25 studies including 3,834 heavily pretreated patients, discontinuation and dose modification were common across bispecific antibody regimens.**
- **Infections and hematologic toxicities were the leading causes of discontinuation and dose modification, while CRS accounted for less than 3%.**
- **Dose modification or interruption occurred in 42% of patients, most often for cytopenias and infections.**
- **Discontinuation rates were higher with GPRC5D-targeted therapies than BCMA-directed agents (p = 0.04).**
- **Findings were consistent across monotherapy and combination bispecific antibody regimens.**
- **Findings were also consistent on sensitivity analyses, with no evidence of publication bias (Egger p = 0.48).**

Conclusions

Treatment discontinuation and dose modification are common with bispecific antibody therapy in RRMM, primarily driven by infections and cytopenias, with meaningful differences observed across antibody targets.

These findings highlight the critical need for improved toxicity mitigation, infection prophylaxis, and optimized dosing strategies to enhance treatment durability in the era of T-cell-redirecting therapies — particularly as these agents move into earlier lines of therapy and broader clinical use.

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