Reduced-Frequency Dosing of FDA-Approved Bispecific Antibodies in Relapsed/Refractory Multiple Myeloma: A Systematic Review of Maintaining Efficacy While Reducing Infection-Related Toxicity

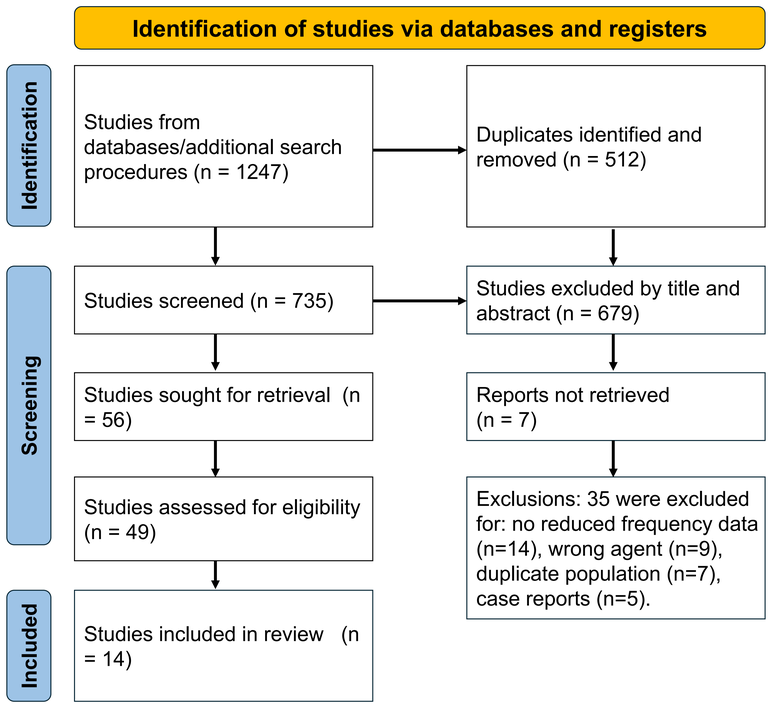
Authors: Mahboob Younus Shaik MD, Sana Dugan MD, Ashley Jenkins MD
Affiliations: CHI St. Vincent Hospital, Hot Springs, Arkansas, USA

Background

- Bispecific antibodies (BsAbs) targeting BCMA and GPRC5D have significantly improved outcomes in relapsed/refractory multiple myeloma (RRMM).
- Standard weekly dosing is associated with high rates of severe infections due to prolonged immunosuppression.
- Reduced-frequency dosing has emerged as a strategy to maintain efficacy while minimizing treatment-related toxicity.

Methods

- PRISMA-guided systematic review
- Databases: PubMed, Embase, Scopus, Cochrane CENTRAL, Web of Science, and major hematology conferences (ASH, ASCO, EHA, SOHO)
- Included prospective trials, cohort studies, and post-hoc analyses evaluating reduced-frequency BsAb dosing.
- Primary outcomes: ORR, PFS, durability of response
- Secondary outcomes: Grade ≥3 infections, hypogammaglobulinemia, treatment discontinuation.



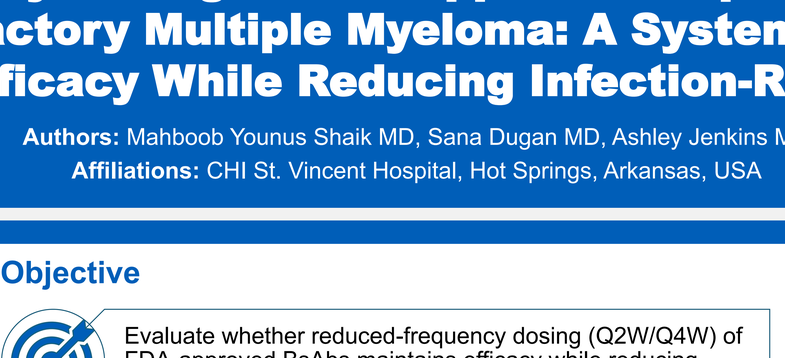
Objective

Evaluate whether reduced-frequency dosing (Q2W/Q4W) of FDA-approved BsAbs maintains efficacy while reducing infection-related toxicity in RRMM.

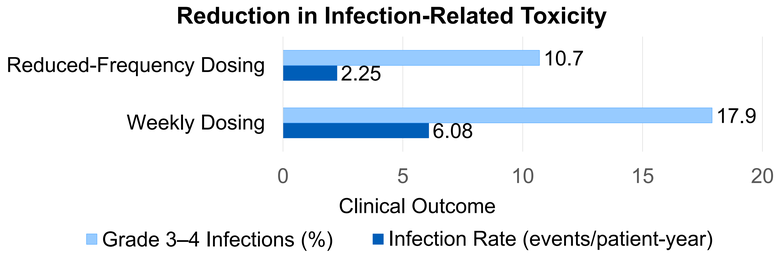
Results

Key Findings:

- 14 studies involving >1,200 patients were included.
- Reduced-frequency dosing maintained clinical efficacy across FDA-approved BsAbs.
- Infection rates consistently decreased following dose de-escalation.
- No study reported loss of response attributable to reduced-frequency dosing.



Graph 1. Clinical efficacy of reduced-frequency bispecific antibody dosing in RRMM. Reduced-frequency dosing maintained high response rates across FDA-approved bispecific antibodies, with Teclistamab and Elranatamab demonstrating preserved responses after dose reduction.



Graph 2. Infection-related toxicity before and after dose de-escalation. Reduced-frequency dosing was associated with lower infection rates and fewer grade 3–4 infections compared with weekly dosing.

Results

Table 1. Key Clinical Outcomes

Parameter	Result
Studies Included	14
Total Patients	>1,200
Teclistamab Q2W	100% response maintained (37/37)
Elranatamab Q4W	92.6% response maintained (25/27)
Talquetamab Q2W	ORR 71%; Median PFS 11.2 months
Infection Rate	6.08 → 2.25 events/patient-year
Grade 3–4 Infections	17.9% → 10.7%
Response Loss After Dose Reduction	None Reported

Key Clinical Message

- Reduced-frequency dosing of FDA-approved bispecific antibodies maintains clinical efficacy while lowering infection-related toxicity, supporting individualized maintenance strategies in relapsed/refractory multiple myeloma.

Conclusion

- Reduced-frequency dosing preserves treatment efficacy while substantially reducing infectious toxicity.
- Current evidence supports biweekly and monthly maintenance schedules for selected patients.
- Prospective randomized studies are needed to optimize patient selection and de-escalation strategies.

References

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