

Efficacy and Safety of Teclistamab in Extramedullary Relapsed/Refractory Multiple Myeloma: A Systematic Review and Meta-Analysis

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INTRODUCTION

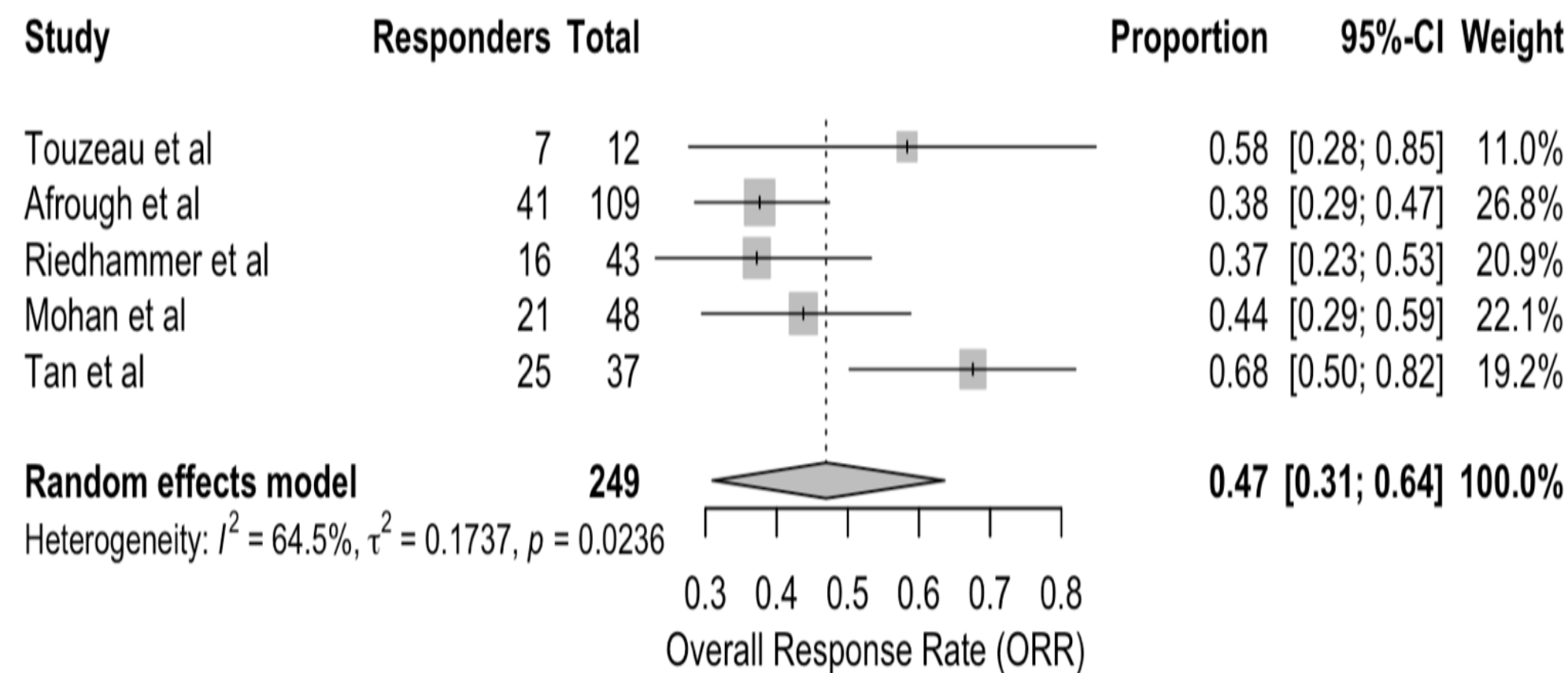
- Extramedullary disease (EMD) in multiple myeloma is associated with:
 - Aggressive disease biology
 - Treatment resistance
 - Poor survival outcomes
- Teclistamab is a B-cell maturation antigen (BCMA) × CD3 bispecific antibody that has demonstrated efficacy in relapsed/refractory multiple myeloma (RRMM).
- However, its efficacy and safety in patients with EMD remain incompletely characterized.
- To date, no dedicated systematic review and meta-analysis has comprehensively evaluated Teclistamab specifically in EMD-associated RRMM.
- Therefore, this study aimed to systematically evaluate the efficacy and safety of Teclistamab in patients with EMD-RRMM.

METHODS

- Study design:** Systematic review and meta-analysis conducted according to PRISMA 2020 guidelines.
- Literature search: Databases searched through May 2026:**
 - PubMed
 - Scopus
 - ClinicalTrials.gov
 - Embase
 - Web of Science
 - Major hematology conference proceedings
- Eligibility:** Studies evaluating Teclistamab in patients with EMD-associated RRMM were included.
- Primary outcome:** Overall response rate (ORR) in patients with EMD.
- Secondary outcomes:**
 - Progression-free survival (PFS)
 - Cytokine release syndrome (CRS)
 - Infections
 - Overall survival (OS)
 - Immune effector cell-associated neurotoxicity syndrome (ICANS)
- Statistical analysis:** Random-effects single-arm proportion meta-analysis using logit transformation.

RESULTS

- Study Selection:** 13 studies were included in the systematic review, with 5 non-overlapping studies comprising 249 EMD-RRMM patients included in the quantitative synthesis.
- Patient Characteristics:** Patients were heavily pretreated, frequently triple-class refractory, and several cohorts included patients with prior BCMA-directed therapy exposure.
- Overall response rate (ORR):**
 - Pooled ORR: 46.9% (95% CI, 30.9–63.6%)
 - Moderate heterogeneity ($I^2 = 64.5\%$)
 - Individual study ORRs ranged from 37.2% to 67.6%
- Prior BCMA-directed therapy:** Responses to Teclistamab remained achievable even after prior BCMA-directed therapy exposure.
- Survival outcomes:**
 - Median PFS: 1.4–8.8 months
 - Median OS: up to 20 months in selected cohorts
- True EMD vs. paraskkeletal disease:**
 - True EMD was associated with markedly inferior outcomes.
 - Median PFS: 1.4 months vs. 6.5 months in paraskkeletal disease.
- Safety:**
 - CRS: ~52–72%, predominantly low grade
 - ICANS: ~3–21%
 - Grade ≥3 infections, neutropenia, and thrombocytopenia were frequently reported.



Forest plot of pooled MMR with random-effects model

CONCLUSIONS

- Teclistamab demonstrated clinically meaningful activity in EMD-RRMM, with a pooled ORR of 46.9%, although lower than the 63% ORR reported in the broader RRMM population of MajesTEC-1.
- True EMD was associated with inferior survival compared with paraskkeletal disease, highlighting its aggressive biology.
- Prospective studies with standardized EMD definitions and optimized combination strategies are needed to improve outcomes.

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