Infectious Complications Associated With Teclistamab-Based Therapy in Relapsed/Refractory Multiple Myeloma: A Systematic Review of Clinical Trials

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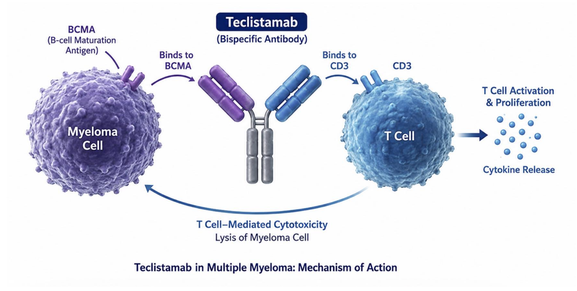
Background

- Teclistamab, a bispecific antibody targeting CD3 on T-cell surfaces and B-cell maturation antigen on myeloma cells, has demonstrated efficacy in relapsed/refractory multiple myeloma (RRMM) as monotherapy and in combination.
- However, infectious complications remain the leading cause of treatment-related mortality. This systematic review characterizes infection incidence, severity, and mortality across teclistamab-based regimens in prospective clinical trials.

Methods

- A comprehensive literature search of peer-reviewed publications was conducted on PubMed, Cochrane, Embase, Scopus, and major conference proceedings through May 2026, to identify interventional trials evaluating teclistamab-based regimens for patients with RRMM.
- Observational studies, retrospective cohorts, and case reports were excluded. Eligible phase 1–3 trials reporting regimen-specific, quantifiable infection outcomes were included. Meta-analysis was not performed due to heterogeneity in trial designs, regimens, and supportive care practices.

Mechanism of Action



Teclistamab in Multiple Myeloma: Mechanism of Action

Results

- Three teclistamab-based trials met the inclusion criteria (n=550).
- **MajesTEC-1 Trial** (phase 1/2, monotherapy, n=165), all-grade infections occurred in 76.4%, with grade ≥3 infections in 44.8% of patients.
- **MajesTEC-3 Trial** (phase 3 teclistamab-daratumumab combination trial, n=291), infections of any grade were reported in 96.5% of patients in the treatment arm. Grade 3 and 4 infections occurred in 54.1%, with infection-related mortality of 4.6%. Twelve of 13 fatal infections preceded the protocol-reinforced intravenous immunoglobulin (IVIG) implementation.
- **RedirecTT-1 Trial** (phase 1b, teclistamab-talquetamab, n=94), infections of any grade occurred in 89% of patients, with grade ≥3 infections reaching approximately 64%.
- A stepwise increase in grade ≥3 infections was observed from monotherapy (44.8%) to doublet (54.1%) to dual-bispecific therapy (64%), suggesting additive immunosuppression.
- Infection-related mortality ranged from 4.6% reported in MajesTEC-3 trial to 12% in the RedirecTT-1 trial. Hypogammaglobulinemia ranged from 74.5% in MajesTEC-1 to 84.5% in MajesTEC-3 trials. Infections were most frequent within the first 6 months of therapy across all regimens.

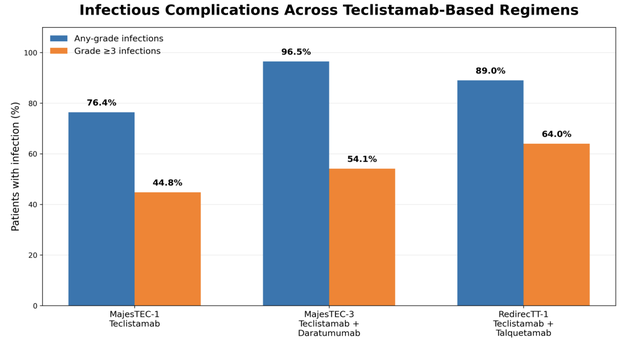


Figure 1. Rates of any-grade and grade ≥3 infections across teclistamab-based regimens.

- COVID-19, pneumonia, and other respiratory tract infections predominated across all trials, with opportunistic (PJP, CMV, adenovirus) and bacterial (sepsis) infections also contributing to grade ≥3 infections and fatal events.
- In MajesTEC-3, reinforced IVIG replacement (Feb 2023 amendment) followed 12 of 13 fatal infections that occurred in the first 6 months and only 1 fatal infection occurred afterward, underscoring the protective role of early IVIG.

Conclusion

Teclistamab-based regimens are associated with substantial infectious morbidity and mortality, with progressively higher rates observed in combination and dual-bispecific strategies.

Infection-related mortality in teclistamab-based regimens ranges from 4.6-12% and clustered within the first 6 months of therapy.

The reduction in fatal infections following IVIG implementation in MajesTEC-3 highlights the importance of early immunoglobulin replacement and structured infection prophylaxis.

Future Directions for Research

Future prospective trials should standardize infection prophylaxis protocols, including early IVIG initiation, and evaluate antimicrobial and antiviral strategies as teclistamab-based combinations move into earlier lines of multiple myeloma therapy.

References

1. Moreau P, Garfall AL, van de Donk NWCJ, et al. Teclistamab in Relapsed or Refractory Multiple Myeloma. N Engl J Med. 2022;387(6):495-505.
2. Costa LJ, Bahlis NJ, Perrot A, et al. Teclistamab plus Daratumumab in Relapsed or Refractory Multiple Myeloma. N Engl J Med. 2026;394(8):739-752.
3. Cohen YC, Magen H, Gatt M, et al. Talquetamab plus Teclistamab in Relapsed or Refractory Multiple Myeloma. N Engl J Med. 2025;392(2):138-149.
4. Guo Y, Quijano Cardé NA, Kang L, et al. Teclistamab: Mechanism of Action, Clinical, and Translational Science. Clin Transl Sci. 2024;17(1):e13717.