Teclistamab Reduces Risk of Progression or Death in Earlier-Line Multiple Myeloma

Key Takeaways

- Teclistamab cut progression/death risk versus PVd or Kd (HR 0.29), with 18-month PFS 69.8% vs 26.9% and median PFS not reached vs 8.2 months.
- Enrollment reflected resistant biology: median two prior lines, 80% lenalidomide-refractory, 85% anti-CD38–refractory, and >90% refractory to the most recent regimen; prior BCMA therapy was excluded.
- Depth of response favored teclistamab, with ≥CR 65.9% vs 16.8% and ORR 84.5% vs 54.2%, and median duration of response not reached vs 13.4 months.
- Overall survival improved at interim analysis, with 18-month OS 79.2% vs 68.6% (HR 0.60) and delayed worsening of myeloma-associated symptoms.
- Safety liabilities centered on neutropenia and infections: grade 3/4 infections 41.6% vs 29.0% and fatal infections 5.5% vs 2.8%; CRS was common but mostly grade 1–2.

Phase 3 MajesTEC-9 findings show teclistamab monotherapy significantly improves progression-free survival and overall survival compared with PVd or Kd.

Teclistamab-cqyv (Tecvayli; Johnson & Johnson) monotherapy significantly reduced the risk of disease progression or death and improved overall survival (OS) compared with investigator-selected standard regimens in patients with relapsed or refractory multiple myeloma (RRMM) who received 1 to 3 previous lines of therapy, according to interim findings from the phase 3 MajesTEC-9 trial (NCT05572515) published in The New England Journal of Medicine.[1,2]

At a median follow-up of about 17.3 months, teclistamab reduced the risk of disease progression or death by approximately 71% compared with pomalidomide, bortezomib, and dexamethasone (PVd) or carfilzomib and dexamethasone (Kd; HR, 0.29; 95% CI, 0.23-0.38; $P < .001$). The estimated progression-free survival (PFS) rate at 18 months was approximately 69.8% with teclistamab compared with 26.9% with PVd or Kd. Median PFS was not reached with teclistamab and was 8.2 months in the control group.[1]

MajesTEC-9 Evaluates Teclistamab Earlier in the Treatment Course

The international, open-label phase 3 trial randomly assigned 593 patients to teclistamab (n = 296) or investigator's choice of PVd or Kd (n = 297). Participants received 1 to 3 prior lines of antimyeloma therapy—including previous treatment with lenalidomide and an anti-CD38 monoclonal antibody—and either experienced disease progression or failed to respond to their most recent regimen. Prior B-cell maturation antigen (BCMA)-directed treatment was not permitted.[1,2]

The median patient age was about 70 years, with approximately 29% of enrolled patients being 75 years of age or older. Patients received a median of 2 prior treatment lines, and the population demonstrated substantial treatment resistance—80% had lenalidomide-refractory disease, 85% were refractory to anti-CD38 therapy, and more than 90% were refractory to their most recent line of treatment.[1]

Teclistamab is a bispecific antibody that simultaneously targets BCMA on myeloma cells and CD3 on T cells, redirecting T-cell activity toward malignant plasma cells.[3] Earlier MajesTEC-1 findings established the activity of teclistamab in heavily pretreated RRMM, with an overall response rate of approximately 63%.[4]

Deep Responses Accompany Survival Benefit

In addition to the improvement in PFS, teclistamab produced substantially deeper responses than the comparator regimens. A complete response or better occurred in 65.9% of patients receiving teclistamab compared with 16.8% receiving PVd or Kd ($P < .001$). Overall response rates were 84.5% and 54.2%, respectively.[1]

Median duration of response was not reached in the teclistamab group compared with 13.4 months with PVd or Kd.[1]

An OS benefit was also observed. The estimated 18-month OS rate was 79.2% with teclistamab compared with 68.6% with PVd or Kd, corresponding to a 40% reduction in the risk of death (HR, 0.60; 95% CI, 0.43-0.83; *P* = .002). Median OS had not been reached in either group at the interim analysis. Teclistamab also significantly delayed worsening of multiple myeloma–associated symptoms.[1]

Infection Risk Remains Central to Teclistamab Management

The efficacy benefit was accompanied by a higher burden of serious toxicity. Grade 3 or 4 adverse events (AEs) occurred in 84.9% of patients treated with teclistamab compared with 76.3% receiving PVd or Kd, and serious AEs occurred in 56.7% and 45.6%, respectively. Neutropenia was the most common grade 3 or 4 AE, affecting approximately 54.3% and 22.3% of patients, respectively.[1]

Grade 3 or 4 infections occurred in 41.6% of teclistamab-treated patients compared with 29.0% of controls, and fatal infections occurred in 5.5% and 2.8%, respectively.[1] Investigators emphasized antimicrobial prophylaxis, infection surveillance, and immunoglobulin replacement when indicated. Current FDA labeling similarly warns that teclistamab can cause severe, life-threatening, or fatal infections.[3]

Cytokine release syndrome occurred in 66.0% of patients receiving teclistamab and was predominantly grade 1 or 2. Two patients experienced grade 3 events. Immune effector cell–associated neurotoxicity syndrome occurred in 4.1%, with most events grade 1 or 2.[1]

Findings Could Expand the Role of BCMA-Directed Bispecific Therapy

The findings provide randomized phase 3 trial data supporting BCMA-directed bispecific therapy considerably earlier in the RRMM treatment course than teclistamab monotherapy is approved for in the US. Teclistamab is currently FDA approved as monotherapy after at least 4 prior lines of therapy and, in combination with daratumumab and hyaluronidase-fihj, after at least 1 prior line containing a proteasome inhibitor and immunomodulatory agent.[3]

MajesTEC-9 supports further consideration of teclistamab monotherapy beginning as early as first relapse, but the findings underscore the importance of infection prevention and monitoring when integrating bispecific antibodies earlier in treatment.[1]

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