Belantamab Mafodotin Triplets Versus Active-Control Triplets in Relapsed or Refractory Multiple Myeloma

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INTRODUCTION

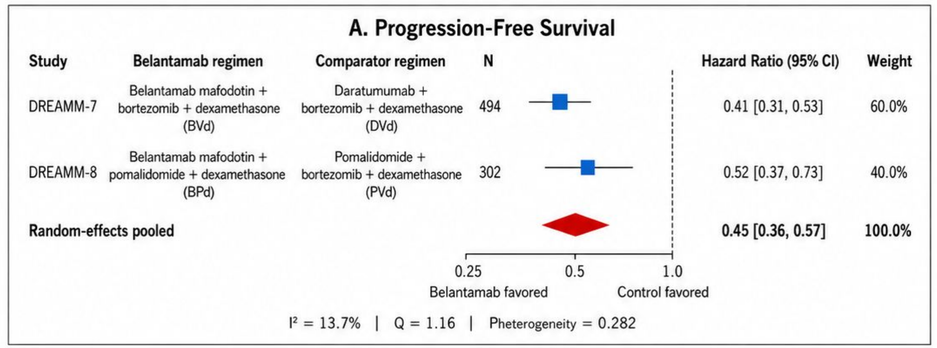
Belantamab mafodotin is a B-cell maturation antigen (BCMA)-directed antibody-drug conjugate that has reemerged as an effective treatment strategy in relapsed/refractory multiple myeloma (RRMM) following positive phase 3 combination trials. DREAMM-7 and DREAMM-8 demonstrated significant clinical activity with belantamab-containing triplets compared with active-control regimens. However, the magnitude and consistency of benefit across these pivotal trials have not been quantitatively synthesized. We therefore performed a meta-analysis evaluating the efficacy and safety of belantamab mafodotin-containing triplets versus active-control triplets in RRMM.

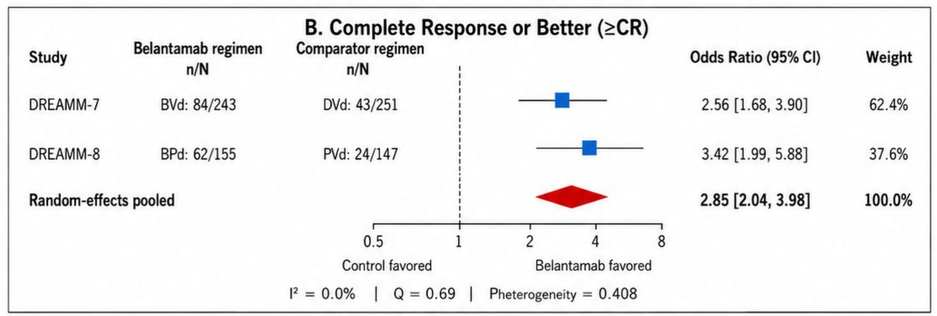
METHODS

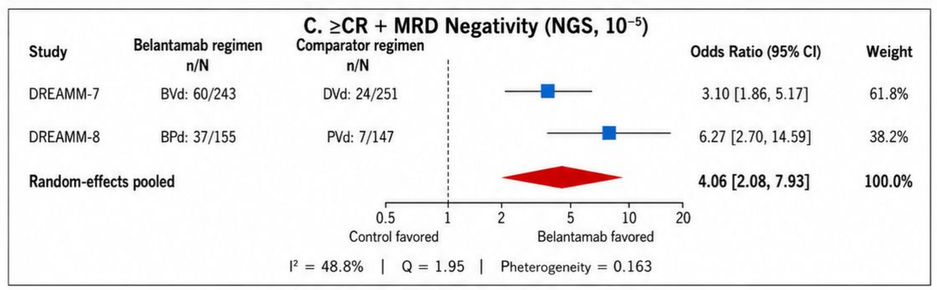
We conducted a systematic review and pairwise meta-analysis of randomized phase 3 trials evaluating belantamab mafodotin-containing triplets versus active-control triplets in adults with RRMM after ≥1 prior line of therapy. Two eligible trials were identified: DREAMM-7 and DREAMM-8. DREAMM-7 compared belantamab mafodotin + bortezomib + dexamethasone (BVd) with daratumumab + bortezomib + dexamethasone (DVd), while DREAMM-8 compared belantamab mafodotin + pomalidomide + dexamethasone (BPd) with pomalidomide + bortezomib + dexamethasone (PVd). The primary outcome was progression-free survival (PFS). Secondary outcomes included depth of response, MRD negativity, and ocular toxicity. Hazard ratios were pooled using an inverse-variance random-effects model, with heterogeneity assessed using the I^2 statistic.

Figure 1. Random-Effects Meta-analysis of Belantamab Mafodotin Triplets in RRMM

DREAMM-7 and DREAMM-8 | 2 phase III randomized trials | 796 patients







Inverse-variance random-effects models. PFS pooled on the log-hazard-ratio scale; binary efficacy outcomes pooled on the log-odds-ratio scale using published primary-analysis event counts. Abbreviations: BVd, belantamab mafodotin + bortezomib + dexamethasone; BPd, belantamab mafodotin + pomalidomide + dexamethasone; DVd, daratumumab + bortezomib + dexamethasone; PVd, pomalidomide + bortezomib + dexamethasone.

RESULTS

Two phase III randomized trials comprising 796 patients were included. Belantamab mafodotin-containing triplets significantly improved progression-free survival compared with active-control triplets, with a pooled HR of 0.45 (95% CI, 0.36–0.57; P<0.0001), corresponding to a 55% lower hazard of disease progression or death. Between-study heterogeneity was low (I^2=13.7%). Belantamab-based therapy was also associated with significantly greater depth of response. The pooled odds of achieving complete response or better (≥CR) were nearly threefold higher with belantamab-containing triplets (OR, 2.85; 95% CI, 2.04–3.98; I^2=0%). The effect was even greater for ≥CR with MRD negativity at 10^{-5}, with a pooled OR of 4.06 (95% CI, 2.08–7.93; I^2=48.8%). Ocular adverse events occurred more frequently with belantamab-containing regimens in both pivotal studies, reinforcing the need for ophthalmologic monitoring and dose modification.

CONCLUSIONS

Across two pivotal phase III trials, belantamab mafodotin-containing triplets demonstrated a substantial and consistent efficacy advantage over active-control triplets in RRMM, reducing the hazard of progression or death by approximately 55% while significantly increasing the likelihood of both complete response and MRD-negative complete response. The concordance of improved PFS and deeper responses across two distinct treatment backbones strengthens the evidence supporting belantamab mafodotin as a highly active, off-the-shelf BCMA-directed treatment strategy. Ocular toxicity remains the principal clinical tradeoff and necessitates proactive ophthalmologic monitoring and appropriate dose modification.