DREAMM-7: A Phase III Study of the Efficacy and Safety of Belantamab Mafodotin with Bortezomib and Dexamethasone (BVd) in Patients with Relapsed/Refractory Multiple Myeloma (RRMM)

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Background

Aim:
To evaluate the efficacy and safety of belantamab mafodotin (belamaf; BLENREP) plus Vd compared with Vd in patients with RRMM

Unmet need
Patients with heavily pre-treated RRMM have a poor prognosis (median OS: 6–9 months); novel, well-tolerated treatments that induce lasting responses are warranted1-2

Belamaf
• First-in-class BCMA–targeting ADC with multimodal mechanisms of action3 approved in the US and the EU4,5
• In the DREAMM-2 study, single-agent belamaf demonstrated deep and durable responses and a manageable safety profile in patients with heavily pre-treated RRMM6
• At 13 months of follow-up, responses with belamaf (2.5 mg/kg; IV Q3W) were sustained7
  • ORR was 32%
  • Estimated median DoR was 11.0 months
  • Estimated median OS was 13.7 months
• At the time of data cut-off,* 10% (10/97) patients remained on study treatment

Combination regimens
• Triple combination regimens, such as DVd, demonstrate potent anti-myeloma activity and are considered standard of care for patients with RRMM8 however, there remains an unmet need for novel treatments, and prospective studies comparing triple combination regimens are required9
• Pre-clinical data suggest increased anti-myeloma activity and survival with belamaf plus bortezomib (a PI) and/or dexamethasone treatment compared with single agents10
• Initial results from the ongoing Phase I/II DREAMM-6 study of BVd indicate an acceptable safety profile for the combination11

Belamaf Mechanisms of Action†

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ADC, antibody-drug conjugate; ADCC/P, antibody-dependent cellular cytotoxicity/phagocytosis; BCMA, B-cell maturation antigen; belamaf, belantamab mafodotin; BVd, belamaf plus bortezomib and dexamethasone; DoR, duration of response; DVd, daratumumab plus bortezomib and dexamethasone; IV, intravenously; ORR, overall response rate; PI, proteasome inhibitor; Q3W, every 3 weeks; RRMM, refractory and relapsed myeloma; Vd, bortezomib and dexamethasone.

Methods

The DREAMM-7 trial (NCT04246047) is an ongoing randomized, open-label, multi-center Phase III study evaluating the efficacy and safety of BVd (Arm A) compared with DVd (Arm B) in patients with RRMM.

### Study Design

**Stratification**
- Patients (~478) ≥1L RRMM

**Randomization**
- 1:1

**Arm A: BVd**
- Belamaf 2.5 mg/kg (IV)
- Bortezomib 1.3 kg/m² (SC)
- Dexamethasone 20 mg (IV/PO)

**Arm B: DVd**
- Daratumumab 16 mg/kg (IV)
- Bortezomib 1.3 kg/m² (SC)
- Dexamethasone 20 mg (IV/PO)

**Screening/ baseline**
- Week 1
- Week 2
- Week 3
- Cycle 1–3+
- Cycle 1–8

**Treatment until disease progression or unacceptable toxicity**
- Cycle 9+, Q4W

**Follow-up period**
- Follow-up for PFS (for patients who discontinue study drug for reasons other than disease progression)
- Disease assessments Q3W until disease progression, death, or start of new anti-cancer therapy

**Follow-up for OS (for patients who discontinue study drug due to disease progression)**
- Disease assessments every 3 months until disease progression, death, or start of new anti-cancer therapy

**End of treatment visit**
- Disease assessments Q3W until disease progression

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*Patients stratified based on number of previous lines of therapy (1 vs. 2/3 vs. ≥4), Revised Multiple Myeloma International Staging System (R-ISS; I vs. II/III), and prior bortezomib exposure (yes vs. no); *bortezomib and dexamethasone administered in Cycles 1–8; †daratumumab: Cycles 1–3, Q1W; Cycles 4–8, Q3W; Cycle 9+, Q4W; 1L, first line of treatment; ADA, anti-drug antibodies; belamaf, belantamab mafodotin; BVd, belamaf, bortezomib and dexamethasone; DVd, daratumumab, bortezomib and dexamethasone; IV, intravenously; OS, overall survival; PFS, progression-free survival; PO, orally; Q3W, every 3 weeks; RRMM, relapsed/refractory multiple myeloma; SC, subcutaneously.*
# Key Objectives and Endpoints

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*Defined as PFS after initiation of new anticancer therapy.

ADA, anti-drug antibody; AE, adverse event; belamaf, belantamab mafodotin; BVd, belamaf plus bortezomib and dexamethasone; cys-mcMMAF, cysteine-maleimidocaproyl monomethyl auristatin F; CRR, complete response rate; DoR, duration of response; DVd, daratumumab plus bortezomib and dexamethasone; EORTC, European Organization for Research and Treatment of Cancer; EORTC QLQ-C30, European Organization for Research and Treatment of Cancer Quality of Life Questionnaire; HRQoL, health-related quality of life; mAb, monoclonal antibody; MRD, minimal residual disease; ORR, overall response rate; OS, overall survival; OSDI, Ocular Surface Disease Index; PFS, progression-free survival; PFS2, PFS after initiation of new anti-cancer therapy; PRO-CTCAE, Common Terminology Criteria for Adverse Events (CTCAE) & Patient-Reported Outcomes-CTCAE; TTBR, time to best response; TTP, time to progression; TTR, time to response; Vd, bortezomib and dexamethasone; VGPR, very good partial response.
**Patient Population**

### Key inclusion criteria

- Age ≥18 years
- Confirmed diagnosis of MM (IMWG criteria)\(^1\)
- Measurable disease (according to serum and/or urine M-protein and/or serum free light chain levels)
- ECOG Performance Status 0–2
- ≥1 prior line of therapy\(^*\)
- History of autologous stem cell transplantation allowed if >100 days prior to initiation of study treatment and no active infections
- Acceptable organ system function
- Informed consent

### Key exclusion criteria

- Intolerance/refractoriness to daratumumab (or other anti-CD38 therapy) or bi-weekly regimen of bortezomib
- Prior exposure to anti-BCMA therapy
- Ongoing ≥Grade 2 peripheral neuropathy or neuropathic pain
- Prior treatment with other mAbs within 30 days, investigational agent or systemic anti-myeloma therapy within 14 days or 5 half-lives (whichever is shorter), plasmapheresis within 7 days of first dose of study drug, or radiotherapy to a large pelvic area
- Prior allogeneic transplant
- Major surgery within 4 weeks prior to the first dose of study drug
- Presence of active renal condition, mucosal or internal bleeding, cirrhosis or current unstable liver or biliary disease, infection, or HIV
- Other malignancies (except in patients who have been disease-free for >2 years or curatively treated non-melanoma skin cancer)
- Current corneal epithelial disease (except mild punctate keratopathy)
- Evidence of cardiovascular risk
- Hepatitis B surface antigen or hepatitis B core antibody present, or positive for hepatitis C at screening, or ≤3 months prior to first dose of study treatment

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\(^*\)Must have documented disease progression during or after the most recent therapy, according to IMWG criteria. No more than 50% of patients with ≥2 prior line of therapy will be enrolled.

BCMA, B-cell maturation antigen; belan, belantamab mafodotin; ECOG, Eastern Cooperative Oncology Group Performance Status; HIV, human immunodeficiency virus; IMWG, The International Myeloma Working Group; mAb monoclonal antibody; MM, multiple myeloma

As of November 2020, the study is enrolling in 15 countries worldwide\(^1\); 157 patients have been screened and 108 patients randomized.

Belamaf is being evaluated in other combination strategies in various MM settings (poster 1419, 2299, and 2302 at this meeting). Further analyses of the pivotal DREAMM-2 study of single-agent belamaf are presented at this meeting (posters 1417, 2278, 3221, 3224, 3248).

The BCMA-targeting MoA of belamaf supports combination with other therapies, including Vd, offering the potential for a manageable safety profile with enhanced efficacy.
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