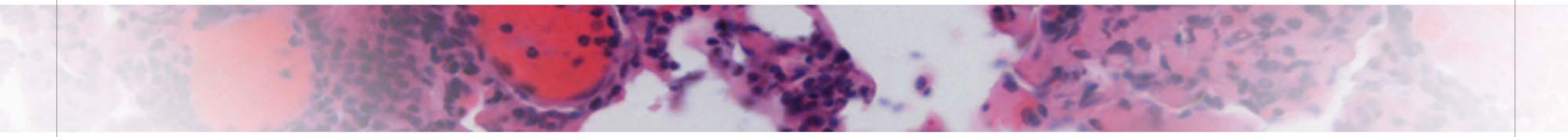
American Society of Hematology
Helping hematologists conquer blood diseases worldwide



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)

Robert Rifkin,[1] Kevin Boyd,[2] Sebastian Grosicki,[3] Kihyun Kim,[4] Francesco Di Raimondo,[5] Meletios Dimopoulos,[6] Katja Weisel,[7] Bertrand Arnulf,[8] Roman Hajek,[9] Vania Hungria,[10] Andrew Spencer,[11] Randy Davis,[12] Antonio Riccio,[13] Chanbin Kim,[14] Jodie Wilkes,[15] Ruth Rutledge,[16] Mala Talekar,[17] Brandon E. Kremer,[17] Ira Gupta,[17] María Victoria Mateos Manteca[18]

[1]Rocky Mountain Cancer Centers, Denver, CO, USA; [2]Royal Marsden Hospital, Sutton, UK; [3]School of Public Health, Medical University of Silesia, Katowice, Poland; [4]Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, South Korea; [5]Department of General Surgery and Medical-Surgical Specialties, University of Catania, Catania, Italy; [6]National and Kapodistrian University of Athens, Alexandra Hospital, Athens, Greece; [7]University Medical Center of Hamburg-Eppendorf, Hamburg, Germany; [8]Hôpital Saint-Louis, Paris, France; [9]Department of Hemato-Oncology, University Hospital, Ostrava, Czech Republic; [10]Clinica São Germano, São Paulo, Brazil; [11]Department of Clinical Haematology, Alfred Health-Monash University, Melbourne, VIC, Australia; [12]GlaxoSmithKline (GSK), Research Triangle Park, NC, USA; [13]GSK, Waltham, MA, USA; [14]GSK, Bethesda, MD, USA; [15]GSK, Stevenage, UK; [16]GSK, Lansdale, MN, USA; [17]GSK, Philadelphia, PA, USA; [18]University Hospital of Salamanca-Instituto de Investigación Biomédica de Salamanca, Cancer Research Center-IBMCC (USAL-CSIC), Salamanca, Spain

Poster No. 3247 | Presented at the 62nd American Society of Hematology Annual Meeting and Exposition (Virtual Format) | December 5–8, 2020

Background

Aim:
To evaluate the efficacy and safety of belantamab mafodotin (belamaf; BLENREP) plus Vd compared with DVd 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 warranted[1,2]

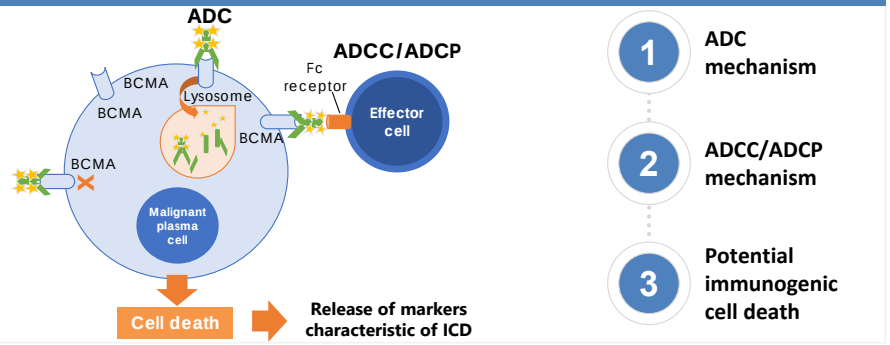
Belamaf

- First-in-class BCMA–targeting ADC with multimodal mechanisms of action[3] approved in the US and the EU[4,5]
- In the DREAMM-2 study, single-agent belamaf demonstrated deep and durable responses and a manageable safety profile in patients with heavily pre-treated RRMM[6]
- At 13 months of follow-up, responses with belamaf (2.5 mg/kg; IV Q3W) were sustained[7]
  - 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 RRMM;[8] however, there remains an unmet need for novel treatments, and prospective studies comparing triple combination regimens are required[9]
- Pre-clinical data suggest increased anti-myeloma activity and survival with belamaf plus bortezomib (a PI) and/or dexamethasone treatment compared with single agents[10]
- Initial results from the ongoing Phase I/II DREAMM-6 study of BVd indicate an acceptable safety profile for the combination[11]

Belamaf Mechanisms of Action†

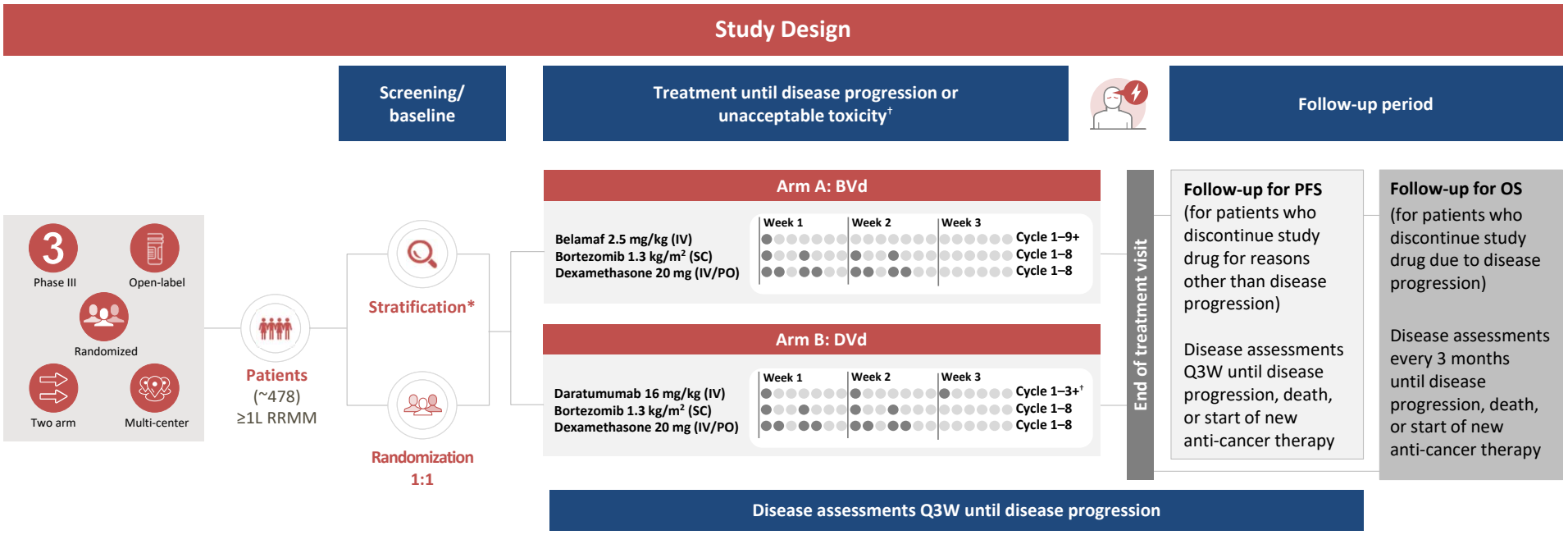


*Data cut: January 2020; †Image adapted from Richardson P, et al. Presented at the 61st Annual Meeting of the American Society of Hematology, December 7–10, 2019, Orlando, FL. Poster 1857.
ADC, antibody-drug conjugate, ADCC/P, antibody-dependent cellular cytotoxicity/phagocytosis; BCMA, B-cell maturation 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, relapsed/refractory multiple myeloma; Vd, bortezomib and dexamethasone.
1. Gandhi UH, et al. *Leukemia* 2019;33:2266; **2.** Chari A, et al. *N Eng J Med* 2019;381:727–38; **3.** Tai YT, et al. *Blood* 2014;123:3128; **4.** US Food and Drug Administration. BLENREP [Package Insert]. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/761158s000lbl.pdf [Accessed Oct 26, 2020]; **5.** European Medicines Agency. BLENREP SmPC. 2020. Available from: https://www.ema.europa.eu/en/medicines/human/EPAR/blenrep#authorisation-details-section [Accessed 26 Oct, 2020]; **6.** Lonial S, et al. *Lancet Oncol* 2020;21:207; **7.** Lonial S, et al. ASCO 2020 Poster 436; **8.** Palumbo A, et al. *N Engl J Med* 2016;375:754; **9.** Boundreault J, et al. *Expert Rev Hematol* 2017;10(3):207–21; **10**. Montes De Oca R, et al. AACR 2020 Poster 6711; **11**. Nooka A, et al. ASCO 2020 Oral 8502.

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



*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; DoR, duration of response; 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

Primary	
Objective	**Endpoint**
Compare the efficacy of BVd vs. DVd	PFS

Key Secondary	
Objective	**Endpoints**
Further assess clinical activity of BVd vs. DVd	MRD negativity rate

Secondary	
Objective	**Endpoints**
• Further assess clinical activity of BVd vs. DVd	• CRR, ORR, DoR, TTR, TTP, OS, PFS2*
• Characterize safety and tolerability of BVd	• AEs, changes in laboratory parameters, and ocular findings
• Further describe exposure to belamaf when administered with Vd	• Plasma concentrations, total mAb, and cys-mcMMAF
• Assess ADAs against belamaf	• Incidence and titers of ADAs
• Evaluate safety and tolerability of belamaf based on self-reported symptomatic AEs when administered with Vd	• Changes from baseline in symptoms and related impact, as measured by PRO-CTCAE
• Evaluate and compare changes in symptoms and HRQoL	• Change from baseline in HRQoL, as measured by EORTC QLQ-C30 and EORTC IL52

Key Exploratory	
Objective	**Endpoints**
• Further assess the efficacy of BVd vs. DVd	• TTBR, ≥VGPR rate
• Further assess the safety and tolerability of BVd	• Changes in safety assessments, including vital signs
• Evaluate self-reported ocular symptomatic AEs with BVd	• Changes from baseline in symptoms and related impacts, as measured by OSDI

*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 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

*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; belamaf, 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

1. Kumar S, et al. *Lancet Oncol* 2016;17:e328–46.

Current Status

As of November 2020, the study is enrolling in 15 countries worldwide[1]; 157 patients have been screened and 108 patients randomized

North America

- United States of America
- Canada

Europe

- Belgium
- France
- Italy
- Netherlands
- Poland
- Russia
- Spain
- United Kingdom

Asia

- China
- Israel
- South Korea

Australia and Oceania

- Australia
- New Zealand

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

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)

Belamaf; belantamab mafodotin; BCMA, B-cell maturation antigen; MoA, mode of action; MM, multiple myeloma

1. National Institutes of Health. 2020. Available from: https://clinicaltrials.gov/ct2/show/NCT04246047 [Accessed Oct 14, 2020]

Disclosures and Acknowledgements

This study was funded by GlaxoSmithKline (GSK; Study 207503). Drug linker technology licensed from Seagen Inc.; monoclonal antibody produced using POTELLIGENT Technology licensed from BioWa.

Editorial assistance was provided by Joanna Nikitorowicz-Buniak, of Fishawack Indicia Ltd. part of Fishawack Health, and funded by GSK.

KB has received consultancy fees and honoraria from Celgene, Janssen, and Takeda. **FDR** has received consultancy fees and honoraria from Amgen, Celgene, GSK, Janssen, and Takeda. **KW** has received consultancy fees and honoraria from Adaptive, Amgen, BMS, Celgene, GSK, Janssen, Karyopharm, Sanofi, and Takeda, and research funding from Amgen, Celgene, Janssen, and Sanofi. **BA** has received consultancy fees and honoraria from Amgen, BMS, GSK, Janssen, Sanofi, and Takeda, research funding from Celgene and Janssen, and is on advisory board of Takeda. **RH** has received consultancy fees and honoraria from AbbVie, Amgen, BMS, Celgene, Janssen, Novartis, Pharma MAR, and Takeda, research funding from Amgen, BMS, Celgene, Janssen, Novartis, and Takeda, and is on advisory board of Amgen and Takeda. **VH** has received consultancy fees from AbbVie, Amgen, BMS, Celgene, Janssen, Sanofi, and Takeda, and is on advisory board of Amgen, BMS, Celgene, Janssen, Sanofi, and Takeda. **RD**, **AR**, **CK**, **JW**, **RRuth**, **MT**, **BEK**, and **IG** are employees of and hold stocks and shares in GSK. **MVMM** has received consultancy fees and honoraria from AbbVie, Amgen, Celgene, GSK, Janssen, Pharmamar-seltia, and Takeda. **RRif**, **SG**, **KK**, **MD**, and **AS** declared no conflict of interest**.**

Presenting author contact: robert.rifkin@usoncology.com

BMS, Bristol-Myers Squibb; GSK, GlaxoSmithKline