DREAMM-2: Single-agent Belantamab Mafodotin (GSK2857916) in Patients With Relapsed/Refractory Multiple Myeloma (RRMM) and Renal Impairment

Poster No. 419

Hans Chulhee Lee[1*], Adam D Cohen[2], Ajai Chari[3], Malin Hultcrantz[4], Ajay K Nooka[5], Natalie Scott Callander[6], Attaya Suvannasankha[7], Ashraf Badros[8], Edward N Libby[9], Suzanne Trudel[10], Paul G Richardson[11], Douglas Weston Sborov[12], Paula Rodriguez Otero[13], Sagar Lonial[5], Eric Zhi[14], Eric Lewis[15], Ira Gupta[14], Joanna Opalinska[14]

[1]MD Anderson Cancer Center, Houston, TX, USA; [2]Abramson Cancer Center, University of Philadelphia, Philadelphia, PA, USA; [3]Icahn School of Medicine at Mount Sinai, New York, NY, USA; [4]Memorial Sloan Kettering Cancer Center, New York, NY, USA; [5]Emory University Hospital, Winship Cancer Institute, Atlanta, GA, USA; [6]University of Wisconsin, Carbone Cancer Center, Madison, WI, USA; [7]Indiana University Simon Cancer Center and Indiana University School of Medicine, Indianapolis, IN, USA; [8]University of Maryland at Baltimore, Baltimore, MD, USA; [9]Division of Medical Oncology, University of Washington, Seattle, WA, USA; [10]Princess Margaret Cancer Centre, Toronto, ON, Canada; [11]Dana Farber Cancer Institute, Boston, MA, USA; [12]Huntsman Cancer Institute, University of Utah, Salt Lake City, UT, USA; [13]Clínica Universidad de Navarra-Pamplona, Navarra, Spain; [14]GlaxoSmithKline, Upper Providence, PA, USA; [15]GlaxoSmithKline, Research Triangle Park, NC, USA

Background

Belantamab mafodotin (belamaf; GSK2857916) is a first-in-class B-cell maturation antigen (BCMA)-binding, humanized, afucosylated, monoclonal antibody-drug conjugate with a multimodal mechanism of action.[1,2]

DREAMM-2 (NCT03525678): Three-weekly (Q3W) intravenous dosing of single-agent belamaf demonstrated deep and durable responses and was well tolerated with an acceptable safety profile in heavily pretreated patients with relapsed/refractory multiple myeloma (RRMM).[3]

Of the 196 heavily pretreated patients with RRMM included in the DREAMM-2 study, results were:[3]

- belamaf 2.5 mg/kg: overall response rate (ORR) 31% (97.5% confidence interval [CI] 20.8–42.6); median progression-free survival (PFS) 2.9 months (95% CI 2·1–3·7); median duration of response (DoR) not reached;
- belamaf 3.4 mg/kg: ORR 34% (95% CI 23.9–46.0); median PFS 4.9 months (95% CI 2.3–6.2); median DoR not reached.

This was sustained during 13 months' follow-up.[4]

Belamaf is not metabolized by the kidney (data on file).

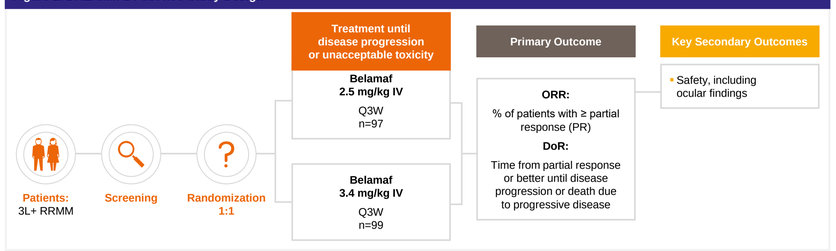
Renal impairment is a frequent complication and poor prognostic factor in RRMM, which may limit treatment with standard regimens.[5]

Additional well-tolerated therapies for patients with RRMM and renal failure are needed.

Aim

To report results from a DREAMM-2 post hoc analysis, assessing outcomes of patients with renal impairment receiving single-agent belamaf (2.5 or 3.4 mg/kg).

Figure 1. DREAMM-2 Post hoc Study Design[3]



3L+, ≥3 prior lines of therapy; IV, intravenous.

Methods

Study design

Details of the DREAMM-2 study design (**Figure 1**) have been previously published.[3] Here, we report outcomes in a subgroup of patients with renal impairment from the DREAMM-2 9-month follow-up. Renal function was assessed according to estimated glomerular filtration rate (eGFR), and categorized as:

- normal (≥90 mL/min/1.73 m^2);
- mildly impaired (≥60–<90 mL/min/1.73 m^2); or
- moderately impaired (≥30–<60 mL/min/1.73 m^2).

Study population

Eligibility for this study was as reported previously.[3]

Key inclusion criteria were:

- age ≥18 years;
- confirmed diagnosis of RRMM;
- no active renal conditions (albumin/creatinine ratio <500 mg/g);
- normal or mildly/moderately impaired renal function based on eGFR (≥30 mL/min/1.73 m^2);
- ≥3 prior lines of therapy and refractory to immunomodulatory agents and proteasome inhibitors, and refractory to/intolerant of an anti-CD38 antibody.

Study endpoints

Efficacy endpoints were assessed according to International Myeloma Working Group (IMWG) 2016 criteria[6] and included ORR, DoR and PFS.

Safety was assessed by adverse events (AEs), which were graded by the investigator according to the National Cancer Institute-Common Toxicity Criteria for Adverse Events (NCI-CTCAE) v4.03.[7] Baseline and subsequent ophthalmic examinations were performed predose and Q3W by an ophthalmologist (or an optometrist if an ophthalmologist was not available) as described previously.[3]

Results

Patient demographics and baseline characteristics

- Patient demographics and baseline characteristics are reported in **Table 1**.
- In general, sex, age, and the number of patients with high-risk cytogenetics differed across renal impairment sub-groups and in both dose cohorts.
- Median prior lines of therapy were balanced across groups.
- Patients in this study predominantly had mild baseline renal impairment (eGFR ≥60–<90 mL/min/1.73 m^2), but approximately one-quarter had moderate impairment (eGFR ≥30–<60 mL/min/1.73 m^2).

Results

Table 1. Patient Demographics and Baseline Characteristics

	Belamaf 2.5 mg/kg				Belamaf 3.4 mg/kg			
	Total (N=97)*	Normal renal function (n=19)	Mild renal impairment (n=48)	Moderate renal impairment (n=24)	Total (N=99)*	Normal renal function (n=17)	Mild renal impairment (n=52)	Moderate renal impairment (n=22)
Sex; n (%)								
Female	46 (47)	8 (42)	26 (54)	11 (46)	43 (43)	2 (12)	22 (42)	14 (64)
Male	51 (53)	11 (58)	22 (46)	13 (54)	56 (57)	15 (88)	30 (58)	8 (36)
Age, years; median (interquartile range)	65.0 (60–70)	63.0 (39–74)	66.0 (40–85)	68.0 (45–85)	67.0 (61–72)	59.0 (44–75)	68.0 (34–84)	70.5 (53–81)
Prior lines of therapy; median (range)	7.0 (3–21)	6.0 (4–10)	7.0 (3–12)	7.0 (3–21)	6.0 (3–21)	6.0 (3–13)	7.0 (3–13)	6.0 (4–21)
High-risk cytogenetics†; n (%)	26 (27)	3 (16)	13 (27)	9 (38)	33 (33)	5 (29)	20 (38)	6 (27)

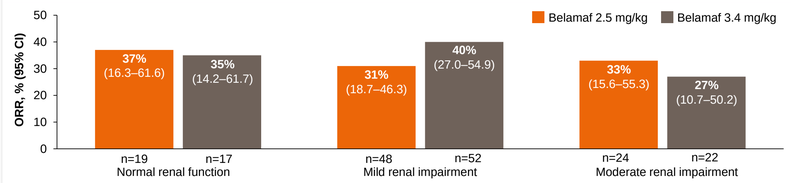
eGFR categorized as normal (≥90 mL/min/1.73 m^2), mildly impaired (≥60–<90 mL/min/1.73 m^2), or moderately impaired (≥30–<60 mL/min/1.73 m^2). *Total N=196 in the intent-to-treat population including patients with severe renal impairment (eGFR ≥15–<30 mL/min/1.73 m^2, n=7) or missing data (n=7); †high risk defined as patients with any of the following cytogenetics: t(4;14), t(14;16) and 17p13del.

Efficacy

Belamaf demonstrated efficacy in patients with mild or moderate renal impairment.

- ORRs were similar in patients with or without renal impairment (**Figure 2**).
- The median DoR (95% CI estimate) was not reached in patients with mild or moderate impairment in the 2.5-mg/kg cohort but in patients with moderate impairment was 5.6 months (2.3–not reached) in the 3.4-mg/kg cohort. For patients with normal renal function receiving the 2.5- or 3.4-mg/kg dose, the median DoR (95% CI) was 4.2 months (1.4–not reached) and 6.2 months (2.1–not reached), respectively.
- The median PFS (95% CI estimate) were similar in patients with or without renal impairment.
  - In the belamaf 2.5-mg/kg cohort: 2.2 months (2.1–3.6) and 3.7 months (1.0–not reached) in the mild and moderate impairment sub-groups, respectively, compared with 3.0 months (1.3–6.2) in the normal renal function sub-group. In the belamaf 3.4-mg/kg cohort: 3.9 months (1.4–6.9) and 3.4 months (0.8–6.4) in the mild and moderate impairment sub-groups, respectively, compared with 2.8 months (1.3–7.3) in the normal renal function sub-group.

Figure 2. ORR in patients with normal renal function or mild or moderate renal impairment



eGFR categorized as normal (≥90 mL/min/1.73 m^2), mildly impaired (≥60–<90 mL/min/1.73 m^2), or moderately impaired (≥30–<60 mL/min/1.73 m^2).

Safety

Overall rates of AEs were similar among all groups (**Table 2**).

- Keratopathy (microcyst-like epithelial changes [MECs], changes in the corneal epithelium observed on eye examination) was the most frequently reported AE in both dose groups, irrespective of renal function.
- Rates of keratopathy (MECs) and albuminuria were similar, regardless of renal function.
- Overall rates of anemia, pyrexia, and thrombocytopenia were higher in patients with mildly or moderately impaired renal function than in those with normal renal function.
- Few patients developed signs of active renal conditions (albumin creatinine ratio ≥500 mg/g): n=1/45 and n=2/37 in the mild impairment sub-group; n=2/20 and n=5/20 in the moderate impairment sub-group for belamaf 2.5 and 3.4 mg/kg, respectively.
- Worsening of renal function (defined as eGFR decrease to ≤60 mL/min/1.73 m^2) was observed in ≤26% of patients, irrespective of renal function across both dose cohorts.
- Three fatal treatment-related serious AEs were reported: 1 patient with normal renal function in the belamaf 2.5-mg/kg cohort due to sepsis, and 2 patients with mild renal impairment in the belamaf 3.4-mg/kg cohort due to cerebral hemorrhage and hemophagocytic lymphohistiocytosis.

Overall Grade 3–4 AEs were comparable across all groups (**Table 3**).

- Keratopathy (MECs), thrombocytopenia, and anemia were the most frequently reported Grade 3–4 AEs across both dose groups, irrespective of renal function.

Table 2. Most Frequent AEs (≥25% in any Group), Serious AEs, and Renal Laboratory Changes According to Renal Function

	Belamaf 2.5 mg/kg			Belamaf 3.4 mg/kg		
	Normal renal function (n=19)	Mild renal impairment (n=48)	Moderate renal impairment (n=24)	Normal renal function (n=18)	Mild renal impairment (n=52)	Moderate renal impairment (n=22)
Hematologic AEs*						
Anemia	1 (5)	13 (27)	7 (29)	5 (28)	21 (40)	12 (55)
Thrombocytopenia	3 (16)	11 (23)	6 (25)	6 (33)	26 (50)	12 (55)
Non hematologic AEs*						
AST increased	5 (26)	12 (25)	2 (8)	1 (6)	16 (31)	6 (27)
Constipation	NR	4 (8)	8 (33)	1 (6)	6 (12)	2 (9)
Cough	2 (11)	6 (13)	2 (8)	2 (11)	5 (10)	10 (45)
Diarrhea	1 (5)	8 (17)	3 (13)	1 (6)	7 (13)	6 (27)
Epistaxis	4 (21)	2 (4)	1 (4)	1 (6)	8 (15)	10 (45)
Fatigue	5 (26)	9 (19)	1 (4)	3 (17)	14 (27)	6 (27)
Headache	5 (26)	3 (6)	2 (8)	1 (6)	7 (13)	4 (18)
Hypercalcemia	1 (5)	5 (10)	5 (21)	NR	9 (17)	7 (32)
Infusion-related reaction	2 (11)	7 (15)	7 (29)	2 (11)	5 (10)	3 (14)
Nausea	5 (26)	10 (21)	7 (29)	4 (22)	16 (31)	9 (41)
Pyrexia	2 (11)	9 (19)	9 (38)	3 (17)	17 (33)	5 (23)
Vomiting	2 (11)	3 (6)	1 (4)	4 (22)	7 (13)	7 (32)
URTI	1 (5)	5 (10)	2 (8)	2 (11)	9 (17)	6 (27)
Ocular AEs*						
Dry eye	1 (5)	9 (19)	1 (4)	3 (17)	7 (13)	8 (36)
Keratopathy (MECs)	18 (95)	33 (69)	15 (63)	14 (78)	40 (77)	14 (64)
Vision blurred	4 (21)	10 (21)	4 (17)	5 (28)	13 (25)	7 (32)
Serious AEs	7 (37)	16 (33)	12 (50)	8 (44)	25 (48)	11 (50)
Renal laboratory changes						
Renal impairment defined by increased albumin creatinine ratio†; n/N (%)	2/14 (14)	1/45 (2)	2/20 (10)	3/14 (21)	2/37 (5)	5/20 (25)
Renal impairment defined by eGFR worsening‡; n/N (%)	1/6 (17)	7/27 (26)	1/16 (6)	2/16 (13)	9/35 (26)	0/14 (0)

eGFR categorized as normal (≥90 mL/min/1.73 m^2), mildly impaired (≥60–<90 mL/min/1.73 m^2), or moderately impaired (≥30–<60 mL/min/1.73 m^2). *Number of patients (%) with AE by preferred term; †patients with albumin/creatinine ratio ≥500 mg/g at baseline; ‡decrease to ≤60 mL/min/1.73 m^2. AST, aspartate aminotransferase; NR, not reported; URTI, upper respiratory tract infection.

Table 3. Most Frequent Grade 3–4 AEs (≥10% in any Group)

	Belamaf 2.5 mg/kg			Belamaf 3.4 mg/kg		
Grade 3–4 AE; n (%)	Normal renal function (n=19)	Mild renal impairment (n=48)	Moderate renal impairment (n=24)	Normal renal function (n=18)	Mild renal impairment (n=52)	Moderate renal impairment (n=22)
Hematologic AEs						
Anemia	1 (5)	9 (19)	6 (25)	5 (28)	13 (25)	9 (41)
Lymphocyte count decreased	2 (11)	8 (17)	2 (8)	NR	5 (10)	2 (9)
Neutropenia*	2 (11)	4 (8)	3 (13)	3 (17)	8 (15)	4 (18)
Thrombocytopenia†	2 (11)	9 (19)	6 (25)	5 (28)	16 (31)	11 (50)
Non hematologic AEs						
AST increased	2 (11)	0 (0)	0 (0)	0 (0)	7 (13)	1 (5)
Fatigue	0 (0)	1 (2)	1 (4)	2 (11)	2 (4)	0 (0)
Hypercalcemia	0 (0)	3 (6)	3 (13)	NR	2 (4)	1 (5)
Hypertension	0 (0)	0 (0)	3 (13)	1 (6)	4 (8)	2 (9)
Hypoxia	NR	NR	NR	2 (11)	NR	1 (5)
Infection-related reaction‡	4 (21)	6 (13)	5 (21)	5 (28)	14 (27)	6 (27)
Infusion-related reaction§	0 (0)	0 (0)	3 (13)	0 (0)	0 (0)	1 (5)
γ-glutamyltransferase increased	1 (5)	2 (4)	1 (4)	1 (6)	4 (8)	3 (14)
Ocular AEs						
Eye disorders¶	8 (42)	13 (27)	8 (33)	5 (28)	15 (29)	4 (18)
Keratopathy (MECs)**	8 (42)	12 (25)	8 (33)	5 (28)	13 (25)	4 (18)

*Includes preferred terms neutropenia, febrile neutropenia, and neutrophil count decreased; †includes preferred terms thrombocytopenia, platelet count decreased and cerebral haemorrhage; ‡includes preferred terms pneumonia, pneumonia influenza, pneumonia legionella, influenza, pneumonia respiratory syncytial viral, brain abscess, nocardiosis, respiratory tract infection, lower respiratory tract infection, upper respiratory tract infection, staphylococcal infection, staphylococcal bacteraemia, sepsis, staphylococcal sepsis, Escherichia sepsis, device-related sepsis, epiglottitis, otitis media, sinusitis, viral infection, device-related infection, vascular device infection, enterocolitis infectious, herpes simplex pneumonia, vaginitis gardnerella, Escherichia urinary tract infection, and cellulitis; §includes preferred terms infusion related reaction, lethargy, and pyrexia; ¶includes preferred terms keratopathy, vision blurred, visual acuity reduced, exophthalmos, glaucoma, ocular hyperaemia, ocular discomfort, keratitis, ulcerative keratitis, and visual impairment; **includes preferred terms keratopathy, keratitis, and ulcerative keratitis.

Conclusions

- Single-agent belamaf represents a new treatment option for patients with RRMM.
- The majority of patients included in this study had mild or moderate renal impairment, representing a common, real-world complication in patients with RRMM and a poor prognostic factor.
- Efficacy and safety of single-agent belamaf were similar in patients with renal impairment versus patients with normal renal function.
- ORR and DoR were similar to those observed in the overall DREAMM-2 population.
- Belamaf may represent an important new treatment in patients with RRMM and renal impairment.
- Further investigation of patients with renal impairment (particularly those with severe renal impairment) receiving single-agent belamaf is planned.

Disclosures

HCL received consulting fees from Takeda, Celgene, Adaptive Biotechnologies, Amgen, GlaxoSmithKline (GSK), Sanofi, and Janssen; and research funding from Takeda, Amgen, Daiichi Sankyo, Janssen, Celgene, and GSK. **ADC** received consulting fees from Celgene, Janssen Oncology, Oncopeptides, Kite Pharma, Takeda, Seattle Genetics, and GSK; personal expenses from GSK, Takeda, Celgene, and Janssen Oncology; and research funding from Novartis. **AC** received consulting fees from Celgene, Novartis, Amgen, Janssen Oncology, Seattle Genetics, Bristol-Myers Squibb, Karyopharm Therapeutics, Genzyme, Oncopeptides, Takeda, Antengene, GSK, and Secura Bio; and research funding from Celgene, Novartis, Janssen, Pharmacyclics, Amgen, Seattle Genetics, and Takeda. **MH** received consulting fees from Intellisphere, LLC; and research funding from Daiichi Sankyo, Amgen, and GSK. **AKN** received consulting fees from Amgen, Janssen Oncology, Celgene, Spectrum Pharmaceuticals, Bristol-Myers Squibb, GSK, Takeda, Oncopeptides, and Karyopharm Therapeutics; personal fees from GSK; and research funding from Amgen, Janssen Oncology, and Takeda. **NSC** received research funding from Cellectar. **AS** received consulting fees from GSK, Janssen, and Karyopharm Therapeutics; and personal fees from GSK, Janssen, BMS, and Celgene. **AB** received consulting fees from Amgen. **ENL** received consulting fees from Adaptive Biotechnologies, Akcea, and Pharmacyclics. **ST** received consulting fees from Celgene, Amge and GSK; honoraria from Celgene, Janssen, Takeda, Sanofi, Karyopharm and Amgen Canada; and research funding from Celgene, Janssen, Amgen, GSK, and Genentech. **PGR** received consulting fees from Celgene, Janssen, Takeda, Karyopharm Therapeutics, Oncopeptides, Sanofi, and Jazz Pharmaceuticals; and research funding from Celgene, Takeda, Bristol-Myers Squibb, and Oncopeptides. **DWS** received consulting fees, honoraria, and personal fees from Janssen. **PRO** received consulting fees from Celgene, Janssen, GSK, Kite, Sanofi, and AbbVie; and personal fees from Celgene. **SL** received consulting fees from Celgene, Bristol-Myers Squibb, Janssen Oncology, Novartis, GSK, Amgen, AbbVie, Takeda, Merck, and Juno Therapeutics; and research funding from Celgene, Bristol-Myers Squibb, and Takeda. **EZ** and **IG** are employees of GSK and have shares in GSK and Novartis. **EL** and **JO** are employees of and have shares in GSK.

Acknowledgments

This study was funded by GlaxoSmithKline (205678). Drug linker technology licensed from Seattle Genetics; monoclonal antibody produced using POTELLIGENT Technology licensed from BioWa.

Editorial assistance was provided by Muchaala Yeboah, PhD, of Fishawack Indicia Ltd and funded by GlaxoSmithKline.

References

1. Tai YT, et al. *Blood* 2014;123:3128–38; **2.** Tai YT & Anderson KC. *Immunotherapy* 2015;7:1187–99. **3.** Lonial S, et al. *Lancet Oncol* 2020;21:207–21; **4.** Lonial S, et al. ASCO 2020 Poster 436 **5.** Blade J, et al. Chapter 80: Multiple myeloma. In: Carreras E, et al. *The EBMT Handbook: Hematopoietic Stem Cell Transplantation and Cellular Therapies*. 7th ed. Cham (CH): Springer, 2019; **6.** Kumar S, et al. *Lancet Oncol* 2016;17:e328–46; **7.** Common Terminology Criteria for Adverse Events (CTCAE) v.4.03. https://evs.nci.nih.gov/ftp1/CTCAE/CTCAE_4.03/CTCAE_4.03_2010-06-14_QuickReference_8.5x11.pdf [Accessed April 8, 2020].

Please find the online version of the poster by scanning the Quick Response (QR) code or via http://tago.ca/ASCO_9

Copies of this poster obtained through QR Code are for personal use only and may not be reproduced without permission from ASCO® and the author of this poster.

Please find the online version of the plain language summary by scanning the QR code or via http://tago.ca/ASCO_22

Presented at the American Society for Clinical Oncology (ASCO) Congress, Virtual Scientific Program, May 29–31, 2020

***For questions, please contact the presenting author: HCLee@mdanderson.org**