Patient-Reported Experiences During and Following Treatment with Belantamab Mafodotin (Belamaf) for Relapsed/Refractory Multiple Myeloma (RRMM) in the DREAMM-2 Study (NCT03525678)

Laurie Eliason,[1] Julia Correll,[2] Mona Martin,[2] Anna Cardellino,[1] Joanna Opalinska,[1] Trisha Piontek,[1] Boris Gorsh,[1] Sandhya Sapra,[3] Rakesh Popat[4]

[1]GlaxoSmithKline, Upper Providence, PA, USA; [2]Evidera, Seattle, WA, USA;
[3]Value, Evidence and Outcomes, GlaxoSmithKline, Upper Providence, PA, USA;
[4]NIHR/University College London Hospital Clinical Research Facility, NHS Foundation Trust, London, UK

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Background

Patients with MM who are refractory to an immunomodulatory agent, a PI, and to an anti-CD38 mAb, are a population with a high unmet need given the poor prognosis in this setting.[1]

Single-agent belamaf (BLENREP) is a BCMA–binding ADC that has demonstrated durable responses with a manageable safety profile in heavily pretreated patients with RRMM.[1,2]

- With belamaf 2.5 mg/kg Q3W, median DoR was 11.0 months, median OS estimate was 13.7 months.[1]
- Belamaf 2.5 mg/kg is approved in the US and the EU for RRMM following ≥4 prior therapies.[3,4]

Insights gained from open-ended discussions with patients who are enrolled in clinical trials and taking experimental treatments can:

- Be used to help complement safety profiles, providing a greater understanding of the timing and severity of side effects.
- Contribute to improved study design and better inform future clinical trial implementation.[5]

Aim

Use qualitative patient interviews to gain an understanding of the patient experience, specifically with symptoms as a result of belamaf treatment in the DREAMM-2 study (NCT03525678), and the impact these symptoms had on overall HRQoL.

Methods

Patient Interviews in DREAMM-2

Patients were refractory to an immunomodulatory agent and PI, refractory and/or intolerant to an anti-CD38 mAb and received single-agent belamaf 2.5 or 3.4 mg/kg Q3W until disease progression or unacceptable toxicity.[2]

All patients were invited to participate in interviews at Cycle 4 of treatment and at end of treatment. If a patient discontinued treatment before Cycle 4, only one interview was conducted.

Interviews (duration: 45 minutes on average) were conducted in patients' native language via telephone, by trained qualitative research interviewers, and were audio recorded with permission obtained through informed consent.

Open-ended interview questions covered the patient symptom experience, treatment-related burden, and adverse events. Disease and treatment-related symptom severity and overall treatment satisfaction were rated on a 0–10 scale (0=not severe to 10=most severe/0=not at all satisfied to 10=extremely satisfied).

A mixed methods approach was used to combine qualitative data from the interviews with quantitative data derived from specific variables such as ratings of symptom severity and treatment satisfaction. Qualitative data was obtained from the conversational aspect of the interview and was coded from the interview transcripts. The coding process allowed the codes to be organized in groups by similarity of content or theme and then summarized by percentages.

Results

Baseline Demographics and Patient Characteristics

Patients enrolled in DREAMM-2 and taking part in the interviews were treated with a median of 6 prior therapies (**Table 1**).

The median time from MM diagnosis was 6.0 years; some patients were first diagnosed a year ago and others had been living with MM for up to 12 years (**Table 1**).

The ORR of interview participants was higher than that of the overall DREAMM-2 clinical study population, which had ORRs of 31/97 (32%) and 35/99 (35%) for the 2.5 and 3.4-mg/kg groups, respectively[1] (**Table 1**).

Table 1. Baseline Demographics and Patient Clinical Characteristics

	Before or at Cycle 4 interviews (n=104)	End of Treatment interviews (n=26)	Total (N=109)
Age at time of consent to interview, years			
Median (range)*	66.0 (40–89)	64.0 (46–89)	66.0 (40–89)
Time since first diagnosed with MM, years			
Median (range)	6.0 (1.1–12.1)	4.5 (4.1–9.1)	5.9 (1.1–12.1)
Prior lines of therapy			
Median (range)	6.0 (3–21)	6.0 (3–21)	6.0 (3–21)
Time on study treatment, weeks			
Median (range)†	24.9 (3–75)	40.7 (12–69)	25.3 (3–75)
ORR (sCR+CR+VGPR+PR), n (%)	59 (56.7)	22 (84.6)	62 (56.9)
Country of residence, n (%)			
United States	69 (66.3)	19 (73.1)	72 (66.1)
Spain	7 (6.7)	3 (11.5)	9 (8.3)
France	8 (7.7)	1 (3.8)	8 (7.3)
United Kingdom	7 (6.7)	1 (3.8)	7 (6.4)
Germany	6 (5.8)	2 (7.7)	6 (5.5)
Canada	5 (4.8)	--	5 (4.6)
Australia	1 (1.0)	--	1 (0.9)
Italy	1 (1.0)	--	1 (0.9)
Race detail, n (%)			
Black or African American	17 (16.3)	5 (19.2)	18 (16.5)
Asian – East Asian Heritage	1 (1.0)	0	1 (0.9)
Asian – South East Asian Heritage	2 (1.9)	0	2 (1.8)
White – Arabic/North African Heritage	2 (1.9)	0	2 (1.8)
White – White/Caucasian/European Heritage	80 (76.9)	21 (80.8)	84 (77.1)
Mixed Asian Race	1 (1.0)	0	1 (0.9)
Multiple	1 (1.0)	0	1 (0.9)

Data represents 13-month follow-up analysis (31 Jan 2020).
*Mean (SD) age at time of consent to interview, in years: 66.0 (9.1) for before or at Cycle 4 interviews, 65.4 (10.0) for end of treatment interviews, and 65.8 (9.1) for total; †Mean (SD) time on study treatment, in weeks: 30.7 (22.4) for before or at Cycle 4 interviews, 42.4 (15.8) for end of treatment interviews, and 30.8 (22.1) for total.

Interview Participation

In total, 130 qualitative interviews were conducted during the study at two possible timepoints.

A total of 109 unique patients (across both dose levels) completed interviews (Cycle 4 and end of treatment).

- A total of 104 (71+33) patients completed interviews before or at Cycle 4 and 58 patients (56%) in that group were identified as responders (i.e. had ≥partial response by IMWG criteria) to treatment (**Table 2**).

A total of 26 patients (across both dose levels) participated in the end of treatment interviews, of whom 21 had also participated in the Cycle 4 interviews (**Table 2**).

- Twenty-two patients (85%) completing end of treatment interviews were identified as responders to treatment.

Table 2. Interview Participant Timing and Treatment Response

Interview Timepoint*	Responders†, n	Non-Responders, n	Number of completed interviews at each timepoint, n
Interview before or at Cycle 4 (1st) interview	58	46	104
End of treatment (1st and only) interview	3	2	5
End of treatment (2nd) interview	19	2	21

Data represents 13-month follow-up analysis (31 Jan 2020).
*For each type of interview, interview windows are 21 days long, starting with Cycle 4 or end of treatment visit. †Responders had ≥partial response by IMWG criteria.

Disease Symptoms

Patients who were responders generally reported a decrease in symptom severity from the start of the study to the time of Cycle 4 interview (**Table 3**).

The Cycle 4 timepoint was chosen to capture an interim point of the study by which patients may have experienced treatment response and changes in disease- and treatment-related symptoms.

- Fatigue was the most frequently reported disease symptom (**Table 3**).
- In responders, bone pain was the most severely rated symptom at the start of the study, but patients reported a decrease in severity by Cycle 4 (**Table 3**).

Table 3. Severity Ratings* for the Most Commonly Reported Disease Symptoms† During Cycle 4 Interviews (n=104)

Symptom	Frequency, %	Responders (n=58)‡		Non-responders (n=46)	
		Mean (SD) severity rating (at start of study)	Mean (SD) severity rating (by Cycle 4 interview)	Mean (SD) severity rating (at start of study)	Mean (SD) severity rating (by Cycle 4 interview)
Fatigue	68	4.6 (2.5)	3.4 (2.4)	4.4 (2.1)	4.5 (2.4)
Neuropathy	43	4.5 (2.6)	3.7 (2.5)	3.9 (1.9)	2.8 (2.0)
Bone pain	37	6.9 (2.1)	3.6 (3.1)	4.9 (2.5)	4.4 (2.3)
Back pain	30	5.2 (2.5)	4.6 (2.9)	4.7 (2.7)	4.2 (2.8)
Weakness	22	4.4 (2.0)	4.1 (2.9)	5.4 (2.1)	4.8 (1.8)
Shortness of breath	21	4.0 (1.9)	2.7 (2.9)	4.1 (2.3)	4.1 (3.0)
Bruising or bleeding easily	16	5.2 (2.7)	2.7 (2.8)	2.8 (1.2)	2.6 (1.5)
Constipation	16	5.8 (2.2)	3.7 (2.3)	3.6 (1.9)	1.5 (1.8)

Data represents 13-month follow-up analysis (31 Jan 2020).
*Disease and treatment-related symptom severity was rated 0–10 (0=not severe;10=most severe); †Most commonly reported symptoms were reported by >15% of patients; ‡Responders had ≥partial response by IMWG criteria.

Treatment-Related Ocular Symptoms

As a known side effect, ocular symptoms were intentionally explored in more detail during the interviews and then summarized separately from other symptoms.

Patients interviewed at end of treatment reported decreased severity in ocular symptoms from the time symptoms were at their worst to the 2-week period prior to their interview (**Table 4**).

Visual impairment was the most commonly reported ocular symptom at both Cycle 4 and end of treatment interviews (**Table 4**).

Table 4. Most Commonly Reported Ocular Symptoms

Symptom	At Cycle 4 Interviews (n=104) Responders = 58 (56%)		At End of Treatment Interviews (n=26) Responders = 22 (85%)		
	Frequency, n (%)	Mean (SD) severity rating* (for symptom "at worst"† during study)	Frequency, n (%)	Mean (SD) severity rating* (for symptom "at worst"† during study)	Mean (SD) severity* (by end of treatment interview)
Visual impairment (includes poor vision, blurred vision, and sensitivity to light)	59 (57)	6.6 (2.6)	17 (65)	8.5 (1.6)	2.9 (2.4)
Eye irritation (includes irritated eyes, dry eyes, itchy eyes, and feeling that something is in the eye)	42 (40)	6.4 (2.0)	11 (42)	7.6 (2.0)	1.6 (2.4)
Eye pain (includes painful eyes, sore eyes, and burning)	12 (12)	6.6 (2.2)	4 (15)	6.6 (2.2)	0.0 (0.0)

Data represents 13-month follow-up analysis (31 Jan 2020).
*Disease and treatment-related symptom severity was rated 0–10 (0=not severe to 10=most severe); †Patients were asked to rate the severity of the symptom they thought was the worst for them during their time on the trial.

Impacts Experienced During Study

Some examples of how patients described improvements in their quality of life, ability to perform daily tasks, and emotional health during the study are shown in **Figure 1**.

Weighing the Risks and Benefits of Study Treatment

Patients had a variety of perspectives (some positive, some neutral, and some negative) regarding staying on study treatment despite new symptoms and the benefits and risks of continued belamaf treatment **(Figure 2).**

Figure 1. Patient Quotations Regarding Life Impacts of belamaf Treatment During the DREAMM-2 Study*

Improved Quality of Life

"Oh yes. I feel it. I mean I haven't felt this good in probably three years."

"I mean it's really helped my quality of life, I'm just really happy with it."

"It's given me some hope for the future and my general health I feel like it has improved."

Physical Functioning/Daily Activities

"I can do things. I can go up and down my steps now without having to sit and rest."

"I can feel my body getting a little stronger… just getting up off the chair without boosting myself up with my arms. I can do that now."

"I feel great. I've got great energy… I was thinking in the beginning I needed to do 1,500 to 2,500 and I've been as high as 10,000 [steps a day]"

Emotional Health

"…I thought I was at the end of my useful life… in my particular situation I'm probably going to get to walk my daughter down an aisle…without your drug that probably wouldn't happen."

"I'm hopeful every day that what I'm in right now is going to propel me toward my goal in life."

"I have noticed that my general health, my general demeanor, my general mindset have definitely improved."

*Taken from Cycle 4 interviews.

Figure 2. Patient Quotations Regarding Weighing the Risks and Benefits of belamaf Treatment During DREAMM-2 Study

Staying on Study Treatment Despite New Symptoms

"I make the call usually to push ahead because I'm out of options now. I've been through every standard treatment. So, it would only be trials, that's all I have available."

"I thought seriously about not continuing, and if there had been another drug for me at this point, approved and ready for me to get it, I might have stopped it, but there is not... so I just decided that I would just put up with not being able to see."

"No [never thought of stopping], knowing [side effects] were temporary, they come and go is not bothering – I'm more about staying alive. Except for my eyes I do feel better…so I'm all for it."

"My doctor has worried about the deposits on my eyes, but they don't really bother me… to me, I never really wanted to get out of the study. I just wanted to keep going because it's just had such a good effect on my numbers."

"It is working on the cancer right now so it seems to be a tradeoff...take the drug... put up with blurry vision and reassess down the road."

"So far, the thing that only happened is the blurry eyes, that's all... No [I didn't think about stopping]. It helps my pain...it works pretty good on my myeloma."

Weighing Risks & Benefits

"Aside from the eyes I had no other side effects, and I don't know if the eyes will recur or if they won't but even if they do, that's okay. I'd rather be alive. I'd rather be alive."

"There are side effects to absolutely any treatment you have and some of the treatments I've had have had much worse than this."

"It was either that [side effects] or go through the possibility of… light chains."

Treatment Satisfaction

Overall, patients reported being generally satisfied with their treatment at the interview.

- Responders reported high treatment satisfaction, while non-responders reported moderate satisfaction (**Figure 3**).

All 26 patients interviewed at the end of treatment indicated they had expected the ocular side effects they experienced.

Six patients considered stopping treatment due to their ocular symptoms; three of whom did stop treatment for this reason.

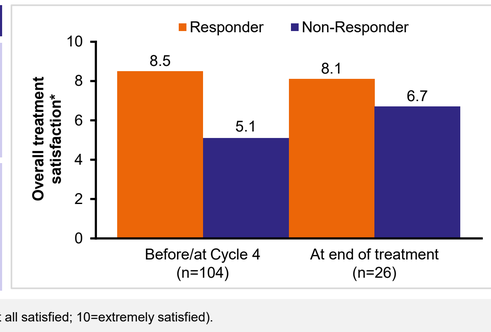
- Two patients specifically reported that their doctor discontinued treatment for this reason.

Figure 3. Patient Treatment Satisfaction*

Example responder quotes

"I'm tickled to death with what the treatment has done to my cancer. I mean it's dropped my levels tremendously."

"It's worth the side effects that I'm having for the eyes ... if I feel that I'm more in control of my body and the myeloma. I feel if I'm in control rather than it being in control of me."



Example non-responder quotes

"So far I'm satisfied because the doctors are doing everything they can... and I'm hoping for the best... not knowing one way or the other we'd have to go with a five then."

"Yeah, I'd give it a seven or eight or something like that. I mean it didn't work for me, but it might work for other people. Just because it didn't work for me don't mean it's [not] going to work for somebody else."

*Overall treatment satisfaction was rated 0–10 (0=not at all satisfied; 10=extremely satisfied).

Conclusions

Overall patient satisfaction with single-agent belamaf treatment in this heavily pretreated population, particularly in the context of the efficacy (median DoR: 11.0 months; median OS: 13.7 months) and manageable safety profile observed in DREAMM-2[1], supports the use of belamaf in patients with RRMM.

Trial-embedded interviews provide valuable insights into a patients' experience with their disease, the course of treatment-related side effects, and the overall impact on patient satisfaction with treatment.

Overall, responders to treatment reported meaningful improvement in key disease symptoms, including bone pain and fatigue.

Many patients reported some type of ocular symptom, but these were shown to improve by end of treatment.

Despite experiencing ocular symptoms, patients reported high satisfaction while on treatment and a desire to remain on treatment, particularly if they were responders.

Disclosures

LE, **AC**, **JO**, **TP**, **BG**, and **SS** are all employees of and shareholders in GlaxoSmithKline. **MM** and **JC** are employees of Evidera. **RP** received consulting fees from AbbVie, Celgene, GlaxoSmithKline, and Takeda; research funding from Takeda, honoraria from Celgene, GlaxoSmithKline, Janssen, and Takeda.

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Abbreviations

ADC, antibody-drug conjugate; BCMA, B-cell maturation antigen; belamaf, belantamab mafodotin; CR, complete response; DoR, duration of response; HRQoL, health-related quality of life; IMWG, International Myeloma Working Group; mAb, monoclonal antibody; MM, multiple myeloma; ORR, overall response rate; OS, overall survival; PI, proteasome inhibitor; PR, partial response; Q3W, every 3 weeks; RRMM, relapsed/refractory multiple myeloma; sCR, stringent complete response; SD, standard deviation; VGPR, very good partial response.

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Presenting author contact: laurie.j.eliason@gsk.com

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