Patient Reported Experience From Part 2 of the First Time in Human Study of the BCMA Antibody Drug Conjugate Belantamab Mafotodin (GSK2857916) for Advanced Relapsed Refractory Multiple Myeloma (DREAMM-1)

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Background

- Despite the introduction of immunomodulators and proteasome inhibitors, outcomes remain poor for patients with relapsed/refractory multiple myeloma (RRMM).[1]
- B-cell maturation antigen (BCMA) is expressed on MM cells.[2,3]
- Belantamab mafodotin (GSK2857916) is a novel anti-BCMA antibody conjugated to microtubule-disrupting agent monomethyl auristatin F.[4]
- The first-in-human study (DREAMM-1; BMA117159; NCT02064387) with belantamab mafodotin in patients with RRMM reported an overall response rate of 60%, and progression-free survival of 12.0 months (95% confidence interval 3.1 to not estimable).[5]
- Due to the encouraging clinical responses observed, we added a qualitative research component part way through the trial to provide a more in-depth understanding of patient experiences and inform strategies for future trials. Embedding this type of research in the trial design may increase the efficiency of the methodology.[6]

Aim

- Here, we report the evaluation of the patient-reported experience of belantamab mafodotin based on the daily bone pain and fatigue diaries and optional end of treatment (EOT) interviews from DREAMM-1.

Methods

Study design and patient population

- DREAMM-1 was an open-label, 2-part Phase I study conducted in 9 centres across the USA, Canada and UK in adults with MM and progressive disease after stem cell transplantation (or considered transplant ineligible), alkylators, proteasome inhibitors and immunomodulators.
  - In Part 1, the recommended dose of 3.4 mg/kg was identified; in Part 2, patients received belantamab mafodotin 3.4 mg/kg once every 3 weeks for up to 16 cycles (~1 year).
- During Part 2, patients were asked to complete bone pain and fatigue patient-reported outcomes diaries and optional EOT interviews, and 6-month follow-up interviews are ongoing.
- Due to the qualitative research being implemented via a protocol amendment, many patients were already off-study and unavailable for participation. The results reported here include an interim analysis of patient EOT interviews. The study is ongoing but closed for recruitment.

Bone pain and fatigue diaries

- Patients completed the diary at baseline and during treatment (Day 1–8 and 15 of each cycle).
- The diary consisted of three questions from the Brief Pain Inventory-Short Form and Brief Fatigue Inventory rated on a scale of 0 (no symptom) to 10 (as bad as you can imagine) and assessed:
  - Bone pain on average in the last 24 hours
  - Bone pain at worst in the last 24 hours
  - Fatigue level at worst in the last 24 hours.

EOT interviews

- Interviews were conducted by telephone at the end of study (within 3 weeks following EOT for 10/13 patients and 8 weeks for the remaining 3). Interviews at 6-month follow-up post EOT are ongoing.
- A semi-structured qualitative interview guide was developed at the onset of the study, with questions focusing on changes in disease and treatment-related symptoms, specifically corneal events, as well as impact of symptoms and daily functioning.
- Patients were asked to rate the severity of their symptoms during the study and within the 2 weeks prior to the interview on a scale of 0 (no symptom) to 10 (as bad as you can imagine) and to describe any changes in symptoms and their impacts.
- Patients were also asked to describe any other symptoms they experienced related to treatment, and discuss overall treatment satisfaction on a scale of 0–10.
- Interview transcripts were analysed using ATLAS.ti (version 7.1.0) software. A coding framework was developed to guide the qualitative analysis. Quantitative sociodemographic, clinical and symptom severity data were analysed descriptively.

Results

Patient demographics

- Nine of 35 patients completed the diary at baseline, and 13 participated in the EOT interviews. Patient demographics are summarised in **Table 1**.

Table 1. Summary of demographic data for diary and interview participants

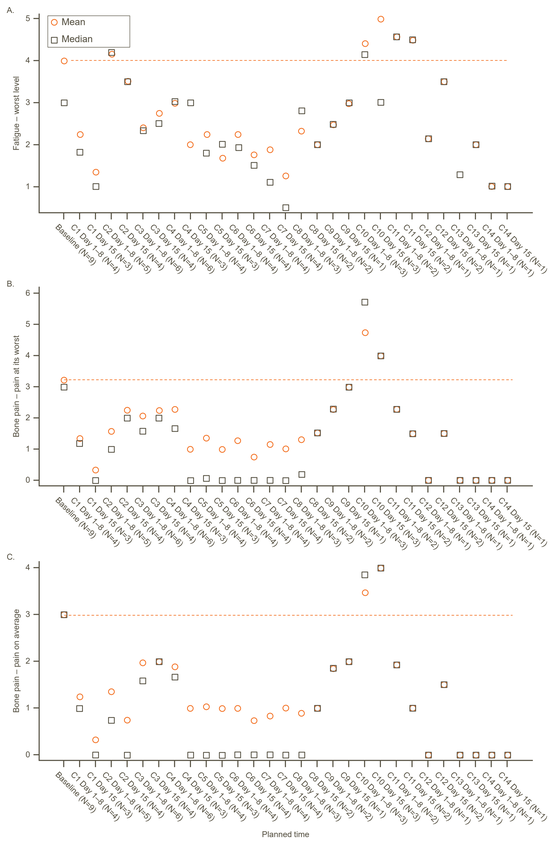
Demographic characteristic		Diary (n=9)	Interview (n=13)
Gender, n (%)	Female	6 (66.7)	7 (53.8)
	Male	3 (33.3)	6 (46.2)
Age at time of consent to interview, (years)	Mean (SD)	59 (6.0)	64 (6.3)
	Median	59	66
	Range	46–66	51–76
Years since diagnosis of multiple myeloma	Mean (SD)	4.1 (1.8)	8.7 (4.7)*
	Median	2.9	7.4
	Range	2.65–6.22	4.08–20.25

*Time since diagnosis data is patient reported for interview patients.
SD, standard deviation

Bone pain and fatigue diaries

- Overall mean scores for bone pain and fatigue severity decreased after baseline, ranging from 0 to 5 points out of 10 (**Figure 1**).
  - This study was limited by a small sample size, and implementation later in the trial; the increased values seen at Cycle 10 was driven by a single patient. Despite this, the results suggest that overall, patients experienced improvements in both fatigue and bone pain.

Figure 1. Mean (orange circles) and median (blue squares) for worst level of fatigue by cycle (A), worst level of pain by cycle (B) and average bone pain by cycle (C) from patient diaries. Dashed lines denote mean at baseline



EOT interviews

- Nearly all patients interviewed (n=12/13, 92%) experienced a partial response or greater by International Myeloma Working Group criteria (**Table 2**).
- Patients reported an improvement in mean severity of bone pain from 6.4 at study start to 4.0 at study end and an improvement in fatigue score from 8.0 to 5.5 (scale 0–10).
- The most commonly reported visual symptoms were blurred vision (n=8) and photophobia (n=7). At the time of the EOT interviews, the mean severity of all visual symptoms had reduced from their worst levels during the study (**Table 3**).
- Impacts include difficulty reading (n=10, 77%) and difficulty driving (n=9, 70%). Only 4 (31%) patients reported decreased independence while on treatment (**Table 4**).
- Overall, treatment satisfaction was very high (mean=8.1, median=9.0; scale 0–10).
- During the interviews, patients discussed visual impacts, quality of life and whether they considered stopping treatment (**Figure 2**).

Table 2. Individual patient characteristics for EOT interviews

Patient	Best confirmed response	Duration of response (months)	Number of dose reductions	Number of dose delays	Highest grade corneal event*	Last corneal event resolved?
1	PR	17.08	3	4	NA	NA
2	VGPR	10.61	3	5	2	No
3	VGPR	11.07	1	6	2	No
4	SD	NA	0	0	2	No
5	sCR	12.45	2	5	3	Yes
6	VGPR	14.29	2	2	3	No
7	VGPR	11.73	3	4	3	No
8	VGPR	13.08	3	4	2	Yes
9	VGPR	10.41	1	1	2	Yes
10	CR	9.69	0	0	1	Yes
11	PR	8.08	2	2	2	No
12	VGPR	12.16	2	5	2	No
13	PR	7.33	2	5	2	Yes

*Defined using CTCAE version 4.03.
CR, complete response; CTCAE, Common Terminology Criteria for Adverse Events; NA, not available; PR, partial response; sCR, stringent complete response; SD, stable disease; VGPR, very good partial response

Table 3. Visual symptoms reported by >1 patient and mean (range) symptom severity reported in EOT interviews.* Symptoms were scored on a 0 to 10-point scale; 0=not severe, 10=extremely severe

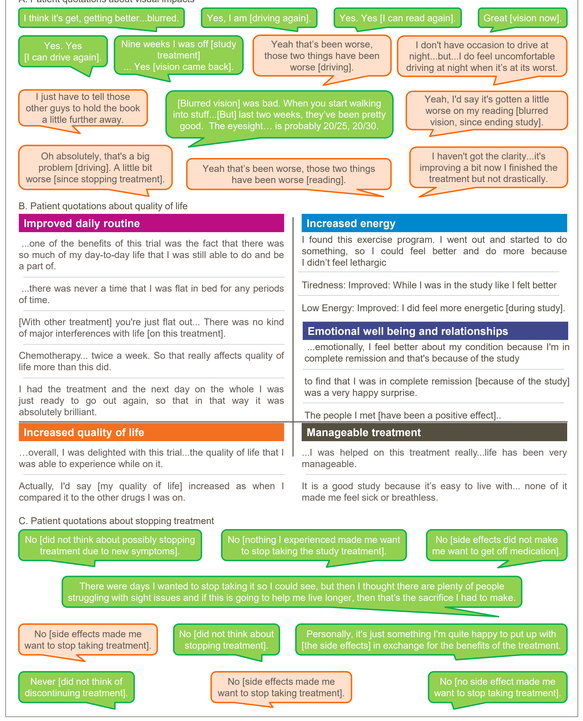
	Number of patients with symptom N=13 n (%)	How bad was the symptom at its worst during the study?	How bad was the symptom over past 2 weeks?	How much does it bother you when it occurs?
Blurred vision	8 (61.5)	7.3 (5–10)	5.3 (0–9)	6.1 (4–10)
Eyes that are sensitive to light	7 (53.8)	7.1 (5–10)	6.4 (4–9)	5.8 (4–10)
Itchy eyes	6 (46.2)	6.7 (5–8)	3.6 (0–6)	4.6 (4–5)
Dry eyes	5 (38.5)	6.8 (5–8)	3.0 (0–6)	4.8 (4–5)
Poor vision	5 (38.5)	6.8 (5–10)	6.3 (4–9)	5.8 (4–10)
Feeling that something is in the eye	4 (30.8)	7.3 (5–8)	4.0 (2–6)	4.7 (4–5)
Irritated eyes	4 (30.8)	7.5 (6–8)	4.7 (2–6)	4.7 (4–5)
Painful eyes	3 (23.1)	6.7 (5–8)	5.0 (4–6)	5.3 (4–7)
Burning	2 (15.4)	7.5 (6–9)	7.0 (6–8)	6.0 (4–8)

*Baseline data is not available.

Table 4. Impacts discussed by >4 patients in EOT interviews

	Spontaneously offered, N=13 n (%)	Offered after probe, N=13 n (%)	Patient said did not apply, N=13 n (%)
Difficulty reading	8 (61.5)	2 (15.4)	3 (23.1)
Difficulty driving	6 (46.2)	3 (23.1)	4 (30.8)
Decreased independence	4 (30.8)	0	3 (23.1)
Difficulty working on a computer	3 (23.1)	3 (23.1)	3 (23.1)
Impaired leisure activities: Travel	2 (15.4)	2 (15.4)	3 (23.1)
Decreased quality of life	0	4 (30.8)	3 (23.1)

Figure 2. Patient quotations regarding (A) visual impacts, (B) quality of life and (C) whether they considered stopping treatment



Conclusions

- Overall, patients treated with belantamab mafodotin 3.4 mg/kg once every 3 weeks as part of the DREAMM-1 study reported improvements in fatigue and bone pain based on patient diaries and EOT interviews, which is in keeping with the high response rate reported.
- Although most patients experienced visual symptoms, they were generally manageable and ongoing improvements were commonly reported after stopping treatment.
- Patients reported high levels of treatment satisfaction; treatment was described as manageable and having less impact on daily life compared with previous treatments.
- These data represent an interim analysis of the EOT interviews. Data from the 6-month follow-up interviews will provide further information on the status of symptoms and patient functioning.
- This study was limited by small sample sizes, but the combination of qualitative and quantitative data provided valuable preliminary insight into the patient experience of belantamab mafodotin, which will inform future studies regarding the impact of treatment on patient symptoms, functioning and tolerability.

References

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Disclosures

- RP: has received honoraria from Janssen, Takeda, Celgene and Amgen, GSK and travel support to attend meetings from Janssen, Takeda and Celgene. JO, LE, JW, GF and AB: employees of and stock/shareholders in GSK. JA: stock/shareholder in GSK. JC and MLM: were employees of Health Research Associates (HRA) at the time of this study. HRA received funding from GSK to conduct the interviews.

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