

Characterization of Ocular Adverse Events in Patients Receiving Belantamab Mafodotin (Belamaf) for ≥12 Months: Post-Hoc Analysis of DREAMM-2 Study in Relapsed/Refractory Multiple Myeloma

Poster No. MM–078

Introduction

Belantamab mafodotin (belamaf; GSK2857916) is a first-in-class, monomethyl auristatin F (MMAF)-containing antibody–drug conjugate (ADC) that binds to B-cell maturation antigen (BCMA) and eliminates multiple myeloma cells by a multimodal mechanism of action.¹

Belamaf is approved for the treatment of adult patients with heavily pretreated relapsed or refractory multiple myeloma (RRMM).^{2,3} Durable responses observed with single-agent belamaf were sustained at the 13-month analysis of the DREAMM-2 study (NCT03525678).⁴

– In patients receiving 2.5 mg/kg belamaf, the estimates for median duration of response and overall survival were 11 months and 13.7 months, respectively.⁴

Corneal events are a known side-effect of MMAF-containing ADCs.⁵

– In DREAMM-2, corneal events including keratopathy (superficial punctate keratopathy and/or microcyst-like epithelial changes [MECs], an eye examination finding with/without symptoms), change in best-corrected visual acuity (BCVA), or symptoms (blurred vision and dry eye) were common adverse events (AEs) reported during treatment.^{6,7}

– Belamaf-related corneal events were adequately managed with dose modifications (delays or reductions) or treatment discontinuation in DREAMM-2; no complete loss of vision has been reported.⁷

- Durable responses to belamaf have been observed with dose modifications.⁶

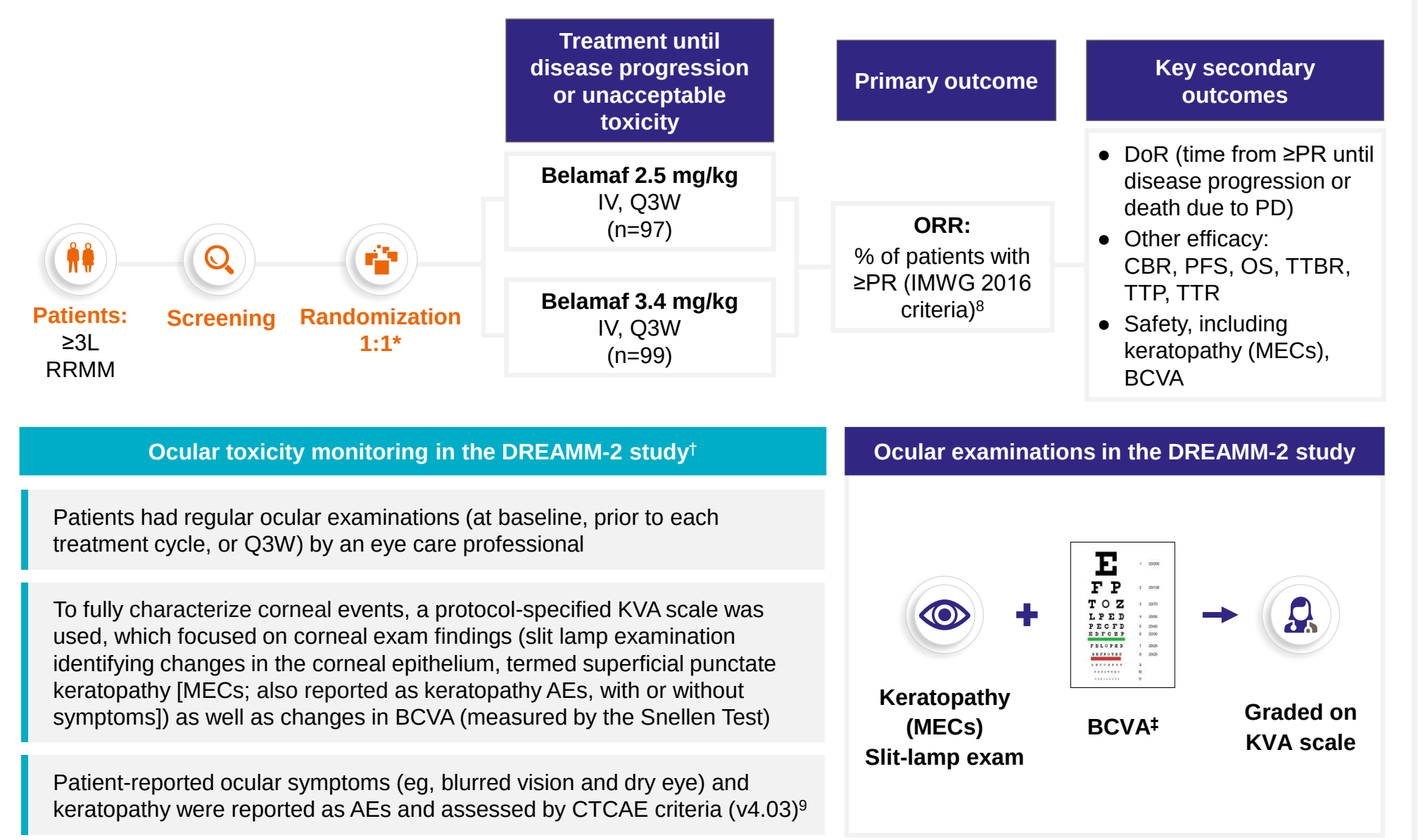
Longer-term management of AEs such as ocular events needs to be characterized more fully to optimize clinical care.⁷

Objective

To characterize the ocular safety profile of belamaf in patients treated for ≥12 months, in a post-hoc analysis of the 2.5 mg/kg arm of the DREAMM-2 study at 13-month follow-up.

Methods

Figure 1. DREAMM-2 study design with focus on ocular toxicity monitoring^{4,6}



*Patients stratified based on number of previous lines of therapy (≤4 vs >4) and presence or absence of HR cytogenetic features; [†]Please check your local belamaf prescribing information for guidance on ocular toxicity monitoring. [‡]BCVA was assessed by manifest refraction using the Snellen eye chart. AE, adverse event; BCVA, best-corrected visual acuity; CBR, clinical benefit rate; CTCAE, Common Terminology Criteria for Adverse Events; HR, high-risk; IMWG, International myeloma working group; KVA, keratopathy and visual acuity; MECs, microcyst-like epithelial changes; ORR, overall response rate; OS, overall survival; PD, progressive disease; PFS, progression-free survival; PR, partial response; Q3W, every 3 weeks; RRMM, relapsed/refractory multiple myeloma; TTBR, time to best response; TTP, time to progression; TTR, time to response.

Disclosures

SL received research funding from Celgene and Takeda, and personal fees from Amgen, Bristol Myers Squibb, Celgene, GlaxoSmithKline, Janssen, Merck, Novartis, and Takeda. **PT** has no disclosures beyond employment. **AKN** has received consulting fees from Amgen, Bristol-Myers Squibb, Celgene, GlaxoSmithKline, Janssen Oncology, Karyopharm Therapeutics, Oncopptides, Spectrum Pharmaceuticals, and Takeda; research funding from Amgen, Janssen Oncology, and Takeda; and personal fees from GlaxoSmithKline. **AJB** has received consulting fees from Amgen, Bristol-Myers Squibb, Celgene, GlaxoSmithKline, Keredon, Sanofi, Santen, and Merck and holds stocks/shares in EyeGate. **NSC** has nothing to disclose. **DS** has received consulting fees from Amgen, GlaxoSmithKline, Janssen, Legend Biotech, Sanofi, and SkylineDX; and honoraria and personal fees from Janssen. **BEZ** has received consulting fees from GlaxoSmithKline. **RP** has

received consulting fees from AbbVie, Celgene, GlaxoSmithKline, and Takeda; research funding from Takeda; honoraria from Celgene, GlaxoSmithKline, Janssen, and Takeda; and travel expenses from GlaxoSmithKline, Janssen, and Takeda. **SDE** has received consulting fees and honoraria from GlaxoSmithKline. **AD, JB, TP, EL, JO, PP**, and **IG** are paid employees of GlaxoSmithKline. **JB, TP**, and **JO** hold stocks/shares in GlaxoSmithKline; and **IG** holds stocks/share in GlaxoSmithKline and Novartis. **AF** has received consulting fees from GlaxoSmithKline, Keredon, Sanofi, Santen, and Merck and holds stocks/shares in EyeGate. **NSC** has nothing to disclose. **DS** has received consulting fees from Amgen, GlaxoSmithKline, Janssen, Legend Biotech, Sanofi, and SkylineDX; and honoraria and personal fees from Janssen. **BEZ** has received consulting fees from GlaxoSmithKline. **RP** has

Acknowledgments

This study was funded by GlaxoSmithKline (Study 205678, NCT03525678). Drug linker technology licensed from Seagen Inc.; monoclonal antibody produced using POTELLIAGENT Technology licensed from BioWa. The authors acknowledge Alessandra Tosolini, BS for her contributions in overseeing the study, and her involvement in the review and interpretation of data presented in this poster. Editorial assistance was provided by Jiah Pearson-Leary, PhD, of Fishawack Indicia Ltd, part of Fishawack Health, and funded by GlaxoSmithKline. This poster was presented at the 26th Congress of the European Haematology Association (Lonial et al, 2021); submitted with permission of the original authors.

Ocular events

All 14 patients experienced keratopathy and 13 patients had ocular symptoms, which are summarized in **Table 3**. Keratopathy and blurred vision led to the most dose modifications (**Table 3**).

Table 3. Drug-related ocular events, and ocular events leading to dose modifications			
	Patients with drug-related ocular adverse events n (%)	Patients with ocular adverse events leading to dose reduction n (%)	Patients with ocular adverse events leading to dose delays n (%)
Keratopathy	14 (100)	10 (71)	13 (93)
Vision blurred	8 (57)	1 (7)	3 (21)
Dry eye	5 (36)	0	1 (7)
Photophobia	3 (21)	0	0
Visual acuity reduced	3 (21)	0	0
Ocular discomfort	2 (14)	0	1 (7)
Visual impairment	2 (14)	0	0
Glaucoma	1 (7)	0	1 (7)
Retinal hemorrhage	1 (7)	0	1 (7)
Ulcerative keratitis	1 (7)	0	1 (7)
Vitreous detachment	1 (7)	0	0

Dose delays and reductions related to ocular adverse events

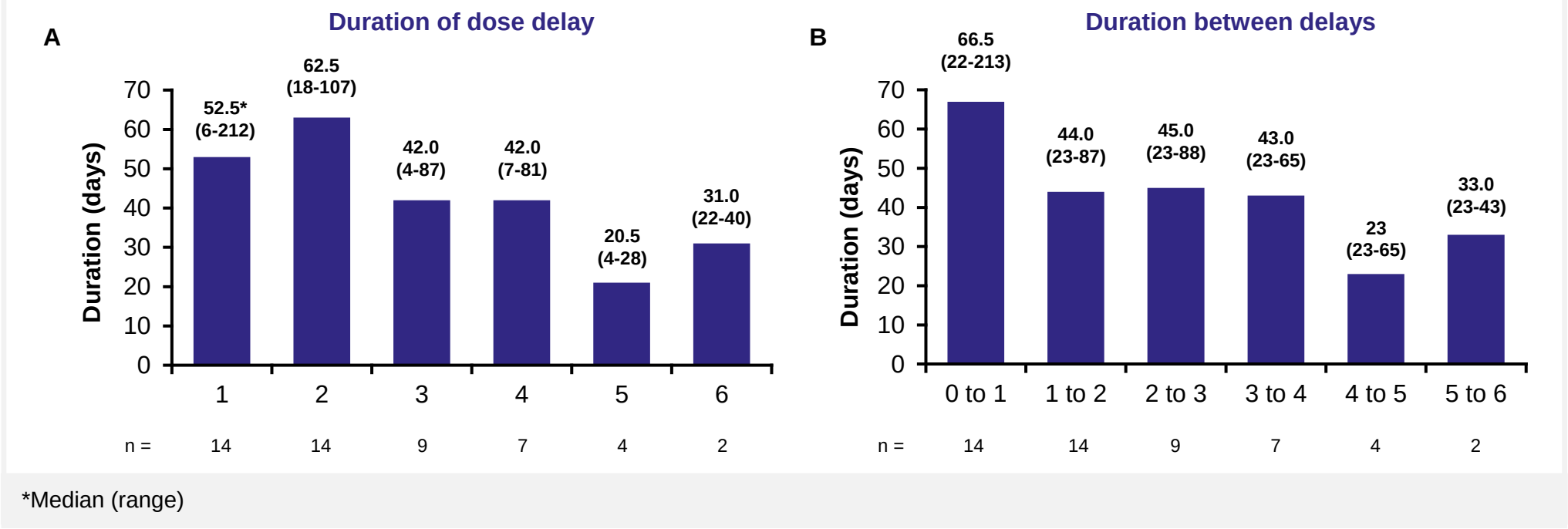
All 14 patients required ≥2 dose delays, with dose reduction (to 1.92 mg/kg) in 12 patients (86%).

- Patients experienced a mean of 3.6 dose delays over the ≥12 months of treatment (median: 3.5, range: 2–6).
- Ten patients (71%) required dose delays of >63 days.

There was a trend towards a decrease in duration of delays over the course of the treatment (**Figure 3A**) with a median duration of 42 days (range: 4–212).

- Earlier dose delays tended to be longer than later delays (**Figure 3A**).
- The median latency until first delay was 66.5 days (range: 22–213; **Figure 3B**); patients experienced shorter duration between delays over the course of therapy.

Figure 3. (A) Median duration of dose delays and (B) median duration between dose delays



Profile plots of individual patients: corneal events (KVA graded), dose modifications (delays and reductions), and duration of response

Dose delays or reductions permitted recovery from ocular events, allowing treatment to be resumed multiple times in all 14 patients (**Figure 4**).

Clinical benefit in patients with long dose delays (>63 days)

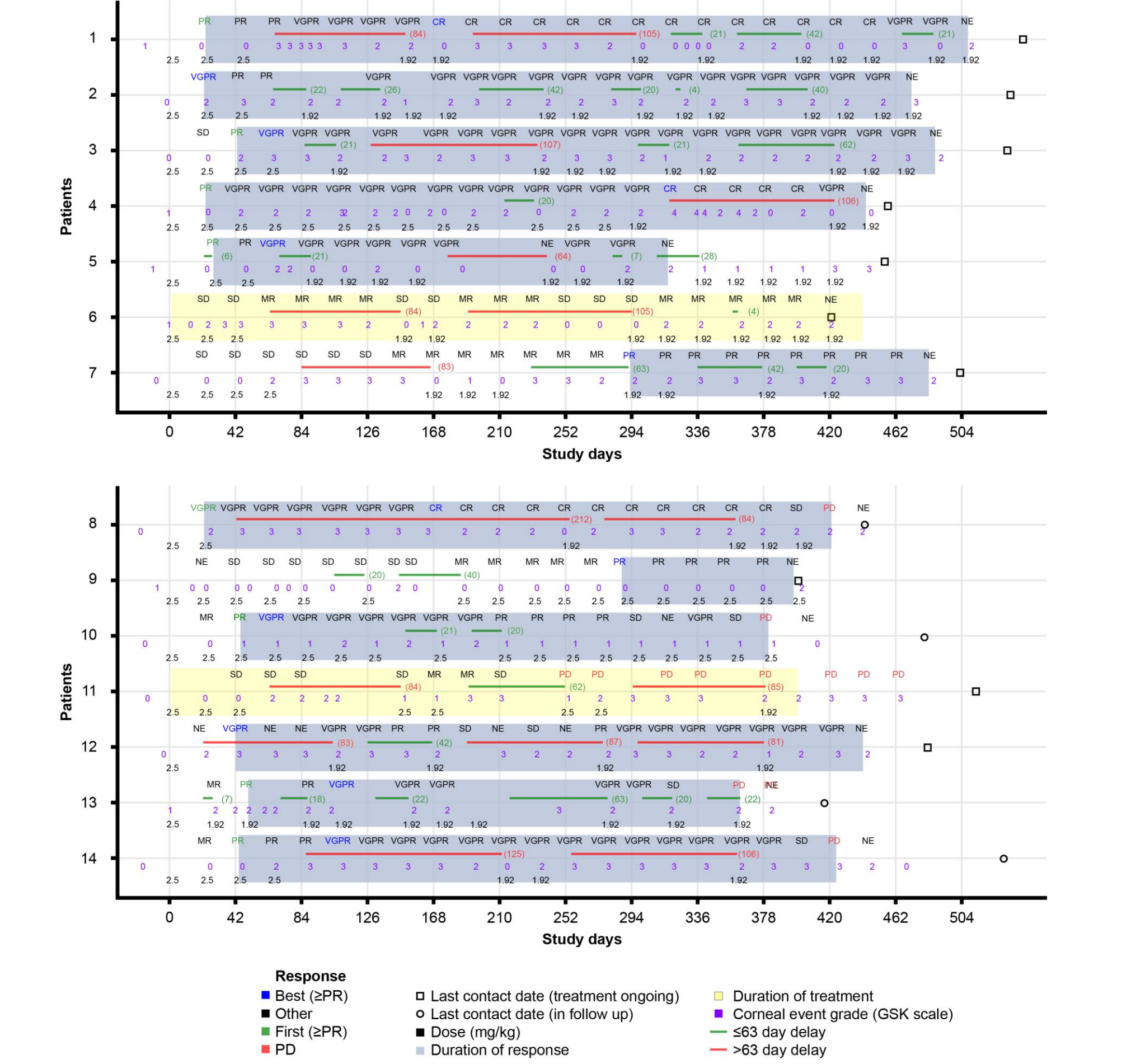
Dose delays or reductions permitted recovery of ocular events, allowing treatment to be resumed multiple times in all 14 patients (**Figure 4**).

- 12 patients had a clinical response (partial response or better) and 11 patients had a clinical response for ≥6 months.
- Of the 10 patients with dose delays >63 days, 5 patients had a response of VGPR or CR (**Figure 4**).

Sagar Lonial¹; Ajay K. Nooka¹; Praneetha Thulasi²; Ashraf Z. Badros³; Bennie H. Jeng³; Natalie S. Callander⁴; Douglas Sborov⁵; Brian E. Zaugg⁶; Rakesh Popat⁷; Simona Degli Esposti⁸; January Baron⁹; Allison Doherty¹⁰; Eric Lewis¹¹; Joanna Opalinska⁹; Prani Paka⁹; Trisha Piontek⁹; Ira Gupta⁹; Asim V. Farooq¹²; Andrzej Jakubowiak¹²

¹Emory University, Winship Cancer Institute, Atlanta, GA, USA; ²Emory Eye Center, Emory University, Atlanta, GA, USA; ³University of Maryland School of Medicine, Baltimore, MD, USA; ⁴University of Wisconsin, Carbone Cancer Center, Madison, WI, USA; ⁵Huntsman Cancer Institute, University of Utah, Salt Lake City, UT, USA; ⁶Moran Eye Center, University of Utah, Salt Lake City, UT, USA; ⁷University College London Hospitals, NHS Foundation Trust, London, UK; ⁸NIHR Biomedical Research Centre at Moorfields Eye Hospital NHS Foundation Trust and UCL Institute of Ophthalmology, London, UK; ⁹GlaxoSmithKline, Upper Providence, PA, USA; ¹⁰GlaxoSmithKline, Collegeville, PA, USA; ¹¹GlaxoSmithKline, Research Triangle Park, NC, USA; ¹²University of Chicago Medical Center, Chicago, IL, USA

Figure 4: Profile plots of patients with corneal events graded on the KVA scale*



*The data in **Figure 4** represent a snapshot of each patient's journey. In a number of cases treatment has continued well after the 504 days presented in **Figure 4**. Some of these patients remain on belamaf treatment >900 days. All relevant information for the complete journey cannot be captured by snapshots when treatment extends well beyond the cutoff. KVA grade at each dose delay is displayed. Duration on treatment is only displayed for non-responders in order to help distinguish between patients in the figure. Time on study drug does not exclude dose delays. AE, adverse event; CR, complete response; KVA, keratopathy and visual acuity; MR, minimal response; NE, not evaluable; PD, progressive disease; SCR, stringent complete response; SD, stable disease; VGPR, very good partial response.

Conclusions

In this subset of 14 patients from the DREAMM-2 study, the median duration of response was 12.5 months. Over the course of belamaf treatment, patients and clinicians should expect dose delays related to ocular events. All patients had at least 2 dose holds, and 10 patients had dose holds longer than 63 days. Dose modifications were effective in managing ocular symptoms and decreasing findings at eye examinations, therefore allowing patients to stay on therapy and gain the clinical benefit of continuing treatment with belamaf. The safety profile of belamaf will be further characterized in ongoing analyses and studies.

Author email address: sloni01@emory.edu