The 7th World Congress on CONTROVERSIES IN MULTIPLE MYELOMA (COMy)

Recovery of Ocular Events (OEs) with Longer-term Follow-up in the DREAMM-2 Study (NCT03525678) of Single-Agent Belantamab Mafodotin (Belamaf) in Patients with Relapsed or Refractory Multiple Myeloma (RRMM)

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Background

Belamaf

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 (BLENREP) is a first-in-class, BCMA-targeting ADC containing MMAF.[3]

In the open-label, randomized Phase 2 DREAMM-2 study of single-agent belamaf (NCT03525678),[4] patients with heavily pre-treated RRMM (refractory to an immunomodulatory agent and a proteasome inhibitor and refractory to/intolerant of an anti-CD38 monoclonal antibody) who responded to belamaf maintained durable responses at 13-month follow-up, with a manageable safety profile.[4]

- With belamaf 2.5 mg/kg Q3W, median DoR was 11.0 months, median OS estimate was 13.7 months[5]

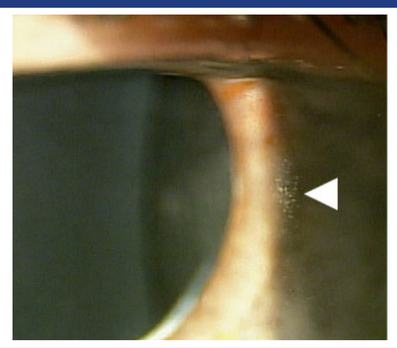
Belamaf 2.5 mg/kg Q3W is approved in the US and EU for the treatment of patients with RRMM.[6,7]

DREAMM-2 ocular events

In patients receiving belamaf in DREAMM-2[4,7]:

- The most frequent ocular symptoms were blurred vision, dry eye, and a decline in BCVA[5,8,9]
- Keratopathy, including superficial punctate keratopathy and/or MECs (observed on slit lamp microscopy with or without symptoms or changes in BCVA; **Figure 1**), are associated with MMAF-containing ADCs and were common in DREAMM-2[8,10]

Figure 1. Slit-lamp eye exam showing MECs



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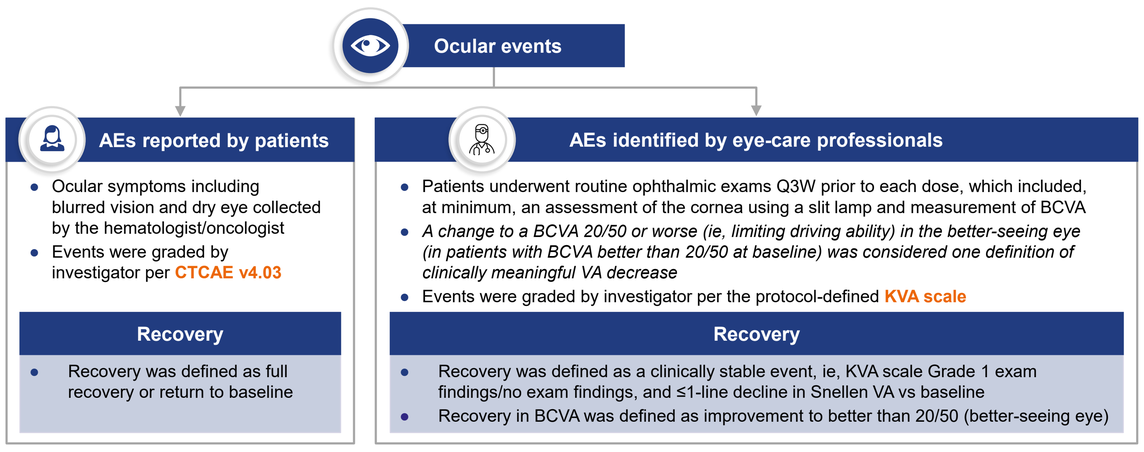
Aims

To report ocular event outcomes for patients receiving belamaf 2.5 mg/kg Q3W from a 13-month follow-up post-hoc analysis of the DREAMM-2 study.

Methods

Figure 2. Ocular event identification and management



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Ocular events were managed by dose modifications in DREAMM-2.

Dose modifications (dose reductions or delays) were based on the severity of eye exam findings and BCVA changes from baseline per KVA scale.

Previous analysis has found that responses to belamaf are durable despite dose modifications; of 31 patients receiving belamaf 2.5 mg/kg who were on a dose hold >63 days, 88% maintained or deepened their response.[11]

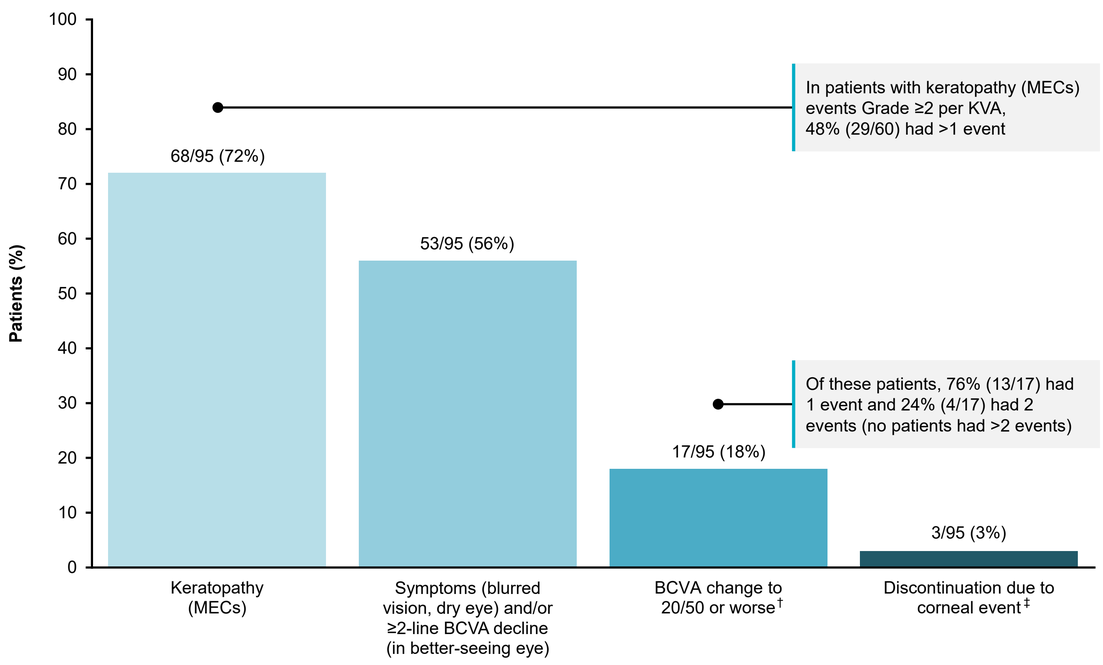
Results

Keratopathy (MECs), symptoms, BCVA changes, and discontinuations due to ocular AEs

68 out of 95 patients (72%) experienced keratopathy with 60 patients having Grade ≥2 events; 29 out of 60 patients (48%) experienced more than one event (**Figure 3**).

53 patients (56%) experienced symptoms or decline in BCVA; 17 patients showed a BCVA change of 20/50 or worse (**Figure 3**).

Figure 3. Frequency of ocular events in patients treated with belamaf 2.5 mg/kg in DREAMM-2 (n=95)*



*Only data from the approved dose of 2.5 mg/kg are presented; †better seeing eye; represents threshold at which activities of daily living eg, legal driving, may become affected[11]; ‡One patient discontinued due to keratopathy (MECs), 1 due to blurred vision, and 1 due to a decline in BCVA; ¶20/200, the threshold for legal blindness in many countries[11]; **CTCAE scale event grading: 1 patient (with a history of cataract surgery in the right eye) developed a central corneal ulcer that resolved 9 days after onset with the use of topical antibiotics. Data on File. Study 205678. GSK Study Register. Available at: https://www.gsk-studyregister.com.

Recovery of Grade ≥2 keratopathy (MECs) in DREAMM-2

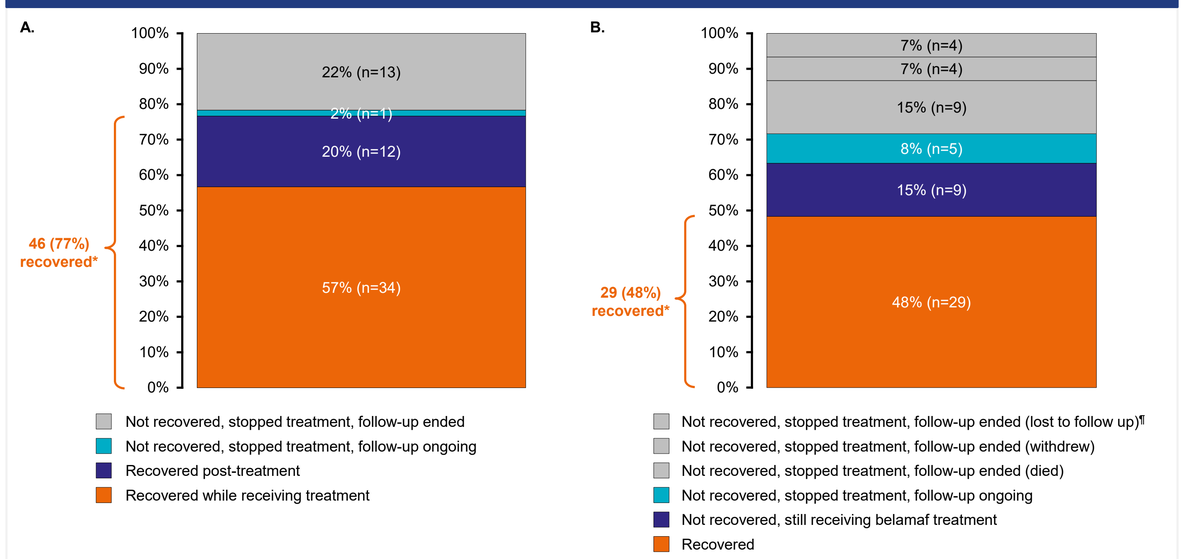
Most (34/60; 57%) patients recovered from their first event while receiving treatment (**Figure 4a**).

Of 60 patients, 46 (77%) recovered; most (57%) patients recovered while receiving treatment and a further 20% recovered after the end of treatment (**Figure 4a**).

At last follow-up, 29 out of 60 patients (48%) recovered (**Figure 4b**).

Of the 31 patients who had not recovered at last follow-up, 9 patients continued to receive treatment, 5 stopped treatment but continued follow-up, and 17 did not complete follow-up (**Figure 4b**).

Figure 4. Recovery* of Grade ≥2 keratopathy (MECs) in DREAMM-2 (belamaf 2.5 mg/kg [60/95 patients]); A) FIRST occurrence of keratopathy (MECs) Grade ≥2†‡; B) LAST follow-up: keratopathy (MECs) Grade ≥2



*Represents patients with events that recovered either prior to end of treatment or after the end of study treatment; recovery was defined as any Grade 1 exam finding or no exam finding compared with baseline; †These patients may have experienced dose modifications (Cohen et al, SOHO 2020; Poster No. MM-250); ‡Median (range) time to event 37 (19–147) days; ¶Patients in survival follow-up but have confirmed they are not coming back to site for further corneal exams.

Recovery of changes in BCVA worse than 20/50 in the better-seeing eye

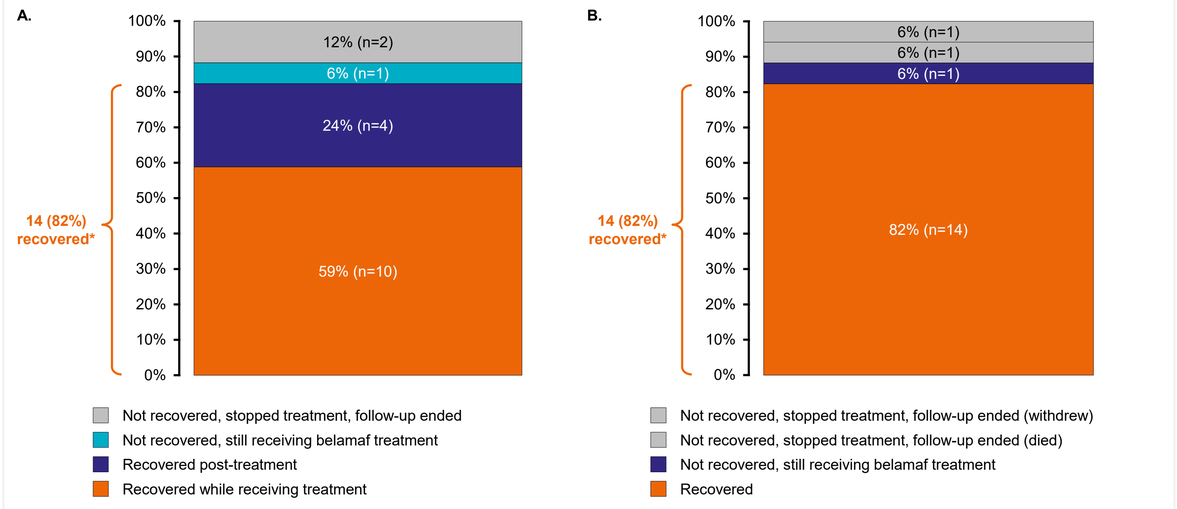
Most (10/17; 59%) patients recovered from their first event while receiving treatment (**Figure 5a**).

Fourteen of 17 (82%) patients recovered; the majority of patients (59%) recovered while receiving treatment and a further 24% recovered after the end of treatment (**Figure 5a**).

Most (14/17 [82%]) patients had recovered at last follow-up (**Figure 5b**).

- At last follow-up, 1 patient had not recovered but continued treatment, 1 patient had died, and 1 patient had withdrawn
- No patients had permanent complete vision change or loss

Figure 5. Recovery* of changes in BCVA worse than 20/50 in the better-seeing eye† (belamaf 2.5 mg/kg [17/95 patients]); A) FIRST occurrence of change to BCVA worse than 20/50 in the better-seeing eye‡¶; B) LAST follow-up: change to BCVA worse than 20/50 in the better-seeing eye



*Represents patients with events that recovered either prior to end of treatment or after the end of study treatment; recovery was defined as any Grade 1 exam finding or no exam finding compared with baseline; †In patients with better than 20/50 BCVA in their better-seeing eye at baseline; ‡These patients may have experienced dose modifications, see Cohen et al, SOHO 2020 Poster No. MM-250; ¶Median (range) time to event 66 (20–442) days.

Conclusions

Long-term follow-up in this DREAMM-2 post-hoc analysis demonstrated that although ocular events were common, the majority of patients recovered while remaining on treatment. No new ocular safety signals were observed at 13-month follow-up.

Though keratopathy (MECs) were frequently observed on eye exam (72% of patients), 44% of patients did not experience symptoms such as a clinically meaningful BCVA decline, and very few patients discontinued treatment.

The changes in vision were generally transient and most (46/60; 77%) patients recovered from the first keratopathy (MECs) event or from clinically meaningful BCVA decline (82%).

Given the nature of heavily pre-treated RRMM, some patients are lost at follow-up (post PD) and therefore it is very challenging, if not impossible, to obtain recovery data on all patients.

Implications for managing belamaf-treated patients

The recovery of most ocular events is consistent with the established safety profile of belamaf.[5]

Events can be asymptomatic so close monitoring by an eye care professional is important.

Ocular events can be managed by dose modifications (guided by both patient-reported ocular symptoms and examination findings [keratopathy, including superficial punctate keratopathy and/or MECs])[12]

Disclosures

SL has received research funding from Celgene and Takeda, and personal fees from Amgen, Bristol-Myers Squibb, Celgene, GlaxoSmithKline, Janssen, Merck, Novartis, and Takeda. **AKN** has received consulting fees from Amgen, Bristol-Myers Squibb, Celgene, GlaxoSmithKline, Janssen Oncology, Karyopharm Therapeutics, Oncopeptides, Spectrum Pharmaceuticals, and Takeda; research funding from Amgen, Janssen Oncology, and Takeda; and personal fees from GlaxoSmithKline. **PT** declares no conflicts of interests. **AZB** has received consulting fees from Amgen. **BHJ** has received consulting fees from GlaxoSmithKline, Kedrion, and Merck; and has stocks/shares in EyeGate. **NSC** has received research funding from Cellectar. **DS** has received honoraria and consulting and personal fees from Janssen. **BEZ** declares no conflicts of interests. **RP** has received consulting fees from AbbVie, Celgene, GlaxoSmithKline, and Takeda; research funding from Takeda; honoraria from Celgene; and honoraria and personal fees from GlaxoSmithKline, Janssen, and Takeda. **SDE** has received consulting fees and honoraria from GlaxoSmithKline. **JByrne** is an employee of GlaxoSmithKline and has stocks/shares in GlaxoSmithKline, Adaptimmune, and Novartis. **JO**, **JBaron**, and **TP** are employees of and have stocks/shares in GlaxoSmithKline. **IG** is an employee of and has stocks/shares in GlaxoSmithKline, and Novartis. **RD** has received consulting fees from Alcon, Dompé, GlaxoSmithKline, Kala, and Novartis; and has stocks/shares in Allergan, Aramis Biosciences, Claris Biotherapeutics, Department of Defense, GelMEDIX, and National Institutes of Health. **AVF** has received consulting fees from GlaxoSmithKline. **AJ** has received consulting fees and honoraria from AbbVie, Adaptive, Amgen, Bristol-Myers Squibb, Celgene, Janssen, Juno, and Karyopharm.

Abbreviations

ADC, antibody–drug conjugate; AE, adverse events; BCMA, B-cell maturation antigen; BCVA, best-corrected visual acuity; belamaf, belantamab mafodotin; CTCAE, Common Terminology Criteria for Adverse Events; DoR, duration of response; KVA, Keratopathy and Visual Acuity; MECs, microcyst-like epithelial changes; MMAF, monomethyl auristatin F; OS, overall survival; Q3W, every 3 weeks; RRMM, relapsed or refractory multiple myeloma; VA, visual acuity.

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