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

Background
Belmaff
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. The BLENREP (Blenantamab Mafodotin) clinical trial is a first-in-class, BCMA-targeting monoclonal antibody.

In the open-label, randomized Phase 2 DREAMM-2 study of single-agent belmaff (NCT03525678), patients with heavily pre-treated RRMM (refractory to an immunomodulatory agent and a proteasome inhibitor and refractory to/tolerant of an anti-CD138 monoclonal antibody) who responded to belmaff maintained durable responses at 13-month follow-up, with a manageable safety profile.4

- With belmaff 2.5 mg/kg, median DoR was 11.0 months, median OS estimate was 13.7 months6
- Belmaff 2.5 mg/kg is approved in the US and EU for the treatment of patients with RRMM.8,9

DREAMM-2 ocellar events
In patients receiving belmaff in DREAMM-2:10
- The most frequent ocular symptoms were blurred vision, dry eye, and a decline in BCVA.5,9
- Keratopathy, including superficial punctate keratopathy and/or MECs (observed on slit lamp microscopy with or without symptoms or changes in BCVA) are identified with MAF-containing ADCs and were common in DREAMM-2.10

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

Methods

Ocular events
- Ocular symptoms including blurred vision and dry eye collected by the hematologist/oncologist.
- Events were graded by investigator per the protocol-defined CTCAE v4.03.
- Recovery of changes from baseline per KVA scale.6,7
- Patients underwent routine ophthalmic exams every 3–4 months, which included, at minimum, an assessment of the cornea using a slit lamp and measurement of BCVA.
- A change to a BCVA ≤20/50 or worse (limiting driving ability) in the better-seeing eye in patients with belmaff 2.5 mg/kg (≥2 events) was considered a definition of clinically meaningful ocular decline.
- Events were graded by investigator per the protocol-defined CTCAE v4.03.

Figure 1. Slit-lamp eye exam showing MECs

Recovery
- Recovery was defined as any Grade 1 exam finding or no examination findings (keratopathy, including superficial punctate keratopathy and/or MECs).
- Recovery was defined as improvement to better than 20/30 (better-seeing eye).

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 (48%) of those patients recovered.

Most (10/11; 91%) patients recovered from their first event while receiving treatment (Figure 4a). 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).

Recovery of changes in BCVA worse than 20/50 in the better-seeing eye
Most (10/11; 91%) patients recovered from their first event while receiving treatment (Figure 5a). Of the 17 (82%) patients who had not recovered at last follow-up (Figure 5b), 2 patients continued to receive treatment, 1 patient had died, and 1 patient had withdrawn.

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.

Implications for managing belmaff-treated patients
The recovery of most ocular events is consistent with the established safety profile of belmaff. Events can be asymptomatic so close monitoring by an eye care professional is important.

References

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 belmaff are durable despite dose modifications: of 31 patients receiving belmaff 2.5 mg/kg who were on a dose hold >63 days, 88% maintained or deepened their response.7

Figure 2. Ocular event identification and management

Other ocular symptoms including blurred vision and dry eye were collected by the hematologist/oncologist. Events were graded by investigator per the protocol-defined CTCAE v4.03.

- Recovery was defined as improvement to better than 20/30 (better-seeing eye).

Figure 3. Frequency of ocular events in patients treated with belmaff 2.5 mg/kg in DREAMM-2

- In patients with keratopathy (MECs), Grade 1 exam finding or no examination findings (keratopathy, including superficial punctate keratopathy and/or MECs).
- In patients with BCVA change to ≤20/50 or worse (in better-seeing eye) that recovered to baseline.

Figure 4: Recovery of Grade ≥2 keratopathy (MECs) in DREAMM-2 (belmaff 2.5 mg/kg [95 patients]).
A) FIRST occurrence of keratopathy (MECs) Grade ≥2: 17/95 (18%) patients.
B) LAST occurrence of keratopathy (MECs) Grade ≥2

Figure 5: Recovery of ocular events (OEs) in patients with RRMM on belmaff 2.5 mg/kg (total of 95 patients), showing common, the majority of patients recovered while remaining on treatment. No new ocular safety signals were obtained at 13-month follow-up.

- Of the 31 patients who had not recovered at last follow-up, 9 patients continued to receive treatment, 1 patient had died, and 1 patient had withdrawn.

- No patients had permanent complete vision change or loss.


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