Impact of Prolonged Dose Delays on Response With Belantamab Mafodotin (Belama; GSK2857916) Treatment in DREAMM-2 Study: 13-Month Follow-Up

**Aims**

To present findings on the impact of dose delays in responses in patients receiving single-agent belanata in a post hoc analysis of DREAMM-2 (NCT03255267).

**Background**

Belanata (GSK2857916) is a first-in-class, monoclonal auristatin F (MMAF)-containing anti-body-drug conjugate (ADC) that binds to CD38 maturation antigen (BCMA) and eliminates multiple myeloma cells by a multistep mechanism of action. The antibody component of belanata enhances antibody-dependent cellular cytotoxicity and phagocytosis. In patients with heavily pretreated relapsed/refractory multiple myeloma (RMM) who have a history of a poor prognosis (overall survival (OS) 6-9 months) and deep and durable responses with single-agent belanata were sustained over 13 months follow-up in the Phase II DREAMM-2 study estimated OS of 13.7 months in patients receiving the 2.5mg/kg who achieved SOHO poster MM24.19.

Conical events are commonly reported with MMAF-containing ADCs. In DREAMM-2, conical keratopathy, corneal capillary, and ocular epithelial changes (MECs), an eye examination finding (without symptoms), change in best-corrected visual acuity (BCVA), or symptoms (blurred vision and dry eye) were the most common adverse events (AEs) reported during belanata treatment. Belanata-related corneal events were adequately managed with dose modifications (delays or reductions) in DREAMM-2. No long-term vision loss has been reported.20

Other studies have also shown improvement in, or resolution of, corneal changes with dose modifications during treatment with other ADCs containing MMAF.21

**Methods**

DREAMM-2 is an ongoing, open-label, two-arm, randomized, multicenter study of belanata with a total (2.5 or 3.4 mg/kg) intravenously every 3 weeks until disease progression or unacceptable toxicity) in patients with relapsed/refractory multiple myeloma.

- Objective response (International Myeloma Working Group (IMWG) criteria 2016) was assessed by an independent review committee.
- Dose modification or hold was assessed. Dose delays (delays or reductions) were permitted to manage AEs, or for medical or surgical reasons unrelated to treatment. For conical events, dose modifications were based on a combination of eye examination (ie, keratopathy [MECs]) and change in BCVA from baseline.

**Results**

**Treatment**

At the data cut-off date (January 31, 2020), patients in both the 2.5 and 3.4 mg/kg groups received a median of 3 treatment cycles (range: 1–7). The median dose intensity was more consistent with the planned dose intensity for the 2.5mg/kg group (median: 2.59 mg/kg (range: 0.5–6.2)) compared with the 3.4 mg/kg group (median: 2.95 mg/kg (range: 0.8–7.3)).

**Dose modifications in the overall population**

In the 2.5- and 3.4-mg/kg groups, 41% (39/95) and 48% (40/83) of patients, respectively, had a dose delay.

- In patients with dose delays in the 2.5-mg/kg group, 36% (43/123) of patients had a single dose delay, and 33% (13/39) of patients had ≥2 dose delays.
- In patients with dose delays in the 3.4-mg/kg group, 48% (34/140) of patients had a single dose delay, 13% (15/114) had two dose delays, and 40% (44/109) of patients had ≥3 dose delays.

The median duration of dose delay was 45 days (range: 12–121) for the 2.5-mg/kg group and 23 days (range: 4–149) for the 3.4-mg/kg group.

Dose modifications due to AEs in the overall population (Table 1).

**Clinical response in patients with prolonged dose delays**

In the 31 patients with prolonged response (PR) in the 2.5-mg/kg cohort, 16 had prolonged dose delays (>63 days; Figure 1A) and 15 had dose delays of ≤63 days (Figure 1B).

- Most of these patients (84% and 84% in the 2.5- and 3.4-mg/kg cohorts, respectively) continued to experience a clinical benefit during the first prolonged delay, with some of these patients (38% and 32%, respectively) deepening their clinical response during dose delay (Table 2).
- Few (13% and 16%, respectively) developed progressive disease.

**Conclusions**

In DREAMM-2, it was common for patients receiving single-agent belanata to experience keratopathy (MECs, an eye examination finding) requiring dose modifications, including prolonging dose delays.

Clinical responses were maintained in over 80% of patients whose AEs were managed with the first prolonged dose delay. Grade 3/4 keratopathy (MECs, an eye examination finding) events improved to Grade ≥2 events in over 80% of patients with their first prolonged dose delays, supporting the use of dose delays as a cemeol management event strategy.

For questions, please contact: Adam Cohen at perimeter@upenn.edu

**References**

2. Farooq A, et al. ASH 2020 Week 302

**Pharmacology & Therapeutics**