DREAMM 4: A Phase I/II single-arm open-label study to explore safety and clinical activity of belantamab mafodotin (GSK2857916) administered in combination with pembrolizumab in relapsed/refractory multiple myeloma (RRMM)

Trial design: DREAMM 4 (NCT03848845)

**Trial objectives**

- **Primary Endpoint**: Determine safety, tolerability, and establish the RP2D of the combination of belantamab mafodotin and pembrolizumab

- **Secondary Endpoints**:
  - ORR
  - CR/PR rate
  - mPFS
  - DLI
  - OS
  - Clinical benefit rate
  - Time to disease progression
  - mTPI
  - ProNAD profile

- **Exploratory Endpoints**:
  - MDIS in patients who achieve CR
  - Clinical activity and tolerability of pembrolizumab
  - Safety monitoring

- **Key inclusion criteria**:
  - ≥18 years of age
  - ECOG PS 0–1
  - ≥3 or more prior lines of anti-myeloma therapies including an IMiD, proteasome inhibitor, and anti-CD38 antibody
  - CD 312 ≥ Grade 2 or previous therapy with an anti-PD-L1, or an anti-PD-L2 agent, or with an anti-CTLA-4 agent
  - Measurable disease
  - Active renal condition, liver or biliary disease, or infection
  - Disease progression is assessed according to IMWG 2016 response criteria

- **Key exclusion criteria**:
  - Any prior anti-HER2 therapy or investigational drug within 14 days
  - Prior treatment with a monoclonal antibody within 30 days
  - Prior therapy with an anti-PD-1, anti-PD-L1, or anti-PD-L2 agent, or with an agent directed to another antibody or co-stimulatory, T-cell receptor (e.g., CTLA-4, OX40, CD137, CD28), or cytokine receptor (e.g., IL-2, IL-7, IL-15) in the past 5 years, or prior treatment due to a Grade 3 or higher hERG
  - Corneal epithelial disease except mild punctate keratopathy
  - Major surgery within the last 4 weeks
  - Active renal condition, liver or biliary disease, or infection
  - Active CNS metastases and/or carcinomatous meningitis
  - Autimmune disease that has required systemic treatment in the past 2 years
  - Diagnosed immunosuppressive therapy within 7 days
  - Prior aleukemic leukemic organ transplant

**Background**

Belantamab mafodotin (GSK2857916) is a first-in-class, anti-BCMA immune conjugate with an anacoplanate, humanized anti-BCMA mAb conjugated by a protease-resistant cysteine BCMA immune-conjugate with an afucosylated, humanized IgG4 Fc, which has a favourable safety profile and clinical activity of belantamab mafodotin as a monotherapy in heavily pretreated participants with MM, with deep and durable response rates reported (NCT03380587; ORR was 59% with a mNPI of 12 months (95% CI: 6.1–not estimable)).

A deleterious safety profile and clinical activity of belantamab mafodotin as a monotherapy in heavily pretreated participants with MM, with deep and durable response rates reported (NCT03380587; ORR was 59% with a mNPI of 12 months (95% CI: 6.1–not estimable)). Of those participants without prior denosumab treatment an ORR of 71.4% (95% CI: 47.8–88.7) was achieved, whereas in participants with prior denosumab treatment and refractory to both immunomodulators and proteasome inhibitors an ORR of 38.5% (95% CI: 13.9–68.4) was achieved.

**Safety monitoring**

An independent safety review committee will review safety data. Safety data will be evaluated on an ongoing basis to support dose-escalation decisions.

**Current status**

- **Enrollment** for Part 1 began in March 2019
- **As of** 16 Sep 2019

**Participants** will be treated until disease progression, intolerable toxicity, informed consent withdrawal, or for a maximum of 35 cycles (approximately 2 years). Disease progression is assessed according to IMWG 2016 response criteria.

**References**

8. Fecteau D3, Talekar M3, Evans J5, and Opalinska J3
9. Trudel S1, Nooka AK2, Fecteau D3, Talekar M3, Evans J5, and Opalinska J3
10. Trudel S1, Nooka AK2, Fecteau D3, Talekar M3, Evans J5, and Opalinska J3