Belantamab mafodotin (GSK2857916) is a novel anti-BCMA monoclonal antibody-drug conjugate (ADC), Belantamab Mafodotin (GSK2857916), in Relapsed/Refractory Multiple Myeloma (RRMM): Final Safety, Efficacy and Pharmacokinetic (PK) Analyses From A Phase I Study

**Introduction**

- Despite the introduction of immunomodulators and proteasome inhibitors (PI), outcomes remain poor for patients with relapsed/refractory multiple myeloma (RRMM).
- The tumour necrosis factor superfamily cell-surface receptor, B-cell maturation antigen (BCMA) is an attractive target for developing novel therapies.

**Methods**

- Study design and patient population
  - This open-label, 2-part Phase I study (BMA117156; NCT02064387) was conducted in 9 centres in the USA, Canada and UK in adults with RRMM and progressive disease after stem cell transplantation (or considered transplantation ineligible). Patients were randomly allocated to one of 3 dose-escalation cohorts (Figure 1).
  - In Part 1 (dose escalation), patients received GSK2857916 (0.03–4.6 mg/kg) administered via IV infusion Q3W. In Part 2 (dose expansion), patients received the selected dose of 3.4 mg/kg GSK2857916 for up to 16 cycles.
- An interim analysis was performed after ~4 months of follow-up (cut-off 28 June 2017), the final analysis presented here was performed after ~18 months of follow-up (cut-off 29 July 2018). Two patients withdrew from the study before the final analysis and their data were included in the final analysis.

**Results**

- **Patient population**
  - In Part 1, 28 patients were enrolled and analysed, and with a mean (range) age of 59 (39–79) years.
  - Thirty-five patients were enrolled in Part 2, with a mean (range) age of 51 (18–75) years; patients completed a median (range) of 12 (7–22) months of follow-up.
- **Safety and efficacy**
  - Safety and efficacy findings from the final analysis of Part 2 have been published.
  - In brief:
    - The most frequent adverse events were infusion-related reactions (60%: 95% confidence interval [CI]: 42–76%); at the recommended Phase 2 dose, and progression-free survival (PFS) of 19 months (95% CI: 3.3–3.7 years).

**Figure 2. Best response to belantamab mafodotin.**

- The best confirmed response was assessed per Response Evaluation Criteria In Solid Tumors (RECIST) Version 1.1 criteria.

**Figure 3. Plasma exposures of A) belantamab mafodotin (Cₚ₅₀) and B) belantamab mafodotin (Cₚ₅₀) by dose level (Part 1).**

- **PK**
  - Combining all dose levels in Part 1, geometric mean clearance of belantamab mafodotin was 18 mL/h, steady-state volume of distribution was 4.1 L/kg, and half-life was 4.7 days (n=19) and the median time to maximum concentration (Tₚ₅₀) was 2.0 h (n=18). Similar PK parameter values were observed for total mAb (mAbs without MMF).
  - The median Tₚ₅₀ for cys-mcMMAF was 240 h (n=20); the geometric mean maximum concentration (Cₚ₅₀) at 3.4 mg/kg was 1290 ng/mL (n=10).

**Figure 4. Baseline BCMA expression in A) Myeloma BCMA expression and B) melanoma BCMA expression and b) myeloma BCMA intensity.**

- **Assessments**
  - **Primary endpoints** were safety, maximum tolerated dose and recommended Phase 2 dose.
  - Secondary endpoints included clinical activity (percentage of patients achieving at least a partial response [PR] overall response rate), safety and tolerability as adverse event (AE) reporting and PK parameters.
  - PI samples were collected during the first cycle in Part 1. PK parameters for the ADC, total mAb and cys-mcMMAF were determined by noncompartmental analysis.
  - MM biomarkers were assessed, including BCMA expression in bone marrow mononuclear cells and plasma cells by immunohistochemistry, and circulating free soluble BCMA (sBCMA) levels by immunoassay in serum.

**Figure 5. Decrease in sBCMA at the end of belantamab mafodotin infusion.**

- **Table 1. Summary of PK parameters.**

- **Conclusions**
  - Belantamab mafodotin was well tolerated and demonstrated rapid deep and durable responses in heavily pre-treated patients with RRMM. With additional follow-up, more complete responses can be identified.
  - The PK profile was characterized by slow clearance, a small volume of distribution and half-life of 4.7 days.
  - No clear relationship between baseline BCMA expression level and patient response was identified.
  - Corneal and thrombocytopenia events were consistent with the known toxicities of other MMF-linked antibody-drug conjugates.
  - Belantamab mafodotin engaged BCMA in a dose-dependent manner. Clinical responses were observed in patients across a wide range of baseline sBCMA levels.
  - Further investigations are needed to understand the value of BCMA expression on MM cells and circulating sBCMA as biomarkers for response to belantamab mafodotin.

**References**


**Disclosures**

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