DREAMM-3: A Phase 3, Open-label, Randomized Study to Evaluate the Efficacy and Safety of Belantamab Mafodotin (GSK2857916) Monotherapy Compared With Pomalidomide Plus Low-dose Dexamethasone (Pom/Dex) in Participants With Relapsed/Refractory Multiple Myeloma (RRMM)

Poster No. 1900

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Background

Target

BCMA is a cell-surface receptor highly and ubiquitously expressed in MM and in other B-cell malignancies at varying levels.[1,2]

BCMA promotes the growth and survival of MM cells and is virtually absent on naïve and memory B cells,[1,3,4] making it an ideal therapeutic target in MM.[5–9]

Belantamab mafodotin

Belantamab mafodotin (GSK2857916) is a first-in-class, anti-BCMA immunoconjugate with an afucosylated, humanized anti-BCMA mAb conjugated by a protease-resistant maleimidocaproyl linker to a microtubule-disrupting agent, monomethyl auristatin F.[1]

Upon binding to BCMA, belantamab mafodotin is rapidly internalized and the cytotoxic moiety is released, antibody-dependent cellular phagocytosis is mediated, antibody-dependent cellular cytotoxicity is enhanced, and immunogenic cell death occurs.[2,10]

In the first-in-human Phase 1 study (DREAMM-1/BMA117159, NCT02064387), **belantamab mafodotin** (3.4 mg/kg Q3W) monotherapy demonstrated a manageable safety profile and deep and durable clinical responses in patients with RRMM.[11,12]

In a cohort of 35 heavily pretreated patients with RRMM results were:

ORR of	Median PFS of	Median DoR of
60%	12.0 months	14.3 months
(95% CI: 42.1, 76.1)	(95% CI: 3.1, NE)	(95% CI: 10.6, NE)

Pomalidomide/dexamethasone combination therapy

The combination of the immunomodulatory agent **pomalidomide with dexamethasone (pom/dex)** is an approved therapy for patients with advanced-stage disease who have progressed after ≥2 prior lines of therapy.[13]

Although pom/dex therapy is a standard-of-care regimen for RRMM, an unmet need remains in this heavily pretreated patient population.

In the Phase 3 MM-003 trial in patients with RRMM receiving **pom/dex** results were:

ORR of	Median PFS of
31%	4.0 months (95% CI: 3.6, 4.7)[14]

In the larger MM-010 (STRATUS) Phase 3b trial of **pom/dex** in RRMM results were:

ORR of	Median PFS of
33% (95% CI: 29.0, 36.2)	4.6 months (95% CI: 3.9, 4.9)[15]

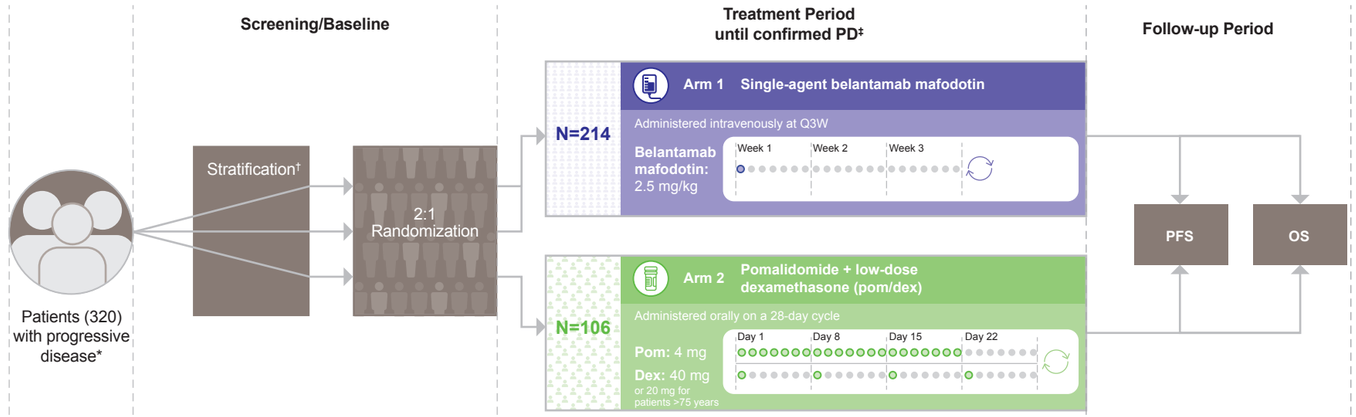
Trial objective

To evaluate the efficacy and safety of single-agent **belantamab mafodotin** compared with **pom/dex**, an established standard-of-care regimen in patients with RRMM treated with ≥2 prior lines of therapy.

Trial design

This study (NCT04162210) is:

- Phase 3
- Open label
- Randomized
- Two-arm
- Multicenter



*Progression on or within 60 days of last treatment, up to 380 patients will be randomized (320+60 to fulfill regional country requirements)
†Stratification based on ISS, number of prior lines of therapy, and prior treatment with anti-CD38 antibody treatment
‡Until PD, death, unacceptable toxicity, withdrawal of consent, lost to follow-up, or end of study, whichever comes first

Study population

Key inclusion criteria:

- Confirmed diagnosis of MM according to IMWG criteria[16]
- ≥18 years of age
- ECOG PS 0–2
- Measurable disease
- Autologous SCT >100 days prior, or transplant ineligible
- ≥2 prior lines of therapy, including ≥2 consecutive cycles of both lenalidomide and a proteasome inhibitor, refractory to or progressing on last line of treatment
- Adequate organ system function
- Agreement to contraception guidelines, including agreement to applicable pregnancy prevention/controlled distribution program as indicated for pom

Key exclusion criteria:

- Prior BCMA-targeted therapy or pom treatment
- Prior allogeneic SCT
- Major surgery <4 weeks prior
- Treatment with an anti-MM monoclonal antibody <30 days prior
- Symptomatic amyloidosis, active POEMS syndrome, or plasma cell leukemia
- Systemic anti-myeloma therapy or investigational drug within <14 days or 5 half-lives, whichever is shorter
- Active renal condition, unstable liver or biliary disease, active infection, or active bleeding
- Known HIV infection, HBV, or HCV positive test result <3 months prior to first dose
- Previous/concurrent malignancies other than MM, unless considered medically stable for >2 years
- Known reactivity to drugs chemically related to belantamab mafodotin, pom, dex, or any of the components of the study intervention

Study objectives and endpoints

Primary endpoint:

- PFS

Key secondary endpoint:

- OS

Additional secondary endpoints:

- ORR
- Clinical benefit rate
- DoR
- Time to response
- Time to progression
- PK/ADA profiles
- Minimal residual disease negativity rate (10^{-5} threshold assessed by next-generation sequencing)
- Safety: incidence of AEs and ocular findings on ophthalmic exam
- Self-reported symptomatic AEs
- HRQoL

Exploratory endpoints:

- Baseline BCMA expression, changes in soluble BCMA and circulating free DNA
- Time to best response
- PFS on subsequent line of therapy
- Further evaluation of changes in safety assessments, including vital signs and ECGs
- Further evaluation of changes in symptoms and HRQoL
- Further PK profiling
- Relationships between belantamab mafodotin exposure and efficacy and safety endpoints
- Health care resource utilization

Current status

Study start is planned for: **Dec 2019**

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Abbreviations

ADA, anti-drug antibody; AE, adverse event; BCMA, B-cell maturation antigen; CI, confidence interval; dex, dexamethasone; DoR, duration of response; ECG, electrocardiogram; ECOG, Eastern Cooperative Oncology Group; HBV, hepatitis B virus; HCV, hepatitis C virus; HIV, human immunodeficiency virus; HRQoL, health-related quality of life; IMWG, International Myeloma Working Group; ISS, international staging system; mAb, monoclonal antibody; MM, multiple myeloma; NE, not estimable; ORR, overall response rate; OS, overall survival; PD, progressive disease; PFS, progression-free survival; PK, pharmacokinetics; POEMS, polyneuropathy organomegaly endocrinopathy monoclonal gammopathy and skin changes; pom, pomalidomide; PS, performance status; Q3W, every 3 weeks; RRMM, relapsed/refractory multiple myeloma; SCT, stem cell transplant.

Disclosures

KW declares a consulting role or honoraria for Amgen, Bristol-Myers Squibb, Celgene, Adaptive Biotech, Janssen, Sanofi, Takeda, GSK, Juno and research funding from Amgen, Celgene, Janssen, Sanofi; **CQ**, **RCJ**, **MN**, **JO,** and **DF** are employees of and hold stocks/shares in GSK; **TGH** and **WB** were employees of GSK at the time of study design and hold stocks/shares in GSK.

Acknowledgments

This study was funded by GlaxoSmithKline (GSK ID: 207495); drug linker technology is licensed from Seattle Genetics; monoclonal antibody is produced using POTELLIGENT Technology licensed from BioWa. Editorial assistance (in the form of writing assistance, assembling figures, collating author comments, grammatical editing and referencing) was provided by Gemma Corr, DPhil, and Fiona Woodward, PhD, at Fishawack Indicia Ltd, UK, and funded by GSK.

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Presented at the American Society of Hematology Annual Meeting, Orlando, FL, USA, December 7–10, 2019