To make an indirect comparison of the efficacy of single-agent belatamab vs. the appropriate comparators and standard of care (SOC) in similar patient populations (received >3 prior lines of therapy, refractory to or-CD38 therapies) in a post hoc analysis of DREAMM-2 (NCT02952678).

### Background

- Patients with RRMM whose disease has progressed following SOC regimens have limited treatment options. Improving the prognosis of patients with heavily pretreated RRMM is a significant challenge and remains an important unmet need in this patient population.

- Belatamab is an antibody-drug conjugate that binds to B-cell maturation antigen (BCMA) and eliminates target cells by mechanisms of action (MOA) of single-agent belatamab demonstrated clinically meaningful, deep and durable responses, along with a manageable safety profile in patients with heavily pretreated RRMM in the DREAMM-2 primary analysis and 13-month follow-up.10

- The efficacy of belatamab versus other treatments, including SOC, has not yet been assessed in head-to-head comparator studies.

- Matching-adjusted indirect comparison (MAIC) and Bucher indirect treatment comparison (ITC) analyses were conducted to compare the efficacy of belatamab with SOC and SOC.

### Methods

#### Study design and population

- DREAMM-2 is a Phase III, open-label, randomized study of belatamab in patients with RRMM (men and women who had previously received >3 lines of therapy), refractory to an immunomodulatory agent and a proteasome inhibitor (PI), had prior exposure to an anti-CD38 antibody and an antibody-drug conjugate, and provided informed consent.10

- Data from the 5.5 mg/kg arm (n=97) were used in this analysis (13-month follow-up), with a cutoff of data as January 31, 2021.

#### Identification of an appropriate comparator: STORM Part 2

- Serum samples were collected in Embra, Madrid, Cochrane Collaboration Central Register of Controlled Trials (CENTRAL), and the Database of Abstracts of Reviews of Effects (DARE) and published online in January 2019 to April 2019 that included patients with late-line RRMM with ≥3 prior lines of therapy.

- After screening, according to prespecified inclusion and exclusion criteria, only one comparator (STORM Part 2) with a comparable patient population was identified for inclusion in the MAIC.

#### STORM Part 2 was a Phase II, open-label study of selinexor (80 mg) vs placebo (20 mg; sel-dex) consisting of patients with RRMM who had received >3 prior lines of therapy and were refractory to daratumumab, immunomodulatory agents, and PI.10

#### MAIC

- Population adjustment was carried out by matching populations on all available clinically validated effect modifiers and prognostic factors.
- Both patient populations were comparable on refractory status to a PI, or an immunomodulatory agent, and daratumumab, there was no need for adjustment.
- The overall response rate (ORR), overall survival (OS), duration of response (DoR), progression-free survival (PFS), and time to response (TTTR) of belatamab vs sel-dex were compared using MAICs.

### Results

#### Efficacy population

The baseline characteristics of the patients enrolled in DREAMM-2 before and after the MAIC adjustment and the corresponding aggregated characteristics for the belatamab patient population are provided in Table 1.

### Efficacy analyses

- Following population adjustments, the OS and DoR were significantly longer for belatamab compared with sel-dex (Table 2, Figure 2, and Table 3), adjusted TTR, PFS, and ORR values were not significantly higher for belatamab versus sel-dex (Table 4).
- Differences in schedules of progression assessment may have affected PFS and TTR, as initial assessments were performed 3 weeks after initiation of therapy in DREAMM-2 and STORM Part 2, respectively.
- Although response rates were equivalent between belatamab and sel-dex, patients achieved deeper responses with belatamab compared with sel-dex (58% vs. 25% of responses were very good partial response for belatamab and sel-dex, respectively).

### Table 1. Demographics and baseline characteristics in DREAMM-2 before and after MAIC adjustment, and baseline characteristics in STORM Part 2

<table>
<thead>
<tr>
<th>Variable</th>
<th>Original</th>
<th>MAIC</th>
<th>STORM Part 2</th>
<th>MAIC</th>
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<tbody>
<tr>
<td>Age (years)</td>
<td>63.0</td>
<td>62.9</td>
<td>60.7-64.2</td>
<td>6.0</td>
</tr>
<tr>
<td>Sex</td>
<td>Male</td>
<td>61</td>
<td>61</td>
<td>59-63</td>
</tr>
<tr>
<td>ECOG Performance Status</td>
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<td>53</td>
<td>53</td>
<td>50-55</td>
</tr>
<tr>
<td>Number of prior lines of therapy</td>
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<td>4</td>
<td>3-6</td>
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<td>Renal function</td>
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<td>9.0</td>
<td>8.0-10.0</td>
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</tr>
<tr>
<td>Serum creatinine level (mg/dL)</td>
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<td>1.8</td>
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<tr>
<td>Extramedullary plasmacytomas</td>
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<td>27</td>
<td>24-30</td>
</tr>
<tr>
<td>Extramedullary plasmacytomas</td>
<td>Yes</td>
<td>4</td>
<td>4</td>
<td>4-5</td>
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<tr>
<td>Number of previous lines of therapy</td>
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<tr>
<td>Baseline β2-microglobulin</td>
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<tr>
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<tr>
<td>Previous therapies</td>
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<td>7</td>
<td>6-8</td>
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</tr>
</tbody>
</table>

#### Figure 2. Bucher indirect treatment comparison (ITC) of belatamab and SOC

- Efficacy analyses showed that belatamab was associated with longer OS and DoR compared with sel-dex, and improved TTR and PFS. These findings were consistent with the primary analysis of DREAMM-2.

### Figure 3. OS Kaplan-Meier plots for belatamab 2.5 mg/kg (DREAMM) and sel+dex (STORM Part 2)

- The Bucher ITC analysis also suggested significantly longer OS with single-agent belatamab versus SOC (Figure 3C).

#### Conclusions

In the MAIC, extramedullary disease at baseline, presence of tibic bone lesions at baseline, and BCMA levels were reported in DREAMM-2 but not in STORM, hence no adjustment could be made for these variables. Additionally, proportion of patients achieving response could not be balanced with regard to time elapsed since MM diagnosis and modality-specific factors.

In the Bucher ITC analysis, limitations included the shared-effect modifier assumption, imbalances in treatment-effect modifiers between compared populations, and comparison against real-world studies.

### MAIC analyses indicated significant improvements in OS and DoR with single-agent belatamab versus sel-dex in patients with heavily pretreated RRMM.

### Limitations

- Subject to the shared treatment effects modifier assumption, Bucher ITC suggested significantly improved OS with belatamab versus SOC.

### Additional analyses will inform safety comparisons.

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**Assessing Efficacy via Indirect Comparison of Single-Agent Belantamab Mafodotin (Belamaf; GSK2857916) in DREAMM-2 Versus STORM or MAMMOTH Studies in Relapsed/Refractory Multiple Myeloma (RRMM)**

**Poster No. MM-209**

**References**


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**Disclosures**

- All contacting authors, excepting authors from GlaxoSmithKline (GSK), Janssen, and Karyopharm Therapeutics; research funding from Bristol-Myers Squibb, Celgene, and Janssen) have no potential conflicts of interest, except for financial support from GSK and Janssen, and for consulting fees from GlaxoSmithKline (GSK), Janssen, and Karyopharm Therapeutics.

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**Acknowledgements**

- Editorial assistance was provided by Kim Flowers-Holmes and Mushika Yeobofor Fishaweko Indics Ltd and funded by GSK. This study was funded by the UK’s National Institute for Health Research (NIHR), the NIHR Health Technology Assessment Programme (HTA), and the Department of Health. Funding for the clinical trial was provided by GSK, (2017/18). Drug development and manufacturing: Cellgene Limited. Lytic bone lesion: Genentech, Inc. Genetically modified antibody produced using POTELLIGENT Technology licensed from Biozoon.