DREAMM-6: Safety and Tolerability of Belantamab Mafodotin in Combination with Bortezomib/Dexamethasone in Relapsed/ Refractory Multiple Myeloma (RRMM)

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Disclosures

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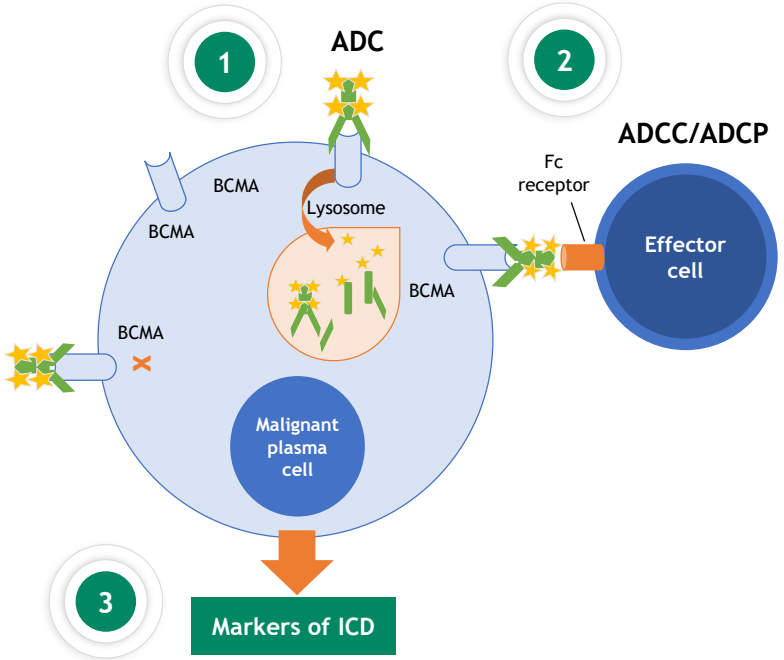
Belamaf Is An Ideal Candidate For Use In Combination With Other Treatments

Belantamab Mafodotin (belamaf; GSK2857916) is a first-in-class anti-BCMA antibody-drug conjugate with a **multimodal MoA**[1,2]



In the Phase II DREAMM-2 study, **single-agent belamaf demonstrated deep and durable responses** in patients with heavily pre-treated RRMM[3,4*]

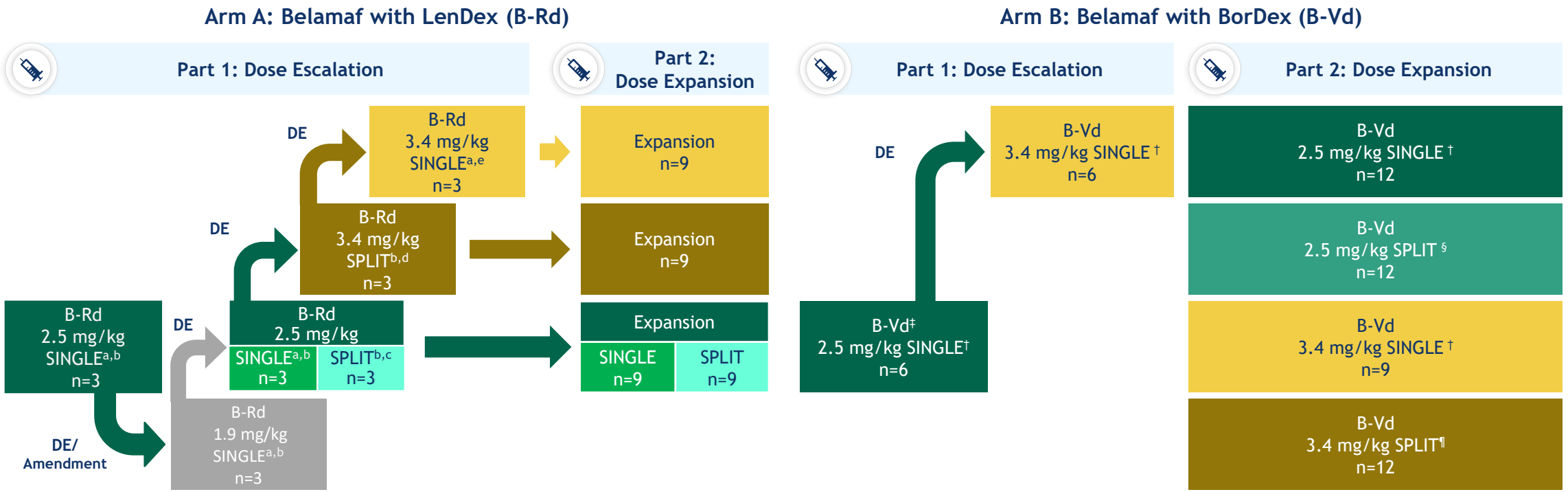
Outcome at 13-month follow-up	Belamaf 2.5 mg/kg (n=97)	Belamaf 3.4 mg/kg (n=99)
ORR†, n (%) (97.5% CI)	31 (32) (21.7-43.6)	35 (35) (24.8-47.0)
Median DoR, months (95% CI)	11.0 (4.2-NR)	6.2 (4.8-NR)
Median PFS, months (95% CI)	2.8 (1.6-3.6)	3.9 (2.0-5.8)
Median OS, months (95% CI)	13.7 (9.9-NR)	13.8 (10.0-NR)

In DREAMM-2, belamaf showed an **acceptable safety profile**[3,4]

*Refractory to an immunomodulatory agent, a proteasome inhibitor, and refractory and/or intolerant to an anti-CD38 monoclonal antibody †Defined as partial response or better.
ADC, antibody-drug conjugate; ADCC/P, antibody-dependent cellular cytotoxicity/phagocytosis; BCMA, B-cell maturation antigen; Belamaf, belantamab mafodotin; CI, confidence interval; DoR, duration of response; DREAMM, DRiving Excellence in Approaches to Multiple Myeloma; ICD, immunogenic cell death; MoA, mode of action; NR, not reached; ORR, overall response rate; OS, overall survival; PFS, progression free survival; RRMM, relapsed or refractory multiple myeloma
1. Tai YT et al. Blood. 2014;123:3128-38; 2. Tai YT & Anderson KC. Immunotherapy 2015; 7:1187-99; 3. Lonial S et al. Lancet Oncol 2020;21:207-21; 4. Lonial S et al. ASCO 2020 poster 436.

DREAMM-6 Study Design

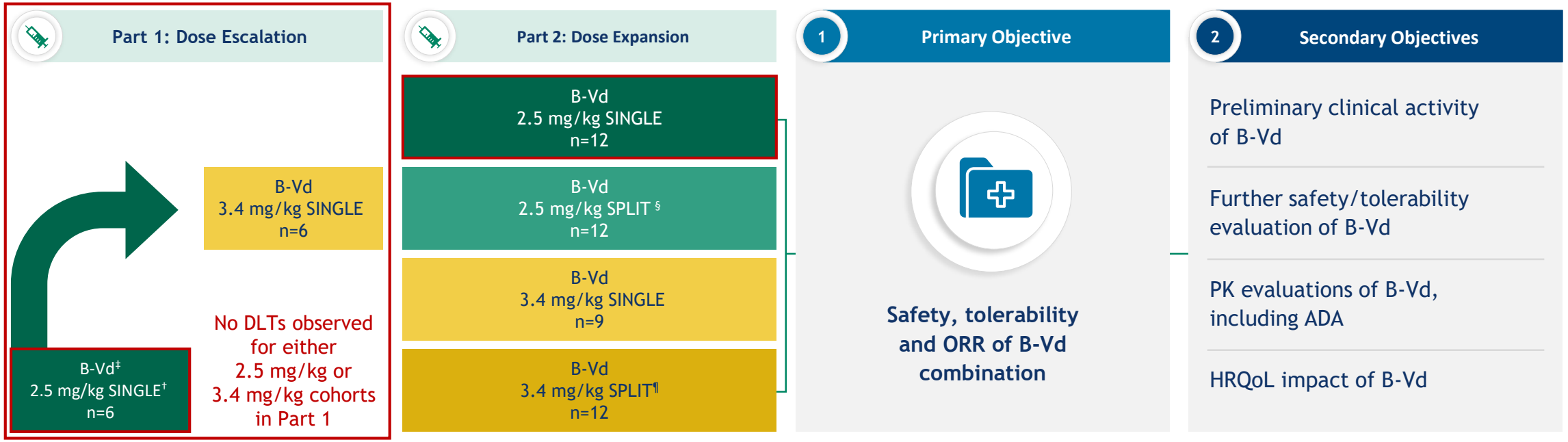
An ongoing, two-part, two-arm, open-label, Phase I/II study of Belamaf in combination with LenDex and BorDex in patients with RRMM previously treated with ≥1 prior therapy (NCT03544281)*



*Combination therapy continued for up to 8 cycles. Thereafter, belamaf monotherapy further continued until disease progression, death, intolerable toxicity, consent withdrawn. Cohorts followed-up for PFS and OS
a. Belamaf SINGLE = full assigned dose of belamaf administered on Day 1 of any 28-day cycle b. Lenalidomide (25 mg on Days 1-21) + dexamethasone (40 mg on Days 1, 8, 15, and 22) of any 28-day cycle; c. belamaf 2.5 mg/kg SPLIT = 1.25 mg/kg on Day 1 and 1.25 mg/kg on Day 8 of any 28-day cycle; d. belamaf 3.4 mg/kg SPLIT = 1.7 mg/kg on Day 1 and 1.7 mg/kg on Day 8 of any 28-day cycle; e. belamaf 3.4 mg/kg SINGLE = May be evaluated based on risk/benefit assessment of GSK2857916 3.4 mg/kg SPLIT;†Belamaf SINGLE = full assigned dose of belamaf administered on Day 1 of any 21-day cycle ‡Bortezomib (1.3 mg/m^2 on Days 1, 4, 8, and 11) + dexamethasone (20 mg on Days 1, 2, 4, 5, 8, 9, 11, and 12) of any 21-day cycle. §Belamaf 2.5 mg/kg SPLIT = 1.25 mg/kg on Day 1 and 1.25 mg/kg on Day 8 of any 21-day cycle. ¶Belantamab mafodotin 3.4 mg/kg SPLIT = 1.7 mg/kg on Day 1 and 1.7 mg/kg on Day 8 of any 21-day cycle.
Belamaf, belantamab mafodotin; BorDex, bortezomib/dexamethasone; B-Rd, Belamaf/lenalidomide/dexamethasone; B-Vd, belamaf/bortezomib/dexamethasone; DE, dose escalation; DREAMM, Driving Excellence in Approaches to Multiple Myeloma; LenDex, lenalidomide/dexamethasone; RRMM, relapsed or refractory multiple myeloma.

DREAMM-6 Arm B Study Design

Belamaf 2.5mg/kg SINGLE dosing in combination with BorDex in patients with RRMM previously treated with ≥1 prior therapy
(NCT03544281)*



*Combination therapy continued for up to 8 cycles. Thereafter, belamaf monotherapy further continued until disease progression, death, intolerable toxicity, consent withdrawn. Cohorts followed-up for PFS and OS.
†Belamaf SINGLE = full assigned dose of belamaf administered on Day 1 of any 21-day cycle. ‡Bortezomib (1.3 mg/m^2 on Days 1, 4, 8, and 11) + dexamethasone (20 mg on Days 1, 2, 4, 5, 8, 9, 11, and 12) of any 21-day cycle. §Belamaf 2.5 mg/kg SPLIT = 1.25 mg/kg on Day 1 and 1.25 mg/kg on Day 8 of any 21-day cycle. ¶Belantamab mafodotin 3.4 mg/kg SPLIT = 1.7 mg/kg on Day 1 and 1.7 mg/kg on Day 8 of any 21-day cycle; ADA, Anti-Drug-Antibodies; BCMA, B-cell maturation antigen; BorDex, bortezomib/dexamethasone; B-Vd, belamaf/bortezomib/dexamethasone; DREAMM, Driving Excellence in Approaches to Multiple Myeloma; HRQoL, health related quality of life; PK, pharmacokinetics; RRMM, relapsed or refractory multiple myeloma.

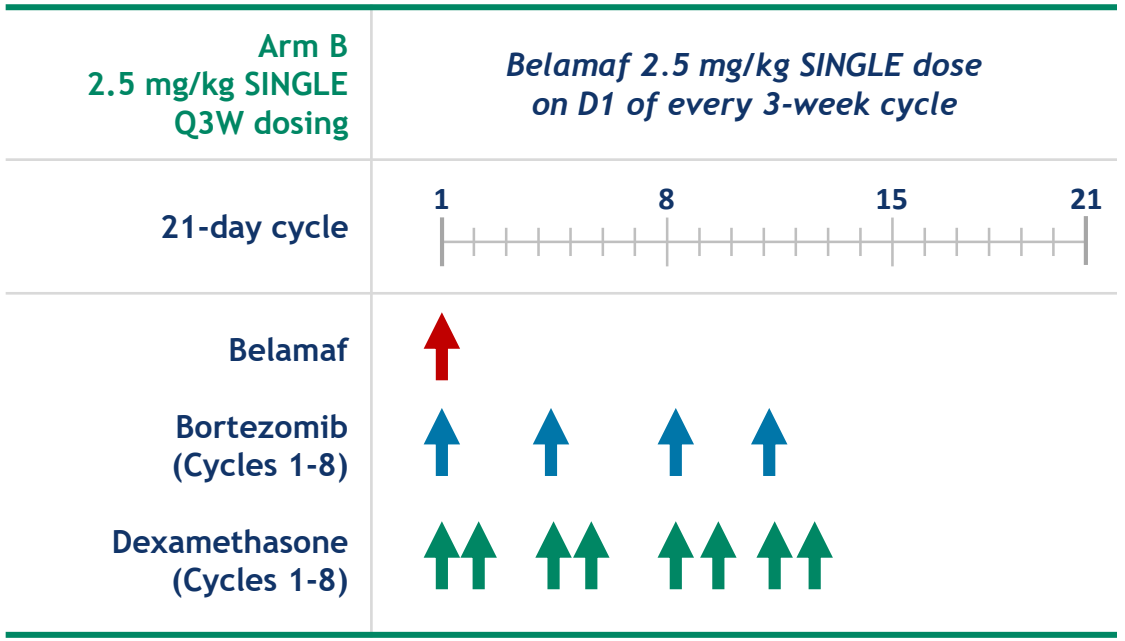
DREAMM-6 Arm B Dosing Schedule

Belamaf 2.5mg/kg SINGLE dosing in combination with BorDex in patients with RRMM previously treated with ≥1 prior therapy
(NCT03544281)*

Key Eligibility Criteria:

- ≥1 prior therapy
- Measurable disease†
- Adequate organ system function
- Prior autologous-stem cell transplant allowed or transplant-ineligible
- Patients refractory to bortezomib were not excluded
- ECOG 0-2
- Not exposed to a mAb therapy within 30 days

B-Vd Dosing Schedule‡



*Combination therapy continued for up to 8 cycles. Thereafter, belamaf monotherapy further continued until disease progression, death, intolerable toxicity, consent withdrawn. Cohorts followed-up for PFS and OS; †Measurable disease defined as serum myeloma protein (M-protein) ≥0.5 g/dL and/or urine M-protein ≥200 mg/24h and/or serum free-light chain (FLC) assay: Involved FLC level ≥10 mg/dL and an abnormal serum FLC ratio (<0.26 or >1.65); ‡Dose delays or reductions can be used to manage adverse events. Belamaf, belantamab mafodotin; BorDex, bortezomib/dexamethasone; B-Vd, belamaf/bortezomib/dexamethasone; DREAMM, Driving Excellence in Approaches to Multiple Myeloma; ECOG, Easter Cooperative Oncology Group performance status; mAb, monoclonal antibody; RRMM, relapsed or refractory multiple myeloma.

DREAMM-6 Arm B: Patient Demographics and Baseline Disease Characteristics

Characteristic	B-Vd‡ (n=18)
Age, years; median (range)	67 (47–83)
Sex, n (%)	
Male	11 (61)
Female	7 (39)
Race, African-American, n (%)	4 (22)
Number of prior lines of therapy, n (%)	
1	4 (22)
2–3	6 (33)
4–6	4 (22)
≥7	4 (22)
Median number of prior lines of therapy (range)	3 (1–11)
ISS Stage, n (%)	
I	4 (22)
II	8 (44)
III	3 (17)
Unknown	3 (17)
ECOG, n (%)	
0–1	15 (83)
≥2	3 (17)
High-risk cytogenetics, n (%)*	6† (33)

*Defined as t(4;14), t(14;16), or del17p13; †Cytogenetic data were not available for 6 patients; ‡Belamaf 2.5 mg/kg SINGLE+ BorDex
B-Vd, belantamab mafodotin/bortezomib/dexamethasone; ECOG, Easter Cooperative Oncology Group performance status; ISS, International Staging System; PI, proteasome inhibitor.

DREAMM-6 Arm B: Time on Treatment

As of data-cut-off date of March 30 2020, belamaf 2.5 mg/kg SINGLE + BorDex patients had a median of 18.2 (range, 6.0–46.4) weeks on treatment

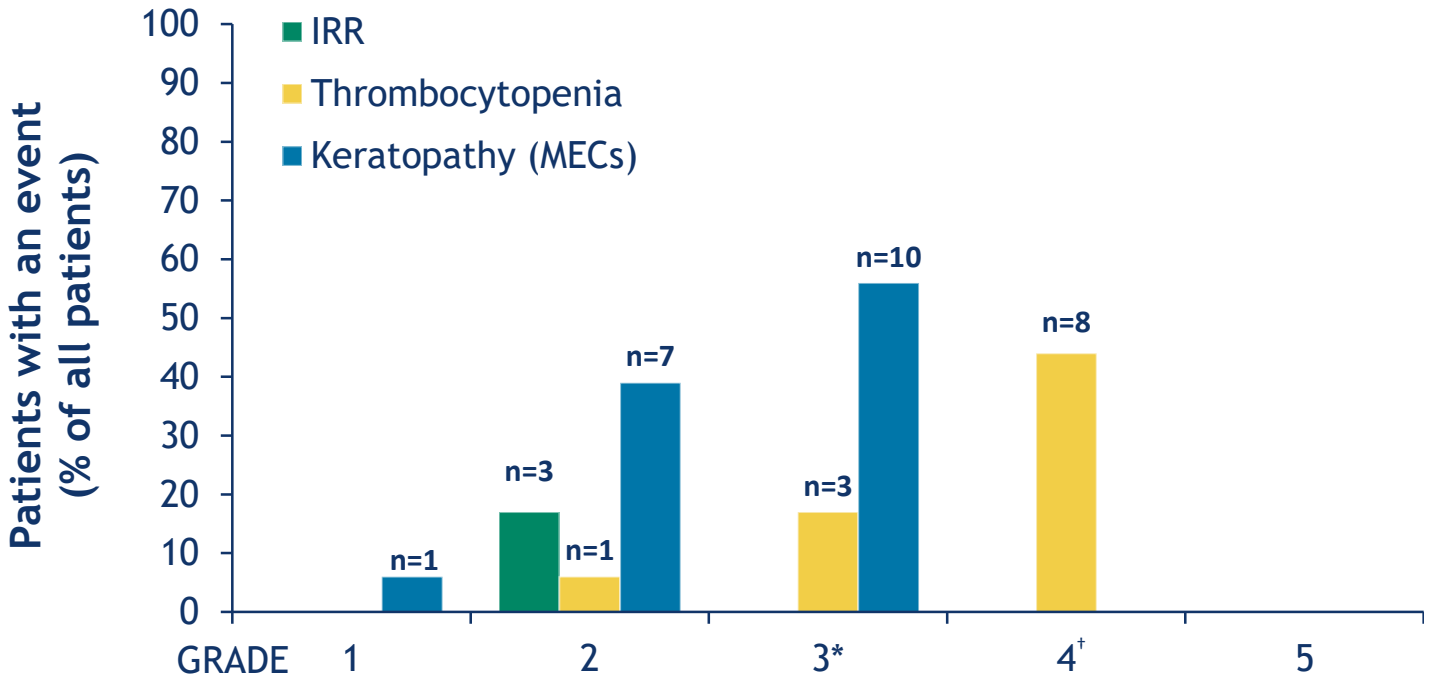
DREAMM-6 Arm B: Overview of Adverse Events

Patients with AE, n (%)	B-Vd¶ (n=18) [Part 1 + Part 2]
AE related to study treatment	**18 (100)**
Grade 3/4 AE	16 (89)
AEs leading to permanent discontinuation of a study treatment	5 (28)†
AEs leading to permanent discontinuation of belamaf	0
AE leading to dose reductions	**13‡ (72)**
Keratopathy (MECs)¥ leading to dose reduction	7 (39)
Thrombocytopenia AE leading to dose reduction	6 (33)
AE leading to dose interruption/delay	**18* (100)**
Keratopathy (MECs)¥ leading to dose interruption/delay	15 (83)
Thrombocytopenia AE leading to dose interruption/delay	7 (39)
Any SAE	**12 (67)**
Fatal SAE	**0**
SAE related to study treatment	**5**(28)**

¶Belamaf 2.5 mg/kg SINGLE+ BorDex; †4/5 discontinued bortezomib, 2/5 discontinued dexamethasone; 4/5 remain on the study receiving belamaf monotherapy; ‡8/13 had an AE leading to a dose reduction in belamaf; ¥Changes to the corneal epithelium observed on eye examination (corneal events/keratopathy/microcyst-like epithelial changes [MECs]); *16/18 had an AE leading to a dose interruption/delay in belamaf; **3/5 SAEs were related to belamaf treatment, 4/5 were related to bortezomib, 2/4 were related to dexamethasone and 1/5 was an undefined causality; AE, Adverse event; B-Vd, belantamab mafodotin/bortezomib/dexamethasone; DLT, dose limiting toxicity; SAE, serious adverse event.

DREAMM-6 Arm B: AESI by Maximum Grade

Belamaf 2.5 mg/kg SINGLE + BorDex (n=18) [Part 1 + Part 2] preliminary AESI data



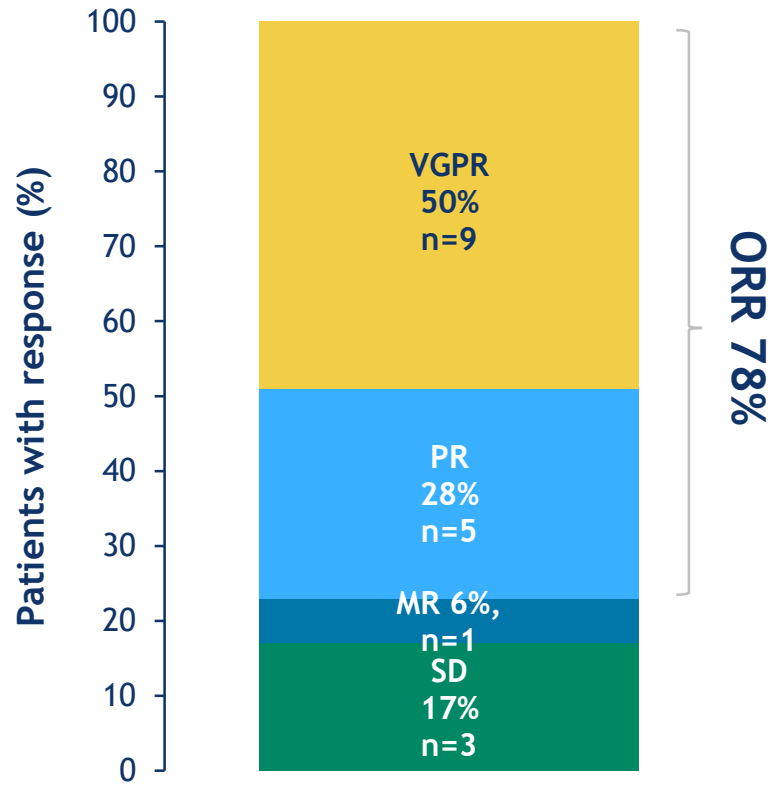
- There were no Grade 5 events
- There were no Grade 4 corneal events
- Dose delays or reductions could be used to manage AE
- B-Vd had a manageable safety profile consistent with that of the individual components
- Data are not sufficiently mature to report resolution of corneal events at this time
- *[In DREAMM-2, at limited follow-up, vision had returned to baseline/near baseline in 69/85 (81%) affected patients. No permanent loss of vision was reported]*[1]

1. Lonial S et al. Lancet Oncol 2020;21:207-21

*Grade 3: Severe or medically significant but not immediately sight-threatening, hospitalization or prolongation of existing hospitalization indicated, limiting self-care or activities of daily living; †Grade 4. Sight-threatening consequences; urgent intervention indicated; blindness(20/200 or worse) in the affected eye. AESI, adverse event of special interest; BorDex, bortezomib/dexamethasone; IRR, infusion related reaction; MECs, microcyst-like epithelial changes; Thrombocytopenia includes MeDRA preferred terms platelet count decreased, thrombocytopenia; Keratopathy (corneal events/MECs) encompasses many preferred terms; most commonly reported symptoms related to corneal events include blurred vision, dry eye, photophobia, foreign body sensation and eye pain; most commonly reported exam findings include keratopathy.

DREAMM-6 Arm B: Investigator-Assessed Best Confirmed Response

Belamaf 2.5 mg/kg SINGLE + BorDex (n=18) [Part 1 + Part 2] preliminary best confirmed response data



In patients with **≥1 prior line** of therapy, **B-Vd** treatment had an **ORR of 78%** (95% CI 52.4–93.6)

CBR was 83% (95% CI 58.6–96.4)

All patients had an **evaluable response**

50% of patients experienced **VGPR**

DoR is not yet reached

In patients with **≥1 prior line** of therapy, **Vd** treatment demonstrated an **ORR of 50%–63%**[1-3]

*Investigator-assessed best confirmed response (International Myeloma Working Group 2016 criteria). No patients had stringent complete response (sCR), complete response (CR), or progressive Disease.
B-Vd, belamaf/bortezomib/dexamethasone; CBR, Clinical Benefit Rate (sCR+CR+VGPR+PR+MR), CI, confidence Interval based on exact method; MR, minimal response; ORR, overall response rate (sCR+CR+VGPR+PR); PR, partial response; SD, stable disease; Vd, bortezomib/dexamethasone; VGPR, very good partial response.

1. Palumbo A, et al. N Engl J Med 2016;375:754-66; 2. San-Miguel F, et al. Lancet Oncol. 2014;15(11):1195-206; 3. Richardson P, et al. Lancet Oncol. 2019;20(6):781-94.

Conclusions

To date, **59 patients** have been treated with **B-Vd** (belamaf and BorDex in combination) in Arm B of DREAMM-6

- Of these, **18** have received **2.5mg/kg Q3W** (SINGLE) **dose of belamaf** in combination with standard-dose BorDex

Preliminary data indicate that the combination of 2.5 mg/kg Q3W belamaf with BorDex has an acceptable safety profile

- The main AEs were:
  - Keratopathy* (MECs; as expected for belamaf, managed with dose modifications)
  - Thrombocytopenia (as expected for both belamaf and Bor)

Preliminary investigator-assessed best response data indicate an **ORR of 78%, a VGPR of 50%,** and CBR of 83% with **belamaf 2.5 mg/kg + BorDex** in participants with RRMM with median 3 prior lines of therapy (range 1–11)

- DoR not yet reached and, response may be expected to deepen over time

This study is currently ongoing. Data for the other dose-schedules in both arms are being collected and will be presented at future meetings

*Corneal events.

Acknowledgements and Further Information

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Belamaf is being evaluated in other clinical trials in various MM settings and is being discussed at this meeting:

- **Posters 452 and 456 -** Belamaf in combination with other agents
- **Posters 436, 419 and 441 -** Belamaf as monotherapy

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