Characterization of infections in patients with relapsed/refractory multiple myeloma treated with belantamab mafodotin–based regimens from DREAMM-7 and DREAMM-8 trials

Digital poster

Poster recording

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Introduction

- BCMA is an established target in RRMM, with approved BCMA-targeting therapies for these patients that include CAR T-cell therapies (cilta-cel and ide-cel) and bispecific antibodies[1]
- However, these T-cell–redirecting therapies have been associated with toxicities; for example, bispecific antibodies in clinical studies of RRMM have demonstrated a high risk of grade ≥3 and fatal infections as well as opportunistic infections not commonly observed in MM[2,3]
  - In phase 2 studies of the bispecific antibodies teclistamab and elranatamab, infections occurred in 76.4% and 69.9% of patients, respectively, with grade 3 or 4 events in 44.8% and 39.8% and fatal events in 9.7% and 6.5%; IVIG was used by 39.4% of patients receiving teclistamab and 43.1% of those receiving elranatamab[2,3]
  - Studies have also shown a risk of infections with BCMA-targeting CAR T-cell therapy (grade 3 or 4 infections in 26.9% with cilta-cel and 24% with ide-cel), despite intensive supportive care that includes IVIG, prophylactic antimicrobials, and G-CSF[4,5]
- Belantamab mafodotin (belamaf) is a BCMA-targeting monoclonal antibody-drug conjugate that has a multimodal mechanism of action[6,7]
- In the phase 3, randomized, DREAMM-7 and DREAMM-8 trials in patients with RRMM after ≥1 prior line of therapy, belamaf-based regimens demonstrated significant and clinically meaningful PFS benefit vs standard of care, with significant OS benefit also observed in DREAMM-7[8-10]
- Our aim is to describe the infections profile and concomitant use of supportive therapies with belamaf-based regimens from DREAMM-7 (data cutoff: October 2, 2023) and DREAMM-8 (data cutoff: January 29, 2024)

Methods

- DREAMM-7 (NCT04246047) compared BVd vs DVd, and DREAMM-8 (NCT04484623) compared BPd vs PVd[8,9]
- Patients were treated per protocol until occurrence of progressive disease, unacceptable toxic effects, withdrawal of consent, or death (whichever occurred first)
  - Antiviral prophylaxis was recommended for patients being treated with daratumumab or bortezomib, per local prescribing information and clinical practice
- Data were analyzed post hoc to summarize infections and infestations (by system organ class; referred to as infections hereafter), use of immunoglobulin, and profile of neutropenia
- Post hoc exposure-adjusted rates were defined as the total number of patients with an event divided by the total exposure time in PYs (per 100 PYs)
- Total exposure time in PYs is the sum of all patients' exposure time calculated as (last dose − first dose + 1) / 365.25

Results

Patient Characteristics

- Conduct of both DREAMM-7 and DREAMM-8, including enrollment, occurred during the COVID-19 pandemic[8,9]
  - From May 2020, through June 2021, 494 patients were randomly assigned to receive BVd (N=243) or DVd (N=251) in DREAMM-7 (median follow-up, 28.2 months)
  - From October 2020, through December 2022, 302 patients were randomly assigned to receive BPd (N=155) or PVd (N=147) in DREAMM-8 (median follow-up, 21.8 months)
  - Baseline characteristics were well balanced between treatment arms in both trials
- The safety population included patients who received ≥1 dose of study treatment, which was 488 patients (BVd, 242; DVd, 246) in DREAMM-7 and 295 patients (BPd, 150; PVd, 145) in DREAMM-8
  - At data cutoff, median duration of exposure to any study treatment was 15.9 months with BVd, 12.9 months with DVd, 16.5 months with BPd, and 8.5 months with PVd

Overview of Infections

- Overall, infections (any grade) occurred in 70% of patients receiving BVd and 67% of those receiving DVd, and 82% vs 68% in patients receiving BPd vs PVd, respectively; exposure-adjusted rates between belamaf-containing regimens (BVd and BPd) and their respective comparator arms (DVd and PVd) were similar (**Table 1**)
  - Grade ≥3 infections were more common with BVd and BPd vs their respective comparators; exposure-adjusted grade ≥3 rates were 23 per 100 PYs with BVd vs 16 per 100 PYs with DVd, and 35 vs 28 per 100 PYs with BPd vs PVd, respectively (**Table 1**)
  - Infections leading to death occurred at similar rates between belamaf-containing regimens and their respective comparators; across all treatment arms, infections were at least resolving or resolved in most patients at data cutoff (**Table 1**)
- The most common infections were COVID-19, upper respiratory tract infection, pneumonia, urinary tract infection, bronchitis, and COVID-19 pneumonia (**Figure 1**)
  - Grade ≥3 pneumonia occurred more frequently with BVd vs DVd, and grade ≥3 COVID-19 and COVID-19 pneumonia were similar between BVd and DVd arms
  - Grade ≥3 pneumonia, COVID-19, COVID-19 pneumonia, and urinary tract infections were more common with BPd vs PVd
- Rates of opportunistic infection were generally low, and none were fatal (**Table 2**)

Table 1: **Summary of Infections**

n (%) unless otherwise noted	DREAMM-7 BVd (N=242)	DREAMM-7 DVd (N=246)	DREAMM-8 BPd (N=150)	DREAMM-8 PVd (N=145)
Any grade	170 (70)	166 (67)	123 (82)	99 (68)
Exposure-adjusted rate per 100 PYs	51	55	59	73
Serious[a]	71/170 (42)	47/166 (28)	74/123 (60)	37/99 (37)
Related to any study treatment	81/170 (48)	73/166 (44)	49/123 (40)	25/99 (25)
Leading to				
Discontinuation of any study treatment	17/170 (10)	12/166 (7)	4/123 (3)	4/99 (4)
Dose reduction of any study treatment	4/170 (2)	3/166 (2)	8/123 (7)	2/99 (2)
Dose interruption/delay of any study treatment	113/170 (66)	96/166 (58)	104/123 (85)	64/99 (65)
At least resolved or resolving at data cutoff[b]	132/170 (78)	137/166 (83)	96/123 (78)	84/99 (85)
Grade ≥3	75 (31)	49 (20)	73 (49)	38 (26)
Exposure-adjusted rate per 100 PYs	23	16	35	28
Grade 5	17 (7)	15 (6)	11 (7)	9 (6)

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BPd, belantamab mafodotin, pomalidomide, and dexamethasone; BVd, belantamab mafodotin, bortezomib, and dexamethasone; DVd, daratumumab, bortezomib, and dexamethasone; PVd, pomalidomide, bortezomib, and dexamethasone; PY, person-year.

[a] Requires/prolongs hospitalization, leads to death, is life-threatening, results in persistent disability/incapacity, or is a congenital anomaly/birth defect.
[b] All infections and infestations categorized as "recovered/resolved," "recovered/resolved with sequelae," or "recovering/resolving."

Table 2: **Summary of Opportunistic Infections[a]**

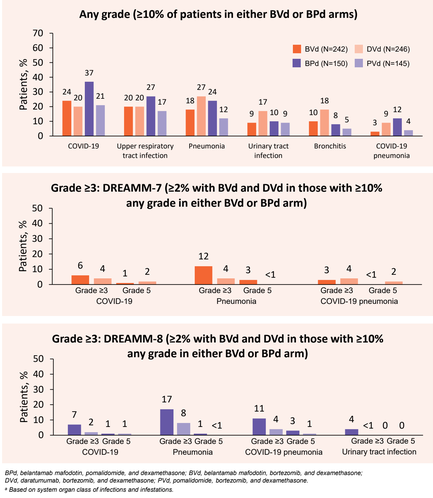
n (%) unless otherwise specified	DREAMM-7 BVd (N=242)	DREAMM-7 DVd (N=246)	DREAMM-8 BPd (N=150)	DREAMM-8 PVd (N=145)
No. of events	3	3	13	1
Patients with an event	3 (1)	2 (<1)	10 (7)	1 (<1)
At least resolved or resolving at data cutoff[b]	1/3 (33)	2/2 (100)	9/10 (90)	0
Patients with a serious event[c]	1/3 (33)	2/2 (100)	7/10 (70)	1/1 (100)
Patients with an event related to any study treatment[c,d]	1/3 (33)	0	5/10 (50)	0
Patients with a fatal event	0	0	0	0

AE, adverse event; BPd, belantamab mafodotin, pomalidomide, and dexamethasone; BVd, belantamab mafodotin, bortezomib, and dexamethasone; DVd, daratumumab, bortezomib, and dexamethasone; MedDRA, Medical Dictionary for Regulatory Activities; PVd, pomalidomide, bortezomib, and dexamethasone.
[a] Includes preferred terms identified in Standardised MedDRA Query.
[b] All events categorized as "recovered/resolved," "recovered/resolved with sequelae," or "recovering/resolving."
[c] Patients may be included in >1 category.
[d] Includes responses of "Yes" and missing response to the following question: "Is there a reasonable possibility that the AE may have been caused by the study treatment?".

Use of Supportive Therapies

- Immunoglobulin replacement therapy and antimicrobial prophylaxis were not mandated per DREAMM-7 and DREAMM-8 trial protocols
- Rates of immunoglobulin use were 8% with BVd vs 4% with DVd, and 18% vs 9% with BPd vs PVd, respectively; when adjusted for treatment exposure per 100 PYs, rates were 6 vs 3 and 13 vs 10

Figure 1: **Summary of the Most Common Infections[a]**



BPd, belantamab mafodotin, pomalidomide, and dexamethasone; BVd, belantamab mafodotin, bortezomib, and dexamethasone; DVd, daratumumab, bortezomib, and dexamethasone; PVd, pomalidomide, bortezomib, and dexamethasone.
[a] Based on system organ class of infections and infestations.

Summary of Neutropenia

- Treatment exposure-adjusted any-grade and grade ≥3 rates of neutropenia were similar between the belamaf-containing arms and their respective comparators (**Table 3**)
  - At data cutoff, neutropenia events were at least resolved or resolving in most patients
  - Concomitant grade 3 or 4 decreased neutrophil count and infection events occurred in a small proportion of patients in the BVd and DVd arms, and occurred in 17% receiving BPd vs 12% receiving PVd

Table 3: **Summary of Neutropenia[a]**

n (%) unless otherwise noted	DREAMM-7 BVd (N=242)	DREAMM-7 DVd (N=246)	DREAMM-8 BPd (N=150)	DREAMM-8 PVd (N=145)
Any grade	43 (18)	41 (17)	95 (63)	66 (46)
Exposure-adjusted rate per 100 PYs	13	14	46	49
At least resolved or resolving at data cutoff[b]	38/43 (88)	36/41 (88)	88/95 (93)	52/66 (79)
Grade ≥3	34 (14)	22 (9)	86 (57)	57 (39)
Exposure-adjusted rate per 100 PYs	10	7	42	42
Concomitant grade 3 or 4 decreased neutrophil count[c] and infection	11 (5)	2 (<1)	26 (17)	18 (12)

BPd, belantamab mafodotin, pomalidomide, and dexamethasone; BVd, belantamab mafodotin, bortezomib, and dexamethasone; DVd, daratumumab, bortezomib, and dexamethasone; PVd, pomalidomide, bortezomib, and dexamethasone; PY, person-year.
[a] Includes preferred terms 'febrile neutropenia,' 'neutropenia,' and 'neutrophil count decreased.'
[b] All events categorized as "recovered/resolved," "recovered/resolved with sequelae," or "recovering/resolving."
[c] Calculated from laboratory data.

Conclusions

- DREAMM-7 and DREAMM-8 were conducted during the COVID-19 pandemic, and immunoglobulin replacement therapy and antimicrobial prophylaxis were not mandated
  - There were low rates of immunoglobulin use throughout both trials (8% with BVd vs 4% with DVd; 18% with BPd vs 9% with PVd; exposure-adjusted rates per 100 PYs for BVd vs DVd were 6 vs 3 and for BPd vs PVd was 13 vs 10)
- Infections with belamaf-based regimens had high rates of resolution and low fatality rates that were comparable with the comparator arm
  - When adjusted for treatment exposure, infections with belamaf-based regimens occurred at similar frequencies to the comparators
- Rates of opportunistic infections with belamaf-based regimens were low, with no fatalities
- Exposure-adjusted any-grade and grade ≥3 rates of neutropenia were similar between belamaf-containing arms and their comparators, with neutropenia events at least resolved or resolving in most patients at data cutoff
- Overall, these results suggest that belamaf-containing regimens have a tolerable infection profile, without the need for intensive supportive care, compared with other BCMA-targeting therapies in patients with RRMM

Abbreviations

AE, adverse event; BCMA, B-cell maturation antigen; belamaf, belantamab mafodotin; BPd, belantamab mafodotin, pomalidomide, and dexamethasone; BVd, belantamab mafodotin, bortezomib, and dexamethasone; CAR, chimeric antigen receptor; cilta-cel, ciltacabtagene autoleucel; DVd, daratumumab, bortezomib, and dexamethasone; G-CSF, granulocyte colony-stimulating factor; ide-cel, idecabtagene vicleucel; IVIG, intravenous immunoglobulin; MedDRA, Medical Dictionary for Regulatory Activities; MM, multiple myeloma; OS, overall survival; PFS, progression-free survival; PVd, pomalidomide, bortezomib, and dexamethasone; PY, person-year; RRMM, relapsed/refractory multiple myeloma.

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