Report BLENREP® - Belantamab mafodotin

Product & Mechanism of action

Substance: Belantamab mafodotin

Brand Name: Blenrep

Originator/licensee:

Classification: NCE

ATC code: L01FX15

Orphan Status:
Eu: Yes
Us: /

Mechanism of action: Belantamab mafodotin, an antibody drug conjugate, consists of a humanised IgG1κ monoclonal antibody targeting the BCMA, conjugated with a cytotoxic agent, maleimidocaproyl monomethylauristatin F.
Belantamab mafodotin binds to BCMA on the surface of myeloma cells causing cell cycle arrest and inducing antibody-dependent cellular cytotoxicity [1].

Authorized indications Licensing status

Authorized Indication:
EMA: Belantamab mafodotin is indicated in adults for the treatment of R/R MM:

- in combination with bortezomib and dexamethasone in pts. who have received at least one prior therapy; and
- in combination with pomalidomide and dexamethasone in pts. who have received at least one prior therapy including lenalidomide [1].

FDA: The US FDA assigns Prescription Drug User Fee Act action date of 23/07/2025 for belantamab mafodotin for MM (Combination therapy, Second-line therapy or greater) [2].

Route of administration: IV

Licensing status
EU CHMP P.O. date: 22/05/2025
FDA M.A. date: /

EU Speed Approval Pathway: No
FDA Speed Approval Pathway: /

ABBREVIATIONS:
AE: Adverse Event
BCMA: B-cell maturation antigen
BVd: Belantamab mafodotin, bortezomib, and dexamethasone
BPd: Belantamab mafodotin, pomalidomide, and dexamethasone
CHMP: Committee for Medicinal Products for Human Use
CI: Confidential Interval
DVd: Daratumumab, bortezomib, and dexamethasone
ECOG: Eastern Cooperative Oncology Group
HR: Hazard Ratio
IMiD: Immunomodulatory drug
IV: Intravenously
M.A.: Marketing Authorization
MM: Multiple myeloma
NR: Not reached
OS: Oral administration
PFS: Progression-Free Survival
PI: Proteasome inhibitor
P.O.: Positive Opinion
PS: Performance Status
Pts: Patients
PVd: Pomalidomide, bortezomib, and dexamethasone
R/R: Relapsed or refractory
R-ISS: Revised International Staging System
SAE: Serious adverse events
SC: Subcutaneously
TRAE: Treatment related AEs
WHO: World Health Organization

Essential therapeutic features

Summary of clinical EFFICACY:

Trial	DREAMM-7 (NCT04246047)	DREAMM-8 (NCT04484623)
Study design	Ongoing phase 3, open-label, global, randomized trial	Ongoing, open-label, global, phase 3, randomized trial
Inclusion criteria	Pts. ≥18 years of age with MM who had received ≥1 line of therapy and had had disease progression during or after the most recent therapy were enrolled. Pts. had to have an ECOG PS of 0-2 and ≥1 aspect of measurable disease. Pts. who were refractory to anti-CD38 therapy or who had been exposed to anti-BCMA therapy were excluded.	Pts. ≥18 years of age with relapsed or refractory myeloma who had been treated with at least one line of therapy including a lenalidomide-containing regimen and who had progressive disease during or after the most recent therapy. Pts. had to have an ECOG PS of 0-2 and ≥1 aspect of measurable disease.
Randomization and treatments	Pts. were randomly assigned in a 1:1 ratio to receive either BVd (n=243) or DVd (n=251). Both treatment groups received bortezomib (SC 1.3 mg/m^2 on days 1, 4, 8 and 11 of 21-day cycles) and dexamethasone (OS or IV 20 mg on the day of and the day after bortezomib administration) for the first eight cycles.The BVd group was treated with IV belantamab mafodotin 2.5 mg/Kg every three weeks, and the DVd group received IV daratumumab 16mg/Kg with decreasing frequency until disease progression. Pts. were stratified according to R-ISS stage at screening, previous exposure to bortezomib, and the number of previous lines of therapy.	Pts. were randomly assigned in a 1:1 ratio to receive either BPd (n=155) or PVd (n=147). Pts. in the BPd group received belantamab mafodotin (2.5 mg/Kg IV on day 1 of cycle 1 and 1.9 mg/Kg on day 1 of cycle 2 onward) with pomalidomide and dexamethasone in 28-day cycles, while those in the PVd group received bortezomib (SC 1.3 mg/m^2 on days 1, 4, 8 and 11 of 21-day cycles) with the same combination in 21-day cycles. Treatment continued until disease progression or other discontinuation criteria. Pts. were stratified according to the number of previous lines of therapy, previous exposure to bortezomib, and whether anti-CD38 antibodies had been received previously.
Endpoints	The primary end point was PFS in the ITT population.	
Results	At a median follow-up of 28.2 months (range, 0.1 to 40.0), median PFS was 36.6 months (95% CI, 28.4 to NR) in the BVd group and 13.4 months (95% CI, 11.1 to 17.5) in the DVd group (HR for disease progression or death, 0.41; 95% CI, 0.31 to 0.53; P<0.001) [2].	At a median follow-up of 21.8 months (range, <0.1 to 39.2), the 12-month estimated PFS with BPd was 71% (95% CI, 63 to 78), as compared with 51% (95% CI, 42 to 60) with PVd (HR for disease progression or death, 0.52; 95% CI, 0.37 to 0.73; P<0.001) [3].

Summary of clinical SAFETY:
DREAMM-7 (NCT04246047): The safety population included all pts., who had received ≥1 dose of any trial drug. All the pts. had ≥1 AE. Grade ≥3 AEs occurred in 95% of the pts. in the BVd group and 78% of those in the DVd group, and SAEs occurred in 50% and 37%, respectively. The most common AEs in both groups were blood disorders and infections: thrombocytopenia (69% of pts. in BVd arm vs. 50% in DVd arm), severe bleeding (7% vs. 6%), anemia (19% vs. 26%) and grade ≥3 pneumonia (12% vs. 4%).
SAEs-related death occurred in 10% (n=23) of pts. in the BVd group and 8% (n=19) in the DVd group; the SAEs that led to death were considered to be related to treatment in 3% (n=7) and 2 pts. (1%), respectively.

DREAMM-8 (NCT04484623): The safety population included all pts. who had received ≥1 dose of any trial drug. AEs of any grade were reported in 99% of the pts., who received BPd and 96% of those, who received PVd. Grade ≥3 AEs occurred in 94% of the pts. in the BPd group and 76% of those in the PVd group, and the percentage of pts. with SAEs was 63% and 45%, respectively.
The most frequently reported AEs in the BPd group were blurred vision (79% of the pts. in BPd group vs 15% of pts. in PVd group), dry eye (61% vs 10%), and foreign-body sensation in the eyes (61% vs 6%). A total of 33 pts. died during the study: 16 in the BPd group and 14 in the PVd group. These deaths were attributed to SAEs.

Ongoing studies:

- ***For the same indication:*** Yes
- ***For other indications:*** No

Discontinued studies (for the same indication): Yes

References:
[1] https://www.ema.europa.eu/en/medicines/human/EPAR/blenrep-0
[2] https://www.nejm.org/doi/full/10.1056/NEJMoa2405090
[3] https://www.nejm.org/doi/abs/10.1056/NEJMoa2403407
[4] https://www.iss.it/documents/20126/8404001/LG92_SIE_MM_v3.5.pdf/e60ca973-8456-16c0-0dda-5f7103b8d11e?t=1678805774591
[5] https://www.epicentro.iss.it/tumori/pdf/2020_Numeri_Cancro-pazienti-web.pdf
[6] https://jnccn.org/view/journals/jnccn/21/12/article-p1281.xml
[7] http://media.aiom.it/userfiles/files/doc/LG/2017_LGAIOM_Mieloma.pdf

NHS impact

Cost of therapy:
In Italy, 100 mg of Blenrep® concentrate for infusion cost € 5.924,13 (ex-factory price).

Epidemiology:
Multiple myeloma is the second most frequent hematologic malignancy. In Italy, the annual incidence is 11.1/100,000 inhabitants [4]. In 2020, 5,700 new cases were diagnosed [5].

POSSIBLE PLACE IN THERAPY:
For pts with R/R MM the choice of appropriate therapy depends on the context of clinical relapse.
PI (bortezomib, carfilzomib), IMiD (pomalidomide) and monoclonal antibodies (daratumumab, elotuzumab) are now considered first-line treatments [6].
Bortezomib in combination with dexamethasone, bortezomib with dexamethasone and liposomal doxorubicin, and lenalidomide with dexamethasone are salvage therapy regimens that have been used for several years in relapsed multiple myeloma [7].

The addition of Belantamab mafodotin to these regimens could represent a further opportunity for these pts.

OTHER INDICATIONS IN DEVELOPMENT: -

SAME INDICATION IN EARLIER LINE(S) OF TREATMENT: -

OTHER DRUGS IN DEVELOPMENT for the SAME INDICATION:
Tanespimycin (NCT00514371); Aplidin (NCT01102426); Venetoclax (NCT02755597)

*Service reorganization: No
*Possible off label use: Yes

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