Belantamab mafodotin (Blenrep®) as monotherapy for the treatment of relapsed or refractory multiple myeloma (MM)

General information [1]

Drug description	Indication
Belantamab mafodotin (also known as GSK2857916) is a humanised IgG1κ monoclonal antibody against the BCMA conjugated with a cytotoxic agent, maleimidocaproyl monomethyl auristatin F	Belantamab mafodotin is indicated as monotherapy for the treatment of MM in adult patients, who have received at least four prior therapies and whose disease is refractory to at least one proteasome inhibitor, one immunomodulatory agent, and an anti-CD38 monoclonal antibody, and who have demonstrated disease progression on the last therapy.

Current treatment [2]

- ❖ Lenalidomide in combination with dexamethasone is recommended for the treatment of MM in transplant-eligible patients who have received at least two prior therapies
- ❖ The following are recommended as subsequent (post-second line) therapies for treating MM in transplant in-eligible patients:
  - daratumumab monotherapy
  - ixazomib, with lenalidomide and dexamethasone
  - pomalidomide, in combination with low-dose dexamethasone
  - panobinostat in combination with bortezomib and dexamethasone
  - lenalidomide in combination with dexamethasone

Regulatory status

EMA [1, 3]	FDA
Approval status for this indication: On 23 July 2020, the CHMP adopted a positive opinion, recommending the granting of a conditional marketing authorisation for Blenrep®, intended for the treatment of relapsed and refractory MM. On 16 October 2017, orphan designation was granted by the European Commission. **Other indications**: none ✓ **Orphan status** ✓ **Accelerated assessment**[1]	**Approval status for this indication**: submitted; not approved

Costs

Currently no cost information available.

Study characteristics [4, 5]

Trial name	*n*	Intervention (I)	Comparator (C)	PE	Characteristics	Biomarker	Funding	Publication(s)
DREAMM-2 NCT03525678	196	belantamab mafodotin 2.5 mg/kg IV every 3 weeks on day 1 of each cycle	belantamab mafodotin 3.4 mg/kg IV every 3 weeks on day 1 of each cycle	the proportion of randomly assigned patients in the ITT population who achieved an overall response (as assessed by an IRC)	open-label, two-arm, multicenter, international, phase 2 trial	-	GlaxoSmithKline	Link

Efficacy (I vs. C)

Overall response (by IRC): 30 (31%; 97.5% CI 20.8–42.6) of 97 patients vs. 34 (34%; 23.9–46.0) of 99 patients

Very good partial response or better: 18 (19%) of 97 patients vs. 20 (20%) of 99 patients

Clinical benefit (minimal response or better, by IRC): 33 (34%; 95% CI 24.7–44.3) of 97 patients vs. 39 (39%; 29.7–49.7) of 99 patients.

Safety (I vs. C)

SAEs: n=38/95 (40%) vs. n=47/99 (47%)

Death[3]**:** n=3/95 (3%) vs. n=7/99 (7%)

Discontinuation[4]**:** n=8/95 (8%) vs. n=10/99 (10%)

[1] This medicine had an accelerated assessment, meaning that it is a medicine of major interest for public health, so its timeframe for review was 150 evaluation days rather than 210.

[3] death due to SAE(s); two deaths were potentially treatment related (one case of sepsis in the 2.5 mg/kg cohort and one case of haemophagocytic lymphohistiocytosis in the 3.4 mg/kg cohort

[4] Permanent treatment discontinuation due to AE(s); keratopathy was the most common reason for treatment discontinuation

Median duration of response: not reached in both groups. At the data cutoff date, 18 vs. 25 patients had a duration of response of 4 months or longer with PFS follow-up ongoing and continued to be on treatment. **OS data (at the time of data cutoff):** not mature; 32 (33%) of 97 patients and 31 (31%) of 99 patients died. **Median PFS:** 2.9 months (95% CI, 2.1–3.7) vs. 4.9 months (2.3–6.2); at the time of data cutoff, 58% and 56% of patients had disease progression or died. **QoL**: not available[2]	

Risk of bias (study level)					
Adequate generation of randomisation sequence	Adequate allocation concealment	Blinding	Selective outcome reporting unlikely	Other aspects which increase the risk of bias	**Risk of bias**
yes	no	no	unclear[5]	yes[6]	unclear
					First published: 08/2020

Abbreviations: AE=adverse event, AJ=adjustment, BCMA=B-cell maturation antigen, C=comparator, CHMP=Committee for Medicinal Products for Human Use, CI=confidence interval, EMA=European Medicines Agency, FDA=Food and Drug Administration, HR=hazard ratio, I=intervention, Int.=intention, IRC=independent review committee, IV=intravenously, MM=multiple myeloma, n=number, NR=not reported, SAE=serious adverse event, OS=overall survival, PFS=progression-free survival, PM=preliminary grade, QoL=quality of life, SAE=serious adverse event.

References:

1. European Medicines Agency (EMA). Medicines. Blenrep. [Available from: https://www.ema.europa.eu/en/medicines/human/summaries-opinion/blenrep.
2. National Institute for Health Research (NIHR). Belantamab mafodotin for relapsed / refractory multiple myeloma – Fourth line [
3. European Medicines Agency (EMA). Medicines. EU/3/17/1925. [Available from: https://www.ema.europa.eu/en/medicines/human/orphan-designations/eu3171925.
4. Lonial S, Lee H, Badros A, Trudel S, Nooka AK, et al. Belantamab mafodotin for relapsed or refractory multiple myeloma (DREAMM-2): a two-arm, randomised, open-label, phase 2 study. Lancet Oncol 2020: 21: 207–21 Published Online December 16, 2019.
5. Supplement to: Lonial S LH, Badros A, et al. Belantamab mafodotin for relapsed or refractory multiple myeloma (DREAMM-2): a two-arm, randomised, open-label, phase 2 study. Lancet Oncol 2019; published online Dec 16.

[2] According to the authors, patient-reported outcomes and health-related QoL outcomes will be reported separately.

[5] Primary analysis data; NCT03525678 is ongoing until 11/2020

[6] The sponsor was involved in study design and implementation, data collection, data analysis, data interpretation, and writing of the report.