

BELANTAMAB MAFODOTIN

INDICATION

Relapsed/refractory multiple myeloma

This treatment is EMA-approved but currently not funded in the UK. It is available for selected patients as part of an individual patient compassionate use scheme

TREATMENT INTENT

Disease modification

GENERAL PRE-ASSESSMENT

1. Ensure all the following staging investigations are done:

- **FBC** & film
- Clotting screen
- U&E
- **LFTs**
- Calcium
- Albumin
- Uric acid
- CRP
- **Baseline detailed ophthalmological work up**
- **Baseline Urine PCR and ACR**
- Baseline random blood glucose level
- **Virology: EBV, CMV, Hep B, Hep C, HIV serology**
- Consider annual flu and pneumococcal vaccination pre therapy
- Calculated creatinine clearance (CrCl)
- Electrophoresis and immunofixation for quantitation of serum paraprotein and immunoglobulins.
- Serum free light chain assay (Freelite)
- β_2 microglobulin
- LDH
- Myeloma FISH should be performed in all patients at diagnosis, and in selected patients at relapse/progression to help guide treatment decisions. Samples should be sent to

Wessex Regional Genetic Laboratory
Salisbury NHS Foundation Trust
Salisbury District Hospital
Salisbury
Wiltshire, SP2 8BJ

- Urine pregnancy testing for pre-menopausal women younger than 55 before each cycle..
- Imaging as per NICE/network guidance and clinical presentation

This is a controlled document and therefore must not be changed

1 of 8

MM.55 BELANTAMAB MAFODOTIN	Authorised by Myeloma lead Dr. Karthik Ramasamy	Review date: June 2023	v.1.4
-------------------------------	---	------------------------------	-------

Additional Investigations

- Plasma viscosity if hyperviscosity suspected If allogeneic transplant an option: Tissue typing of patient and siblings and CMV serology
- Counselling about risks in pregnancy - Animal reproductive studies have not been conducted with belantamab mafodotin, and should not be administered to pregnant or lactating women.
- Consent - ensure patient has received adequate verbal and written information regarding their disease, treatment and potential side effects. Document in medical notes all information that has been given.
- Fertility - all patients should be offered fertility advice, as appropriate.
- Hydration - fluid intake of at least 3 litres /day should be attempted.
- Document patient's height and weight, dose on actual body weight.
- Document patient's performance status.
- Treatment must be agreed at the relevant MDT.

REGIMEN SPECIFIC PRE-ASSESSMENT

1. Patients must be referred by the treating Consultant for ophthalmology review prior to start of treatment, pre cycle for the cycles 1-3, then 6- 8 weekly thereafter or based on clinical need
2. Obtain written consent for the treatment with this compassionate scheme including total number of doses (16 doses)
3. Coolant eye masks are recommended for one hour from start of infusion of BELANTAMAB MAFODOTIN
4. Hypromellose eye drops must be administered continuously throughout treatment, starting on day 1 of cycle 1 of BELANTAMAB MAFODOTIN .

DRUG REGIMEN

To initiate a new cycle of belantamab mafodotin, ANC $\geq 1.0 \times 10^9/L$, Haemoglobin $\geq 80g/l$ and Platelets $\geq 50 \times 10^9/L$

Day of administration	Dose	Method of administration
Mandatory on C1 D1 only	Paracetamol 1g PO, Chlorphenamine 10 mg IV/PO, Dexamethasone 20mg IV bolus or PO	To be given 1 hour prior to Belantamab mafodotin infusion
Day 1 of each cycle	Belantamab mafodotin (GSK2857916) 2.5mg/kg	Intravenous infusion in 250ml 0.9% sodium chloride over 30 minutes

CYCLE FREQUENCY

The cycle is repeated every 21 days until disease progression or unacceptable toxicity, but the current agreement with the company within this compassionate scheme is to supply free of charge

This is a controlled document and therefore must not be changed

2 of 8

MM.55 BELANTAMAB MAFODOTIN	Authorised by Myeloma lead Dr. Karthik Ramasamy	Review date: June 2023	v.1.4
-------------------------------	---	------------------------------	-------

stock for up to 16 doses.

DOSE MODIFICATIONS:

Dose modifications for adverse corneal events:

Category	Eye examination findings	Recommended dose modifications
Mild	Corneal examination finding(s) Mild superficial keratopathy Change in best corrected visual acuity (BCVA): Decline from baseline of 1 line on Snellen Visual Acuity	Continue treatment at current dose.
Moderate	Moderate superficial keratopathy Change in BCVA: Decline from baseline of 2 or 3 lines (and Snellen Visual Acuity not worse than 20/200)	Withhold treatment until improvement in examination findings and BCVA to mild severity or better. Consider resuming treatment at a reduced dose of 1.9 mg/kg.
Severe	Severe superficial keratopathy Corneal epithelial defect Change in BCVA: Decline from baseline of more than 3 lines	Withhold until improvement in examination findings and BCVA to mild severity or better. For worsening symptoms that are unresponsive to appropriate management, consider discontinuation.

Dose modifications for other AEs:

Adverse reaction	Grade	Recommendation
Thrombocytopenia	Grade 2-3	Consider withholding belantamab and/or reducing the dose to 1.9 mg/kg.
	Grade 4	Withhold belantamab until platelet count improves to Grade 3 or better. Consider resuming at a reduced dose of 1.9 mg/kg.
Infusion-related reactions	Grade 2	Interrupt infusion and provide supportive treatment. Once symptoms resolve, resume at lower infusion rate by at least 50%.
	Grade 3 or 4	Interrupt infusion and provide supportive treatment. Once symptoms resolve, resume at lower infusion rate reduced by at least 50%. If anaphylactic or life-threatening infusion reaction, permanently discontinue the infusion and institute appropriate emergency care

This is a controlled document and therefore must not be changed

3 of 8

MM.55 BELANTAMAB MAFODOTIN	Authorised by Myeloma lead Dr. Karthik Ramasamy	Review date: June 2023	v.1.4
-------------------------------	---	------------------------	-------

Pneumonitis:

Grade	Management
2	Continue treatment when toxicity resolves to G 0-1
3-4	Permanently discontinue

Renal and Hepatic Impairment

Renal	Hepatic
<p>No dose adjustment is required in patients with mild or moderate renal impairment (eGFR \geq30 mL/min).</p> <p>There are insufficient data in patients with severe renal impairment to support a dose recommendation</p> <p>In patients with significant proteinuria, we recommend holding dose until ACR drops to 50 or below.</p>	<p>No dose adjustment is required in patients with mild hepatic impairment (bilirubin greater than ULN to less than or equal to 1.5 \times ULN or aspartate transaminase [AST] greater than ULN).</p> <p>There are insufficient data in patients with moderate hepatic impairment and no data in patients with severe hepatic impairment to support a dose recommendation. But, we would recommend holding Belantamab until LFT's normalise.</p>

INVESTIGATIONS/ASSESSMENTS – during treatment

- FBC, U&Es, LFTs, Ca⁺⁺, glucose, Urine protein/creatinine ratio – every 3 - 4 weeks.
- Ig's, paraprotein, usually monthly after first 2 months, Freelite assay if appropriate.
- Consider bone marrow assessment after four cycles for non-secretory Myeloma
- Ophthalmology assessments every cycle before dosing, or based on clinical need after cycle 3

CONCURRENT MEDICATIONS

- Hypromellose 0.3% eye drops throughout the treatment period: 1 drop in each eye four times a day
- Coolant eye mask for one hour during infusion
- Allopurinol 300 mg daily for 7 days for cycle 1 only
- Prophylactic aciclovir 200 mg TDS (consider reducing to 200mg BD if CrCl<10ml/min) for the duration of treatment and for 3 months afterwards.
- Consider prophylactic co-trimoxazole 960mg OD on M/W/F if heavily pre-treated or previous autograft.
- Consider prophylactic levofloxacin 500mg od for 12 weeks (cycles 1-4), at clinician discretion, only in patients deemed at high risk of infections. Adjust dose for renal function
- Proton pump inhibitor or H2 antagonist at clinician's discretion on days of steroids
- Bone protection as per NSSG Bone Protection protocol MM.

This is a controlled document and therefore must not be changed

4 of 8

MM.55 BELANTAMAB MAFODOTIN	Authorised by Myeloma lead Dr. Karthik Ramasamy	Review date: June 2023	v.1.4
-------------------------------	---	------------------------	-------

Drug interactions

No formal drug interaction studies have been performed with belantamab mafodotin. Based on available in vitro and clinical data, there is a low risk of pharmacokinetic or pharmacodynamic drug interactions for belantamab mafodotin.

EMETIC RISK

Low risk

EXTRAVASATION RISK

Not known

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS

In part 2 (dose expansion study) of Phase 1 study trial, 23 (66%) of 35 patients had adverse events that led to dose reductions, and 25 (71%) patients had adverse events that led to dose interruptions or delays. Blurred vision was the most common adverse event that led to dose reduction (11 [31%] of 35 patients), followed by thrombocytopenia (four [11%]) and keratitis (three [9%]). Two patients discontinued treatment because of adverse events, one because of thrombocytopenia and the other because of thrombocytopenia and increased blood creatinine phosphokinase.

➤ **Deaths on the study:**

As of the data cut-off date, three deaths have occurred in part 2, all of which were attributed to progressive myeloma and not deemed treatment related. Adverse events of clinical interest related to belantamab included infusion-related reactions, thrombocytopenia, and corneal events.

➤ **Infusion-related reactions:**

To fully assess the incidence and severity of infusion-related reactions, premedication was prohibited before the first infusion. In part 2, eight (23%) patients had infusion-related reactions (as defined by a grouped term); most (in five of eight patients) were grade 1 or 2 and all occurred with the first dose. After the first infusion, premedications were permitted and included paracetamol (eight [23%] of 35 patients), antihistamines (seven [20%]), steroids (two [6%]; dexamethasone and hydrocortisone), and sodium chloride (one [3%]).

➤ **Thrombocytopenia:**

Thrombocytopenia of any grade occurred in 20 (57%) of 35 patients and grade 3 or 4 thrombocytopenia occurred in 12 (34%). The median time to first occurrence of thrombocytopenia was 7 days (range 1–185) and the median duration for patients with a resolution date (n=9) was 8 days (range 6–16). Two (6%) patients discontinued treatment and seven (20%) required dose reduction or delays because of thrombocytopenia.

➤ **Corneal events:**

Corneal events were reported in 22 (63%) of 35 patients in part 2. These were predominantly mild to moderate (grade 1 or 2 in 19 of 22 patients) with three (9%) patients having grade 3 corneal events (one with keratitis, one with eye pain and keratitis, and one with dry eye). The median time to onset of corneal events was 23 days (range 1–84) and the median duration for patients with a resolution

This is a controlled document and therefore must not be changed

5 of 8

MM.55 BELANTAMAB MAFODOTIN	Authorised by Myeloma lead Dr. Karthik Ramasamy	Review date: June 2023	v.1.4
-------------------------------	---	------------------------------	-------

date (n=13) was 30 days (range 5–224). 31 (89%) of 35 patients had corneal findings on ophthalmological examination, characterised by a superficial punctate keratitis (in 27 [77%] of 35 patients) often associated with epithelial (microcystic) oedema (22 [63%]), stromal oedema (five [14%]), or opacities (eight [23%]).

As of June 26, 2017, data on corneal examination were available for 13 patients with an end-of-treatment visit. 11 of these 13 patients had corneal abnormalities on ophthalmological examination; most (nine of 11) were considered mild. Although visual acuity, assessed by the Snellen method, decreased in most patients during treatment, possible or definite worsened vision (change from baseline in best-corrected visual acuity score ≥ 0.3) was evident in three of 13 patients (right eye) and five of 12 patients (left eye) with available data, by the end of treatment.

Management of corneal events included dose reduction in 14 (40%) patients; dose interruptions, delays, or both in 15 (43%) patients; and supportive measures, such as the use of artificial tears and increasing the duration or frequency of steroid eye drop treatment. **No patient in part 2 permanently discontinued study treatment because of a corneal event.**

TREATMENT RELATED MORTALITY

<5%

REFERENCES

1. Trudel S, Lendvai N, Popat R et al. Targeting B-cell maturation antigen with GSK2857916 antibody–drug conjugate in relapsed or refractory multiple myeloma (BMA117159): a dose escalation and expansion phase 1 trial. *Lancet Oncol.* 2018 Dec;19(12):1641-1653. doi: 10.1016/S1470-2045(18)30576-X. Epub 2018 Nov 12.
2. Belantamab investigator’s brochure (May 2019)
3. Lonial et al. Belantamab mafodotin for relapsed or refractory multiple myeloma (DREAMM-2): a two-arm, randomised, open-label, phase 2 study. *Lancet Oncology.* Volume 21, ISSUE 2, P207-221, February 01, 2020
4. Product information from EMA website for BLENREP 100 mg powder for concentrate for solution for infusion: https://www.ema.europa.eu/en/documents/product-information/blenrep-epar-product-information_en.pdf

MM.55 BELANTAMAB MAFODOTIN	Authorised by Myeloma lead Dr. Karthik Ramasamy	Review date: June 2023	v.1.4
-------------------------------	---	------------------------------	-------

REVIEW

Name	Revision	Date	Version	Review date
Faouzi Djebbari (Advanced Haematology Pharmacist)	New protocol	November 2019	1.0	June 2020
NSSG myeloma Group	Annual protocol review and update	October 2020	1.1	June 2021
Quality manager	Nursing care plan added	May 2021	1.2	June 2021
NSSG myeloma Group	Annual protocol review 2021	June 2021	1.3	June 2022
NSSG Myeloma Group	Updated concurrent medication section	Nov 2022	1.4	June 2023

This is a controlled document and therefore must not be changed

7 of 8

MM.55 BELANTAMAB MAFODOTIN	Authorised by Myeloma lead Dr. Karthik Ramasamy	Review date: June 2023	v.1.4
-------------------------------	---	------------------------	-------

Nursing Care Plan: Belantamab Mafodotin

BELANTAMAB MAFODOTIN: Antibody-drug conjugate (this is a monoclonal antibody which has a chemotherapy drug attached to it). Belantamab mafodotin attaches to BCMA proteins on myeloma cells and is then absorbed into the cell. Once inside the myeloma cell the chemotherapy part of the drug (mafodotin) is released and kills the cell. Mafodotin cannot be given directly to patients as it is too toxic. Molecules of the drug residing on BCMA proteins on the outside of myeloma cells also act as flags to the body’s immune system that these cells can be targeted for destruction.

Indication: Relapsed/refractory Myeloma.

Administered: On day 1 of each 21 day cycle for up to 16 doses or until disease progression.

Emetic Risk: Low.

Extravasation Risk: Not known.

Alopecia: No.

Side Effects: Corneal events, vision disturbances, blurred vision, fever, fatigue, anaemia, thrombocytopenia, proteinuria and raised AST blood levels.

Infusion related reactions up to and including grade 2 can be managed by stopping the infusion and giving rescue medications if required. If the patient recovers sufficiently (to grade 1 or below) the infusion can be recommenced and half the original rate. In the even or a more severe reaction, the SpR in collaboration with the Consultant will determine whether the patient can be re-challenged.

Regime Specific Considerations:

- Patients should attempt to drink 3 litres of water a day.
- Bloods (including glucose level) are required at the start of each cycle. Patients with unstable blood counts (especially low platelets) may require more frequent monitoring.
- Urine testing for protein creatinine ratio and albumin creatinine ratio
- Coolant eye masks are recommended for one hour from the start of infusion. The eye mask should be changed after 30 minutes to ensure cooling is effective.
- Hypromellose eye drops (1 drop in each eye QDS) must be administered continuously throughout treatment, starting on day 1 of cycle 1. Please ensure patient/carer is able to administer these.
- Ophthalmology assessments are required before starting treatment, every 3 weeks for the first 2 months then monthly thereafter or based on clinical need.
- Premeds on C1D1 are mandatory. Administer 1 hour pre Belantamab infusion.

This is a controlled document and therefore must not be changed

8 of 8

MM.55 BELANTAMAB MAFODOTIN	Authorised by Myeloma lead Dr. Karthik Ramasamy	Review date: June 2023	v.1.4
-------------------------------	---	------------------------------	-------