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Health Technology Briefing
October 2022

Belantamab mafodotin with bortezomib and dexamethasone for previously treated relapsed/refractory multiple myeloma

Company/Developer	GlaxoSmithKline UK Ltd

☐ New Active Substance ☒ Significant Licence Extension (SLE)

NIHRIO ID: 28712	NICE TSID: 11811	UKPS ID: 663873

Licensing and Market Availability Plans

Currently in phase III clinical development.

Summary

Belantamab mafodotin is in clinical development in combination with bortezomib and dexamethasone for the treatment of relapsed and refractory multiple myeloma (MM) in adult patients who have previously received at least one prior therapy. MM is a rare form of cancer characterised by excessive production (proliferation) and improper function of certain cells (plasma cells) found in the bone marrow. Myeloma develops due to DNA changes during the development of the plasma cell, producing an abnormal cell that begins to proliferate and produce more cancerous cells. Patients with MM often go through many cycles of treatment options to improve overall survival, which can sometimes lead to poor survival outcomes for patients whose disease has become resistant to the currently available therapy options.

Belantamab mafodotin is administered intravenously and designed to attach to a protein called B-cell maturation antigen (BCMA), which is present on the surface of abnormal plasma cells. Once inside the tumour cell, the cell-killing component of the drug is released, killing the cells by interfering with their ability to divide and grow, whilst also stimulating the immune system to attack the myeloma cells, and slow progression of the disease. Triple combination therapies have shown to be more effective in treatment of relapsed/refractory MM. If licensed, belantamab mafodotin with bortezomib and dexamethasone will offer a novel treatment option for patients with relapsed and refractory MM, who have previously received at least one treatment.

This briefing reflects the evidence available at the time of writing and a limited literature search. It is not intended to be a definitive statement on the safety, efficacy or effectiveness of the health technology covered and should not be used for commercial purposes or commissioning without additional information. A version of the briefing was sent to the company for a factual accuracy check. The company was available to comment.

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Proposed Indication

Belantamab mafodotin in combination with bortezomib and dexamethasone for treating adult patients with relapsed/refractory multiple myeloma who have received at least one prior therapy.[1]

Technology

Description

Belantamab mafodotin (Blenrep) is a humanised IgG1κ monoclonal antibody attached to a cytotoxic agent, maleimidocaproyl monomethyl auristatin F (mcMMAF).[2,3] The antibody has been designed to attach to a protein called B-cell maturation antigen (BCMA), which is present in high levels on the surface of myeloma cells.[3] Belantamab mafodotin binds to cell surface BCMA and is rapidly internalised.[2] Once inside the tumour cell, the cytotoxic agent is released disrupting the microtubule network, leading to cell cycle arrest and apoptosis. The antibody enhances recruitment and activation of immune effector cells, killing tumour cells by antibody-dependent cellular cytotoxicity and phagocytosis.[2] The cytotoxic molecule kills the cells by interfering with their ability to divide and grow and also stimulates the immune system to attack the myeloma cells, and these actions combined are expected to slow down progression of the disease.[3]

Belantamab mafodotin is in clinical development in combination with bortezomib and dexamethasone for relapsed/refractory MM patients who have previously received at least one prior anti-myeloma therapy. In the phase III clinical trial DREAMM-7 (NCT04246047), 2.5mg/kg of belantamab mafodotin (IV), 1.3mg/m^2 bortezomib (SC) and 20mg dexamethasone (IV or orally) will be administered on a routine schedule every three weeks.[1,4]

Key Innovation

Relapsed and refractory multiple myeloma (MM) is a significant clinical challenge, with poor survival outcomes for patients whose disease has become resistant to the current standard of care. Due to the limited options currently available, these patients are often retreated with drugs from the same classes after they relapse.[5] Belantamab mafodotin is a first-in-class, novel therapeutic agent that selectively targets the cancerous cells and elicits an immune response whilst delivering the cytotoxic payload directly to the cancerous cell.[6] Furthermore, triple combination drug regimens are considered a standard of care for patients with relapsed/refractory MM, having demonstrated superior antimyeloma activity to monotherapy and dual combination regimens.[4]

If licensed, belantamab mafodotin in combination with bortezomib and dexamethasone would provide a novel triple combination treatment option with an acceptable benefit-risk profile for patients with relapsed/refractory MM who may have become resistant to the currently available treatment regimens, and currently have limited treatment options available.[4-6]

Regulatory & Development Status

Belantamab mafodotin currently has Marketing Authorisation in the EU/UK for monotherapy treatment of multiple myeloma 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.[2]

Belantamab mafodotin is also currently in clinical trials for the following indications:[7]

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- As a monotherapy treatment of multiple myeloma in adult patients, who have received at least two prior therapies
- In combination with pomalidomide and dexamethasone for relapsed/refractory multiple myeloma
- Relapsed or refractory acute myeloid leukaeimia

Belantamab mafodotin has been granted:

- EMA Orphan designation for MM in October 2017.[8]
- FDA Orphan designation for MM in June 2017.[9]

Patient Group

Disease Area and Clinical Need

MM, also known as myeloma, is a type of bone marrow cancer. Bone marrow is the spongy tissue at the centre of some bones that produces the body's blood cells.[10] The bone marrow produces different types of blood cells.[11,12] Myeloma develops when DNA is damaged during the development of a plasma cell. This abnormal cell then starts to multiply and spread within the bone marrow.[12] The abnormal plasma cells then begin to proliferate and produce more abnormal cells, known as myeloma cells.[11,12] Myeloma affects multiple places in the body where bone marrow is normally active in an adult, such as in the bones of the spine, skull, pelvis, the rib cage, long bones of the arms and legs and the areas around the shoulders and hips.[12] The cause of MM is not well understood however, there is a close link between MM and a condition called monoclonal gammopathy of unknown significance (MGUS).[10] MGUS is where there is an excess of protein molecules, called immunoglobulins, in a patient's blood. Every year, around 1 in every 100 people with MGUS go on to develop MM. MM is more common in males, adults over 60 and black people.[10] Symptoms often include bone pain, bone fractures, spinal cord compression, repeated infections and unusual bleeding. Treatment can often help to control the condition for several years, but most cases of MM cannot be cured.[10]

Myeloma is the 19th most common cancer in the UK, accounting for 2% of all new cancer cases (2016-2018). There have been around 6,000 new myeloma cases and around 3,100 myeloma deaths in the UK every year (2016-2018). Over the last decade, myeloma incidence rates have increased by around a tenth (11%) in the UK.[11] In England (2020-21), there were 107,457 finished consultant episodes (FCE) for MM (ICD-10 code: C90.0), with 103,209 hospital admissions that resulted in 92,913 day cases and 66,906 FCE bed days.[13] In England (2017), there were 5,034 patients diagnosed and 2,611 deaths registered where MM and malignant plasma cell neoplasms were the underlying cause.[14] For patients diagnosed between 2013 and 2017, followed up to 2018, the 1-year and 5-year survival rates were 82.7% and 52.3% respectively.[15]

Recommended Treatment Options

NICE guidelines recommend the following treatment options for relapsed or refractory MM after receiving 1 prior treatment:[16]

- Carfilzomib, dexamethasone and lenalidomide for multiple myeloma after one treatment with bortezomib
- Carfilzomib and dexamethasone for multiple myeloma after one treatment
- Bortezomib monotherapy for relapsed multiple myeloma
- Lenalidomide plus dexamethasone for multiple myeloma after one treatment with bortezomib

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- Daratumumab, bortezomib and dexamethasone (Cancer Drugs Fund only)

Clinical Trial Information

Trial	**DREAMM 7,** NCT04246047, DREAMM 7: A Multicenter, Open-Label, Randomized Phase III Study to Evaluate the Efficacy and Safety of the Combination of Belantamab Mafodotin, Bortezomib, and Dexamethasone (B-Vd) Compared With the Combination of Daratumumab, Bortezomib and Dexamethasone (D-Vd) in Participants With Relapsed/Refractory Multiple Myeloma **Phase III:** Active, not recruiting **Location(s):** 9 EU countries, UK, US, Canada and other countries **Primary completion date:** April, 2023
Trial Design	Randomised, parallel assignment, open label
Population	N=575 (estimated); adults 18 years and older; confirmed diagnosis of multiple myeloma as defined by the International Myeloma Working Group (IMWG) criteria; previously treated with at least 1 prior line of multiple myeloma (MM) therapy; must have documented disease progression during or after their most recent therapy
Intervention(s)	Patients will receive belantamab mafodotin 2.5 mg/kg (IV) Q3W on Day 1 of each cycle; bortezomib 1.3 mg/m^2 (subcutaneously) on Days 1, 4, 8, and 11 of Cycles 1-8 (21-day cycles); and dexamethasone 20 mg (IV or orally) on the day of, and the day after, bortezomib treatment.[4]
Comparator(s)	Patients will receive daratumumab 16 mg/kg (IV) in 21-day cycles: Cycles 1-3 Q1W, Cycles 4-8 Q3W, and from Cycle 9 onwards Q4W; dexamethasone and bortezomib schedules will be the same as in Arm A.[4]
Outcome(s)	Primary Outcomes: Progression-free survival (PFS) [time frame: Up to 34 months] See trial record for full list of other outcomes.
Results (efficacy)	-
Results (safety)	-

Estimated Cost

Belantamab mafodotin100mg powder for concentrate for solution for infusion vials is available for £5,707.83.[17]

Relevant Guidance

NICE Guidance

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- NICE technology appraisal guidance in development. Ciltacabtagene autoleucel for treating relapsed and lenalidomide-refractory multiple myeloma after 1 to 3 therapies (GID-TA10905). Expected date of issue to be confirmed.
- NICE technology appraisal guidance in development. Melphalan flufenamide with dexamethasone for treating relapsed or refractory multiple myeloma (GID-TA10744). Expected date of issue to be confirmed.
- NICE technology appraisal guidance in development. Carfilzomib with daratumumab and dexamethasone for treating relapsed or refractory multiple myeloma (ID2709). Expected publication date to be confirmed.
- NICE technology appraisal. Carfilzomib with dexamethasone and lenalidomide for previously treated multiple myeloma (TA695). April 2021
- NICE technology appraisal. Carfilzomib for previously treated multiple myeloma (TA657). November 2020
- NICE technology appraisal. Lenalidomide plus dexamethasone for multiple myeloma after 1 treatment with bortezomib (TA586). June 2019
- NICE technology appraisal. Daratumumab with bortezomib and dexamethasone for previously treated multiple myeloma (TA573). April 2019
- NICE technology appraisal. Bortezomib monotherapy for relapsed multiple myeloma (TA129). October 2007.
- NICE guideline. Myeloma: diagnosis and management (NG35). February 2016.

NHS England (Policy/Commissioning) Guidance

- NHS England. Clinical Commissioning Policy: Bendamustine for relapsed multiple myeloma (all ages). 2020. 200604/P
- NHS England. Clinical Commissioning Policy: Second allogeneic haematopoietic stem cell transplant for relapsed disease (all ages). 2017. 16068/P
- NHS England. 2013/14 NHS Standard Contract for Cancer: Chemotherapy (Adult). B/15/S/a.
- NHS England. 2013/14 NHS Standard Contract for Cancer: Radiotherapy (All Ages). B01/S/a.
- NHS England. 2013/14 NHS Standard Contract for Haematopoietic Stem Cell Transplantation

Other Guidance

- British Society for Haematology (BSH) and the UK Myeloma Forum (UKMF). Guidelines on the diagnosis, investigation and initial treatment of myeloma. 2021.[18]
- European Society of Medical Oncology (ESMO). Multiple myeloma: EHA-ESMO Clinical Practice
- Guidelines for diagnosis, treatment and follow-up. 2021.[19]
- National Comprehensive Cancer Network (NCCN). NCCN clinical practice guidelines in oncology: multiple myeloma. 2020.[20]

Additional Information

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2 Electronic Medicines Compendium (EMC). *BLENREP 100 mg powder for concentrate for solution for infusion*. Available from: https://www.medicines.org.uk/emc/product/12545#ORIGINAL.

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