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Newcastle University

Health Technology Briefing
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Belantamab mafodotin for treating relapsed or refractory multiple myeloma

Company/Developer	GlaxoSmithKline UK Ltd

☐ New Active Substance ☒ Significant Licence Extension (SLE)

NIHRIO ID: 33657	NICE ID: 10756	UKPS ID: 651396

Licensing and Market Availability Plans

Currently in phase III clinical trials.[1]

Summary

Belantamab mafodotin is in clinical development for the treatment of relapsed and refractory multiple myeloma (MM) patients. MM is a rare form of cancer characterized 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 a new type of medicinal product for MM patients, 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. If licensed, belantamab mafodotin will offer a novel treatment option for patients with relapsed and refractory MM, who have previously received at least two types of treatment, including a proteasome inhibitor and an immunomodulatory agent.

Proposed Indication

Treatment for Relapsed/Refractory Multiple Myeloma.[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 for relapsed/refractory MM patients who have previously received least 2 prior anti-myeloma therapies, including at least 2 consecutive cycles of both lenalidomide and a proteasome inhibitor. In phase III clinical trial (NCT04162210), belantamab mafodotin will be administered by intravenous (IV) infusion at 2.5 milligram (mg)/kilogram (kg) on day 1 of every 3 weeks schedule.[1]

Key Innovation

Relapsed and refractory multiple myeloma 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.[4] 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.[5,6]

If licensed, belantamab mafodotin would provide a novel treatment option with an acceptable benefit-risk profile for patients with relapsed/refractory MM who have become resistant to the currently available treatment regimens, and currently have limited treatment options available.[1,4,5]

Regulatory & Development Status

Belantamab mafodotin currently has Marketing Authorization 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:[7]

- In combination with Bortezomib and Dexamethasone for relapsed/refractory multiple myeloma after at least 1 prior therapy (DREAMM-7)
- In combination with Pomalidomide and Dexamethasone for relapsed/refractory multiple myeloma after at least 1 prior therapy (DREAMM-8)

Belantamab mafodotin has also been granted the following regulatory designations/awards:

- EMA Orphan designation for MM in October 2017.[8]
- FDA approval for the treatment of patients with relapsed or refractory MM in August 2020.[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] 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 cell then begin to proliferate and produce more abnormal cells, known as are myeloma cells.[11] 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.[10] Symptoms often include bone pain, bone fractures, spinal cord compression, repeated infections and unusual bleeding.[10] Treatment can often help to control the condition for several years, but most cases of multiple myeloma 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 5034 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[16]:

- Panobinostat in combination with bortezomib and dexamethasone is recommended for adult patients who have received at least 2 prior regimens including bortezomib and an immunomodulatory agent.
- Ixazomib, with lenalidomide and dexamethasone is recommended for patients who have already received 2 or 3 lines of therapy.
- Lenalidomide in combination with dexamethasone is recommended in people who have received 2 or more prior therapies.

Clinical Trial Information

Trial	**DREAMM 3,** NCT04162210, A Phase III, Open-Label, Randomized Study to Evaluate the Efficacy and Safety of Single Agent Belantamab Mafodotin Compared to Pomalidomide Plus Low-dose Dexamethasone (Pom/Dex) in Participants With Relapsed/Refractory Multiple Myeloma) **Phase III:** Recruiting

	Location(s): 10 EU countries, UK, US, Canada and other countries **Primary completion date:** June 2022
Trial Design	Randomized, parallel assignment, open label
Population	N=380, 18 years and older, Histologically or cytologically confirmed diagnosis of Multiple myeloma (MM) and: Has undergone autologous stem cell transplant (SCT), or is considered transplant ineligible; Has received at least 2 prior lines of anti-myeloma treatments, including a proteasome inhibitor and an immunomodulatory agent, and must have documented disease progression on, or within 60 days of, completion of the last treatment.
Intervention(s)	Belantamab mafodotin will be administered intravenously at 2.5 milligram (mg)/kilogram (kg) on Day 1 (D1) of every 3 weeks (Q3W) schedule
Comparator(s)	Pomalidomide will be administered orally at the approved starting dose of 4 mg daily on Days 1 to 21 of each 28-day cycle, with dexamethasone administered orally at a dose of 40 mg once weekly (Days 1, 8, 15, and 22)
Outcome(s)	Primary Outcomes: Progression-free survival (PFS) [Time Frame: Up to 20 months] See trial record for full list of other outcomes
Results (efficacy)	-
Results (safety)	-

Estimated Cost

Blenrep 100mg powder for concentrate for solution for infusion vials is available for £5707.83.[17]

Relevant Guidance

NICE Guidance

- NICE technology appraisal guidance in development. Selinexor with bortezomib and low-dose dexamethasone for treating relapsed refractory multiple myeloma (GID-TA10646). 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. 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. Isatuximab with pomalidomide and dexamethasone for treating relapsed and refractory multiple myeloma (TA658). November 2020.
- NICE technology appraisal. Ixazomib with lenalidomide and dexamethasone for treating relapsed or refractory multiple myeloma (TA505). February 2018.
- NICE technology appraisal. Panobinostat for treating multiple myeloma after at least 2 previous treatments (TA380). January 2016

- NICE technology appraisal. Lenalidomide for the treatment of multiple myeloma in people who have received at least 2 prior therapies (TA171). June 2009

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
- (Adult). B04/S/a.

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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