Health Technology Briefing
October 2021

Elranatamab for treating relapsed /refractory multiple myeloma

Company/Developer	Pfizer Limited (UK)

☒ New Active Substance ☐ Significant Licence Extension (SLE)

NIHRIO ID: 30958	NICE ID: 10692	UKPS ID: 661025

Licensing and Market Availability Plans

Currently in phase II clinical trials

Summary

Elranatamab is in clinical development for relapsed/refractory multiple myeloma (MM). MM is a rare, incurable cancer of the blood that develops from plasma cells in the bone marrow (the spongy tissue inside the inner part of some bones) where large amounts of abnormal plasma cells are produced and interfere with the production of red and white blood cells and platelets. People with MM will experience periods of time without symptoms followed by periods when the illness comes back (relapsed MM). Eventually the periods without symptoms will shorten and the illness will become resistant to treatment (refractory MM). Most patients will experience serial relapse to existing treatments at some point during their disease course (relapsed MM), hence the need for newer treatment options.

Elranatamab is a novel type of cancer immunotherapy that brings an antigen (a substance that induces an immune response in the body) found on the cancer cells closer to a person's own T-cells (a type of white blood cell that is part of the immune system) to kill the cancer cells. Elranatamab is administered by subcutaneous injection, which is intended to allow higher doses than intravenous administration without increasing adverse events. If licensed, elranatamab will offer a new treatment option for patients with relapsed/refractory MM.

Proposed Indication

Treatment of patients with multiple myeloma (MM) who are relapsed/refractory to at least one proteasome inhibitor (PI), one immunomodulatory drug (IMiD) and one anti-CD38 monoclonal antibody (mAb).[1,2]

Technology

Description

Elranatamab (PF-06863135) is a humanised bispecific monoclonal antibody (IgG2a) that targets B-cell maturation antigen (BCMA), a member of the tumour necrosis factor receptor superfamily which is highly expressed in MM, and the CD3 receptor found on the surface of cancer-fighting T-cells, bridging them together to activate an immune response.[2,3]

Elranatamab is in clinical development for MM who are relapsed/refractory to at least one PI, one IMiD and one anti-CD38 mAb. In the phase II clinical trial (MagnetisMM-3; NCT04649359), participants will receive a weekly 76 mg subcutaneous injection of elranatamab following a priming dose of 44 mg.[1,2]

Key Innovation

Despite the improvement in depth and duration of response to standard first-line treatments and prolonged survival, MM remains incurable for the majority of patients due to the eventual emergence of drug-resistant myeloma clones and often imminent relapse.[4]

Bispecific antibodies are a novel type of cancer immunotherapy that bind to and engage two different targets simultaneously. One arm binds directly to specific antigens on cancer cells and the other activates and brings a person's own T-cells from the immune system closer to kill the cancer cells. Subcutaneous administration of elranatamab is intended to allow higher doses than intravenous administration without increasing adverse events.[2]

If licensed, elranatamab will offer a new treatment option for patients with MM who are relapsed/refractory to at least one PI, one IMiD and one anti-CD38 mAb.[1,2]

Regulatory & Development Status

Elranatamab does not currently have Marketing Authorisation in the EU/UK for any indication.

Elranatamab both as monotherapy and in combination with daratumumab/daratumumab + Pomalidomide + dexamethasone is in phase II clinical development for Relapsed/Refractory MM.[5,6]

Elranatamab has the following regulatory designations/awards:

- Orphan drug designation in the EU in July 2021 for MM.[7]
- PRIME status for MM by the EMA in March 2021.[8,9]
- Fast Track Designation by the US Food and Drug Administration (FDA) in January 2021.[2,8]

Patient Group

Disease Area and Clinical Need

Multiple Myeloma (MM) is a type of bone marrow cancer that is characterised by uncontrolled proliferation of monoclonal plasma cells in the bone marrow.[10,11] MM can affect multiple organs and systems including the bones, kidneys, blood, and immune system.[12] Refractory myeloma is defined as disease that is nonresponsive while on primary or salvage therapy, or progresses within 60 days of last therapy.[13] The causes of MM are unknown however, there are some factors that increase the risk of getting MM such as age (risk increases with age), gender (more common in men), having rare medical condition called monoclonal gammopathy of undetermined significance (MGUS), having a family history of MM or MGUS, and lowered immunity.[14] Multiple myeloma may not cause any symptoms in the early stages but eventually leads to a wide range of problems including bone pain, bone fractures and spinal cord compression, anaemia, fatigue, calcium elevation, thickened blood, bruising and unusual bleeding, kidney problems, and infections.[15]

Myeloma is the 19th most common cancer in the UK, accounting for 2% of all new cancer cases (2016-2018). In England, between 2016 and 2018, there were around 5,041 new myeloma cases every year.[16] In England, in 2020-21, there were 110,505 finished consultant episodes (FCE) and 106,047 hospital admissions with a primary diagnosis of MM (ICD-10 code: C90.0), resulting in 70,400 FCE bed days and 95,378 day case.[17] In England, 2013-2017, the age-standardised net survival rates for myeloma were 82.7% for one year and 52.3% for five years.[18]

Recommended Treatment Options

NICE guidelines recommend the following treatment options for relapsed or refractory MM:[19]

- Ixazomib, with lenalidomide and dexamethasone, for adults who have already had two or three lines of therapy.
- Panobinostat in combination with bortezomib and dexamethasone for adults who have received at least two prior regimens including bortezomib and an immunomodulatory agent.
- Lenalidomide in combination with dexamethasone for adults who have received two or more prior therapies.
- Isatuximab plus pomalidomide and dexamethasone, for treating relapsed and refractory MM in adults who have had lenalidomide and a proteasome inhibitor, and whose disease has progressed on their last treatment, only if they have had 3 previous lines of treatment.
- Daratumumab monotherapy for adults whose previous therapy included a proteasome inhibitor and an immunomodulator, and whose disease progressed on the last therapy, only if they have daratumumab after three previous therapies.
- Pomalidomide, in combination with low-dose dexamethasone for adults at third or subsequent relapse: that is, after three previous treatments including both lenalidomide and bortezomib.

Clinical Trial Information	
Trial	**MagnetisMM-3;** NCT04649359; MagnetisMM-3 an open-label, multicenter, non-randomized phase 2 study of elranatamab (PF-06863135) monotherapy in participants with multiple myeloma who are refractory to at least one proteasome inhibitor, one immunomodulatory drug and one anti-CD38 antibody **Phase II** - Recruiting **Location(s):** EU, USA, Canada, Australia, and Japan **Primary completion date:** 16 September 2022
Trial Design	Non-Randomised, parallel assignment, open label
Population	N= 150 (planned); participants with MM and refractory to at least one PI, one IMiD and one anti-CD38 mAb; relapsed/refractory to last anti-myeloma regimen; has not received (cohort A) or has received (cohort B) prior BCMA-directed therapy (ADC or CAR T cells); aged 18 years and older.
Intervention(s)	Participants will receive a weekly 76 mg subcutaneous injection of elranatamab following a priming dose of 44 mg.[2]
Comparator(s)	No comparator.
Outcome(s)	Primary outcome: - Objective response rate [Time Frame: assessed approximately every 4 weeks [up to approximately 2 years] See trial record for full list of other outcomes.
Results (efficacy)	-
Results (safety)	-

Estimated Cost
The cost of elranatamab is not yet known.

Relevant Guidance

NICE Guidance

- NICE technology appraisal guidance in development. Selinexor with bortezomib and low dose dexamethasone for treating relapsed or refractory multiple myeloma (ID3797). Expected publication date to be confirmed.

- NICE technology appraisal guidance in development. Belantamab mafodotin for treating relapsed or refractory multiple myeloma after 3 therapies (ID2701). Expected publication date to be confirmed.

- NICE technology appraisal guidance in development. Idecabtagene vicleucel for treating relapsed and refractory multiple myeloma in people who have received at least 3 prior therapies (ID1442). Expected publication date 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: October 2022.

- NICE technology appraisal guidance in development. Melphalan flufenamide with dexamethasone for treating relapsed or refractory multiple myeloma (ID3862). Expected publication date: June 2022

- NICE technology appraisal guidance in development. Ixazomib with lenalidomide and dexamethasone for treating relapsed or refractory multiple myeloma (CDF review of TA505) (ID1635). Expected publication date: March 2022

- NICE technology appraisal guidance. Isatuximab with pomalidomide and dexamethasone for treating relapsed and refractory multiple myeloma (TA658). November 2020

- NICE technology appraisal guidance. Lenalidomide for the treatment of multiple myeloma in people who have received at least 2 prior therapies (TA171). June 2019

- NICE technology appraisal guidance. Daratumumab with bortezomib and dexamethasone for previously treated multiple myeloma (TA573). April 2019.

- NICE technology appraisal guidance. Daratumumab monotherapy for treating relapsed and refractory multiple myeloma (TA510). March 2018.

- NICE technology appraisal guidance. Ixazomib with lenalidomide and dexamethasone for treating relapsed or refractory multiple myeloma (TA505). February 2018.

- NICE technology appraisal guidance. Pomalidomide for multiple myeloma previously treated with lenalidomide and bortezomib (TA427). January 2017.
- NICE technology appraisal guidance in development. Panobinostat for treating multiple myeloma after at least 2 previous treatments (TA380). January 2016
- NICE guideline. Myeloma: diagnosis and management (NG35). May 2018.
- NICE guideline. Haematological cancers: improving outcomes (NG47). May 2016.
- NICE quality standard. Haematological cancers (QS150). June 2017.

NHS England (Policy/Commissioning) Guidance

- NHS England. Clinical Commissioning Policy: Second allogeneic haematopoietic stem cell transplant for relapsed disease (all ages). 2017. 16068/P
- NHS England. Clinical Commissioning Policy: Haematopoietic stem Cell Transplantation (HSCT) (All ages): Revised. 2015. B04/P/a
- 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

- European Society of Medical Oncology (ESMO). Multiple myeloma: EHA-ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. 2021.[20]
- National Comprehensive Cancer Network (NCCN) Guidelines Insights. Multiple Myeloma, Version 3. 2018.[13]
- NHS England. NHS manual for prescribed specialist services. Chapter 29: blood and marrow transplantation services (adults and children). 2018/2019.[21]
- The UK Myeloma Forum (UKMF) and the British Society for Haematology (BSH). Guidelines for screening and management of late and long-term consequences of myeloma and its treatment. 2017.[22]

- European Society of Medical Oncology (ESMO). Clinical Practice Guidelines for diagnosis, treatment and follow-up: Multiple myeloma. 2017.[23]
- NHS England. National chemotherapy algorithms – multiple myeloma. 2015.[24]
- The International Myeloma Working Group. Revised International Staging System for Multiple Myeloma: A report from IMWG. 2015.[25]

Additional Information

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