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Health Technology Briefing
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Anitocabtagene autoleucel for relapsed or refractory multiple myeloma

Company/Developer	Gilead Sciences Ltd

☒ New Active Substance ☐ Significant Licence Extension (SLE)

NIHRIO ID: 35154	NICE ID: Not available	UKPS ID: 674689

Licensing and Market Availability Plans

In phase II clinical development.

Summary

Anitocabtagene autoleucel (anito-cel) is in clinical development for treatment of relapsed or refractory multiple myeloma in adult patients. Multiple myeloma is a rare form of cancer characterised by excessive production (proliferation) and improper function of certain cells (plasma cells) found in the bone marrow. Plasma cells are a type of white blood cell which produce a large amount of antibodies. 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 multiple myeloma 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 treatments that are currently available.

Anitocabtagene autoleucel is a type of chimeric antigen receptor (CAR) T cell therapy, which consists of a patients' T cells which have been genetically modified to attach to a protein called B-cell maturation antigen (BCMA), which is present on the surface of myeloma cells. When anitocabtagene autoleucel binds to BCMA on myeloma cells, it triggers a response from the immune system which kills myeloma cells. BCMA is not found as frequently on healthy cells, which remain largely unharmed during treatment which reduces side effects. If licensed, Anitocabtagene autoleucel will offer a novel treatment option for patients with relapsed and refractory MM who have received three or more previous lines of treatment.

Proposed Indication

Treatment of adults with relapsed or refractory multiple myeloma (RRMM).[1]

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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Technology

Description

Anitocabtagene autoleucel (CART-ddBCMA, anito-cel) is a type of chimeric antigen receptor (CAR) T cell therapy consisting of autologous T cells genetically modified *ex vivo* to express a binding domain that specifically recognises B-cell maturation antigen (BCMA).[1-3] BCMA is highly expressed on multiple myeloma (MM) cells, with limited expression outside of terminally differentiated B cells and normal plasma cells, and is involved in promoting multiple myeloma cell survival and proliferation.[2] In preclinical studies, anitocabtagene autoleucel consistently activated specific signals resulting in cytokine (interleukin-2, interferon-γ) secretion, and induced BCMA-specific cytotoxicity in tumour cell lines.[2]

Anitocabtagene autoleucel is in phase II clinical development (iMMagine-1; NCT05396885) for the treatment of adults with RRMM.[1] In the phase II trial anitocabtagene-autoleucel is given as single dose via intravenous (IV) infusion.[2]

Key Innovation

Treatments for RRMM are aimed at disease control rather than cure. Historically, patients with triple and penta-refractory disease (RRMM resistant to at least two immunomodulatory drugs, two different proteosome inhibitors and one CD38 monoclonal antibody) have demonstrated median progression-free survival (PFS) of 3.5 and 2.3 months and median overall survival (OS) of 14.7 and 6.6 months, respectively.[2,4] Due to the poor survival in this highly refractory patient population, novel treatment strategies are critically needed to improve outcomes in patients with MM.[2] Anitocabtagene autoleucel uses autologous T cells which have been genetically modified to include a chimeric antigen receptor (CAR), which binds to BCMA and initiates immune response against MM cells.[3] This leaves healthy cells which have lower or no expression of BCMA largely unharmed.[3] In a phase I trial (NCT04155749), treatment with anitocabtagene autoleucel had a 100% overall response rate, with progression free survival (PFS) of 92.1% at 6-months, 75.9% at 12 months and 63.7% at 18 months.[5] Treatment with Anitocabtagene autoleucel was generally well tolerated, with no reported cases of delayed neurotoxicity, no cases of Guillain-Barré syndrome, no cranial nerve palsies, and no Parkinsonian-like syndromes for the entire population through the follow-up period.[5] Anitocabtagene autoleucel may meet the criteria for an advanced therapy medicinal product (ATMP) classification by the European Medicines Agency (EMA). The scientific recommendation for an ATMP classification is issued by the EMA's Committee for Advanced Therapies (CAT).[6] If licensed, anitocabtagene autoleucel will offer an additional treatment option for patients with RRMM who currently have few, well tolerated therapies available.

Regulatory & Development Status

Anitocabtagene-autoleucel does not have marketing authorisation in the UK/EU for any indication.

Anitocabtagene autoleucel is also in phase III clinical development for patients with RRMM who have received 1-3 previous lines of treatment.[7]

Patient Group

Disease Area and Clinical Need

Multiple myeloma is a plasma cell dyscrasia, which is one of a heterogeneous group of disorders caused by the monoclonal proliferation of lymphoplasmacytic cells in the bone marrow.[8] Multiple myeloma is characterised by the uncontrolled proliferation of malignant plasma cells within the bone marrow, as well

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as clinical symptoms, such as bone destruction and kidney injury.[9] RRMM is defined as a disease which becomes non-responsive or progressive while the patient is on salvage therapy (treatments given after other treatments have failed), or within 60 days of the last treatment in patients who had achieved a minimal response or better on prior therapy. The genomic complexity and clonal evolution of MM over the course of treatment are thought to contribute to drug resistance and disease progression.[10] The cause of MM is unknown but is closely associated with a condition called monoclonal gammopathy of unknown significance (MGUS) which is characterised by an excess number of protein molecules (immunoglobulins) present in the blood. Estimates suggest approximately 1 in every 100 people with MGUS go on to develop MM on an annual basis.[11] Additional risk factors for MM include older age - cases affecting those under 40 years of age are rare; male sex, and ethnicity, with black people being more likely to develop multiple myeloma compared to other ethnicities. The symptoms of MM can include bone pain (notably in the spine, hips or chest), nausea, constipation, loss of appetite, physical and mental fatigue, frequent infections, reduced kidney function, anaemia, weight loss, loss of muscle control in the lower extremities, and excessive thirst.[12] MM patients experience a variety of disease-related events and subsequent disability, such as bone destruction leading to pain, height reduction and body shape changes, bone marrow failure, renal failure, immunodeficiency, and the psychosocial burden of a diagnosis of cancer.[13]

Between 2017-2019, there were approximately 6,240 new cases of multiple myeloma in the UK each year, which is around 17 every day.[14] Multiple myeloma is the 19th most common cancer in the UK, accounting for 2% of all new cancer cases (2017-2019). In females in the UK, myeloma is the 18th most common cancer, with around 2,600 new cases every year (2017-2019). In males in the UK, myeloma is the 16th most common cancer, with around 3,600 new cases every year (2017-2019).[14] Myeloma incidence rates are projected to rise by less than 1% in the UK between 2023-2025 and 2038-2040.[14] The survival rate of myeloma for 10 or more years is 29.1% (2013-2017).[14] In England, between 2023-2024, there were 167,351 finished consult episodes (FCE) for MM (ICD10 code: C90.0), resulting in 99,531 FCE bed days and 154,272 day cases.[15]

Recommended Treatment Options

The National Institute for Health and Care Excellence (NICE) recommends the following regimens for the treatment of RRMM:[16-21]

- Daratumumab monotherapy
- Ixazomib with lenalidomide and dexamethasone
- Isatuximab with pomalidomide and dexamethasone
- Pomalidomide with low-dose dexamethasone
- Panobinostat in combination with bortezomib and dexamethasone
- Teclistamab

Clinical Trial Information

Trial	**iMMagine-1** NCT05396885; A Phase II Study of CART-ddBCMA for the Treatment of Patients with Relapsed or Refractory Multiple Myeloma **Phase II –** Recruiting **Location:** United States **Estimated Primary Completion Date:** May 2024
Trial Design	Open label, single group assignment

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Population	N (estimated) = 110; ages 18 years and older; subjects with relapsed or refractory multiple myeloma treated with at least 3 prior regimens of systemic therapy including proteasome inhibitor, immunomodulatory drugs (IMiD) and anti-CD38 antibody and are refractory to the last line of therapy
Intervention(s)	Single dose of 115±10 x 10^{e-6} CAR+ anitocabtagene autoleucel cells infused intravenously
Comparator(s)	No comparator
Outcome(s)	Primary outcome: Overall response rate per International Myeloma Working Group (IMWG) criteria, as assessed by an independent review committee (IRC). [time frame: 24 months] See trial record for full list of other outcomes.
Results (efficacy)	-
Results (safety)	-

Estimated Cost

The cost of anitocabtagene autoleucel is not yet known.

Relevant Guidance

NICE Guidance

- NICE technology appraisal guidance in development. Idecabtagene vicleucel for treating relapsed or refractory multiple myeloma after 2 to 4 therapies. (GID-TA11075). Expected date of issue to be confirmed.
- NICE technology appraisal guidance in development. Talquetamab for treating relapsed or refractory multiple myeloma after 3 treatments. (GID-TA10969). Expected date of issue to be confirmed.
- NICE technology appraisal guidance in development. Elranatamab for treating relapsed and refractory multiple myeloma after 3 or more treatments. (GID-TA10918). Expected publication date: 08 January 2025.
- NICE technology appraisal guidance in development. Teclistamab for treating relapsed and refractory multiple myeloma after 3 or more treatments. (GID-TA11418). Expected publication date: 13 November 2024.
- NICE technology appraisal. Ixazomib with lenalidomide and dexamethasone for treating relapsed or refractory multiple myeloma. (TA870). February 2023.
- NICE technology appraisal. Daratumumab monotherapy for treating relapsed and refractory multiple myeloma. (TA783). April 2022.
- NICE technology appraisal. Isatuximab with pomalidomide and dexamethasone for treating relapsed and refractory multiple myeloma. (TA658). November 2020.
- NICE technology appraisal. Pomalidomide for multiple myeloma previously treated with lenalidomide and bortezomib. (TA427). January 2017.
- NICE guideline. Myeloma: diagnosis and management (NG35). February 2016

NHS England (Policy/Commissioning) Guidance

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- NHS England. Clinical Commissioning Policy: Bendamustine for relapsed multiple myeloma (all ages). 2020. 200604/P
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- 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.[22]
- European Society of Medical Oncology (ESMO). Multiple myeloma: EHA-ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. 2021.[23]
- National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines) Multiple Myeloma. 2024.[24]

Additional Information

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