Health Technology Briefing
August 2023

I-131-Apamistamab for acute myeloid leukaemia

Company/Developer	Immedica Pharma

☒ New Active Substance ☐ Significant Licence Extension (SLE)

NIHRIO ID: 12923	NICE TSID: 9536	UKPS ID: 670529

Licensing and Market Availability Plans

Currently in phase III clinical development

Summary

I-131-Apamistamab is in clinical development for the treatment of adult patients with relapsed, or refractory acute myeloid leukaemia (AML), prior to bone marrow transplant. AML is a type of blood cancer where excess immature white blood cells are made by the bone marrow, these immature cells do not function like healthy blood cells in fighting off infections or carrying oxygen around the body, which causes the symptoms of AML. It is an acute cancer which means it progresses quickly and aggressively, needing immediate treatment, and is most common in people aged 60 years and over.

I-131-Apamistamab is a monoclonal antibody (a type of protein) that has been designed to recognise and attach to the surface of white blood cells and to the stem cells in the bone marrow that make them. The antibody is attached to a molecule containing a form of iodine, ^{131}I, which emits low-level radiation. When administered, the antibody attaches to these cells in the bone marrow, so the radiation can kill the immature cells without affecting other tissues elsewhere in the body. This clears the bone marrow so that donor stem cells can be given as a transplant. I-131-Apamistamab administered intravenously (into the veins). If licensed, I-131-Apamistamab will offer an additional treatment option for patients with relapsed or refractory AML prior to bone marrow transplant.

Proposed Indication

Treatment of adult patients with active, relapsed or refractory acute myeloid leukaemia prior to allogeneic hematopoietic stem cell transplant (HSCT).[1]

Technology

Description

I-131-Apamistamab (Iomab-B) is an investigational medicinal product that is a radioimmunoconjugate consisting of apamistamab, a murine IgG1 anti-CD45 monoclonal antibody labeled with iodine 131 (I-131), a radio immunotherapeutic property. The monoclonal antibody is a carrier for I-131 resulting in the targeted destruction of cells expressing CD45. CD45 is tyrosine phosphatase expressed on virtually all leukocytes, including myeloid and lymphoid precursors in bone marrow and mature lymphocytes in lymph nodes; it is also expressed on most myeloid and lymphoid leukemic cells, but not on mature erythrocytes or platelets.[2]

In the phase III trial (SIERRA, NCT02665065), I-131-Apamistamab was administered via intravenous infusion (IV) in conjunction with a reduced intensity conditioning (RIC) regimen containing fludarabine and low-dose total body irradiation (TBI) prior to allogeneic HSCT, (also known as bone marrow transplant) to patients with relapsed/ refractory AML.[1,3]

Key Innovation

Radiopharmaceutical therapy (RPT) is a novel therapeutic modality for the treatment of cancer, providing several advantages over existing therapeutic approaches.[4] It combines the precision of targeted therapy with the power of radiation therapy. One of the major benefits is Its ability to target cancer cells, with less damage to healthy cells and minimal toxicity.[5] AML is more common in the elderly, with poor prognosis and limited treatment options because advanced age is often accompanied by frailty and comorbidities, which have an important impact on the tolerance these patients have to intensive treatment modalities such as traditional chemotherapy.[6] Lower toxicity rates seen with I-131-Apamistamab mean that patients who were previously ineligible for potentially curative allogeneic HSCT can now receive that treatment, yielding higher survival rates.[7]

If licensed, I-131-Apamistamab will offer an option to patients which would increase their chance of getting allogeneic HSCT and possibly achieving a cure, with minimal toxicity.

Regulatory & Development Status

I-131-Apamistamab does not currently have Marketing Authorisation in the EU/UK for any indication.

I-131-Apamistamab is not currently in phase II/ III development for any other indications.

I-131-Apamistamab received an orphan drug designation in the EU in October 2016 for patients receiving allogenic HSCT.[8]

Patient Group

Disease Area and Clinical Need

Leukaemia is cancer of the white blood cells. Acute leukaemia is classified according to the type of white blood cells affected, if the monocyte or granulocyte cells (which originate from myeloid stem cells) are affected it is referred to as AML.[9,10] It develops when immature myeloblasts start multiplying uncontrollably, resulting in increased numbers in the blood and bone marrow, the abnormal/immature myeloblasts could now be considered as leukaemia cells. AML can be described as having too many leukaemia cells in the bone marrow and the blood, these cells can sometimes spread to the lymph nodes, spleen, liver, central nervous system (brain and spinal cord) and other organs. In addition, excessive numbers of myeloblasts or leukaemia cells begin to accumulate in the bone marrow, preventing it from producing other healthy blood cells.[11] Primary refractory disease is failure to achieve complete remission (CR) after two courses of intensive induction therapy, while relapse is diagnosed in AML patients who have achieved CR but show an increase of blasts in the bone marrow to ≥5%, reappearance of blasts in the blood or development of extramedullary disease. [12] Symptoms include tiredness, breathlessness, weight loss, frequent infections, pale skin, fever, night sweats, nosebleeds, bone and joint pain, swollen lymph nodes.[9,10]

AML incidence is strongly related to age, with the highest incidence rates being in older people, about 40% of new cases are diagnosed in people aged 75 and over in the UK (2016-2018). There were 3,089 new cases of AML each year in the UK (2016-2018), and 2,678 deaths annually (2017-2019).[13,14]In 2017, there were 4,102 registrations of newly diagnosed cases of AML (ICD-10 code: C92) and the directly age-standardised rate per 100,000 population of newly diagnosed cases was 9.8 among males and 6.2 among females in England.[15] Survival statistics for people with AML diagnosed in England showed that younger people have a better prognosis:[16]

- In people younger than 40 years, more than 50 out of 100 will survive their leukaemia for 5 years or more after they are diagnosed.
- In people aged 50-59, around 25 out of 100 will survive their leukaemia for 5 years or more after diagnosis. The survival rate drastically reduces with age.

In England (2021-22), there were 65,908 finished consultant episodes (FCE) and 62,118 admissions for myeloid leukaemia (ICD-10 code: C92), which resulted in 127,374 FCE bed days and 54,654-day cases.[17]

Recommended Treatment Options

For the majority of relapsed/refractory AML patients, allogeneic HSCT is the only curative treatment approach. Salvage therapy is given in order to reduce the leukaemia load prior to transplantation. Patients achieving complete remission prior to allogeneic HSCT have a more favourable outcome.[18] Intensive salvage regimens commonly consist of an anthracycline and high-dose cytarabine backbone, but for elderly patients, low-intensity regimens are recommended which aim to reduce treatment-related mortality and improve quality of life through improved control of disease. The low-intensity salvage options that do exist for elderly patients essentially consist of hypomethylating agents, and palliative strategies.[12]

Treosulfan with fludarabine is recommended as an option for conditioning treatment before allogenic HSCT for people with malignant diseases for whom a reduced intensity regimen would be suitable.[19]Gilteritinib is also recommended for the treatment of relapsed/refractory FLT3-mutation-positive acute myeloid leukaemia in adults. [20]

Clinical Trial Information

Trial	**SIERRA;** NCT02665065; A multicentre, pivotal phase 3 study of Iomab-B prior to allogeneic hematopoietic cell transplant versus conventional care in older subjects with active, relapsed or refractory acute myeloid leukaemia. **Phase III -** Active, not recruiting. **Location(s):** United States and Canada **Primary completion date:** June 2022
Trial Design	Randomised, parallel assignment, open label, active comparator controlled
Population	N=153 adults, 55 years and over with active, relapsed, or refractory AML.
Intervention(s)	I-131-Apamistamab in conjunction with a RIC regimen containing fludarabine and low-dose TBI prior to allogeneic HCT
Comparator(s)	Conventional care of physician's choice of over 20 available agents including chemotherapies and/or targeted therapies such as Venetoclax (Bcl-2), FLT3 inhibitors, IDH inhibitors, and Mylotarg
Outcome(s)	Primary outcome criteria: • Durable Complete Remission (dCR) [Time Frame: 6 months from the time of initial CR or CRp]. Defined as CR or CRp lasting 180 days or more from the time of initial CR or CRp is documented with evidence of subsequent relapse. See trial record for the full list of other outcomes
Results (efficacy)	I-131-Apamistamab met the primary endpoint of durable Complete Remission (dCR) of 6-months following initial complete remission after bone marrow transplant with high statistical significance (p-value of <0.0001), 22% of patients achieved dCR in the I-131-Apamistamab arm compared to 0% in the control arm.[21]
Results (safety)	I-131-Apamistamab was well-tolerated with a favourable safety profile, in transplanted patients, the incidence of sepsis was four times lower in the I-131-Apamistamab arm than the control arm (6.1% vs 28.6%). Rates of other treatment-related adverse events were lower in favour of I-131-Apamistamab including febrile neutropenia (43.9% vs. 50%), mucositis (15.2% vs 21.4%), and acute graft vs host disease (26.1% vs 35.7%).[21]

Estimated Cost

The cost of I-131-Apamistamab is not yet known.

Relevant Guidance

NICE Guidance

- NICE technology appraisal. Treosulfan with fludarabine for malignant disease before allogeneic stem cell transplant (TA640). August 2020.
- NICE technology appraisal. Gilteritinib for treating relapsed or refractory acute myeloid leukaemia. (TA642). August 2020
- NICE guidelines. Haematological cancers: improving outcomes (NG47). May 2016.
- NICE quality standard. Haematological cancers (QS150). June 2017.

NHS England (Policy/Commissioning) Guidance

- NHS England. 2013/14 NHS Standard Contract for Cancer: Chemotherapy (Adult). B15/S/a.
- NHS England. Clinical Commissioning Policy: Haematopoietic Stem Cell Transplantation NHSCB/B04/P/a. April 2013

Other Guidance

- European Leukaemia Network. Diagnosis and management of AML in adults: 2022 recommendations from an international expert panel. 2022[22]
- European Society for Medical Oncology. Acute myeloid leukaemia in adult patients: ESMO clinical practice guidelines for diagnosis, treatment, and follow-up. 2020[23]
- West Midlands Cancer Alliance (NHS). West midlands guidelines for the treatment of adult acute myeloid leukaemia. 2020[24]

Additional Information

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