

Health Technology Briefing February 2022

Lisocabtagene maraleucel for treating chronic lymphocytic leukaemia or small lymphocytic lymphoma

Company/Developer

Bristol-Myers Squibb

New Active Substance

Significant Licence Extension (SLE)

NIHRIO ID: 20409

NICE ID: 10539

UKPS ID: 663428

Licensing and Market Availability Plans

Currently in phase I/II clinical development.

Summary

Lisocabtagene maraleucel is in clinical development as a treatment option for chronic lymphocytic leukaemia (CLL) or small lymphocytic lymphoma (SLL). CLL is a type of cancer that affects white blood cells and tends to progress slowly over many years. It mostly affects people over the age of 60. CLL and SLL are different forms of the same cancer in which the bone marrow produces too many white blood cells (lymphocytes), which are not fully developed and fail to work properly. In SLL, cells build up in the lymph nodes, whereas in CLL the cancer cells can be found in the blood and bone marrow. Over time this can cause a range of problems, such as an increased risk of developing infections, persistent tiredness, swollen glands in the neck, armpits or groin, and unusual bleeding or bruising. Most patients develop resistance to the currently available treatment options, creating a need for novel therapies for this condition.

Lisocabtagene maraleucel is Chimeric Antigen Receptor T-cell (CAR-T) therapy product targeting the protein CD19. CAR-T cell therapy involves injecting genetically modified T cells into the patient to specifically target patient's tumour cells. The modified T-cells are expected to activate more T-cells within the patient and attach to CD19 on the cancer cells in order to eliminate them. If licensed, lisocabtagene maraleucel will act as the first CART therapy treatment option for adult patients with CLL or SLL.

Proposed Indication

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 unavailable to comment.

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Treatment of relapsed or refractory Chronic Lymphocytic Leukaemia (CLL) or Small Lymphocytic Lymphoma (SLL).¹

Technology

Description

Lisocabtagene maraleucel (JCAR017, Liso-cel) is a second-generation Chimeric Antigen Receptor T-cell (CAR-T) therapy product targeting CD19.² It is a novel CAR-T cell therapy used as a third line treatment that is manufactured using a lentiviral vector and a 4-1BB co-stimulation domain. Its manufacturing separately transduces and expands autologous CD4+ and CD8+ T-cells, respectively, and these are administered to the patient at a fixed 1:1 ratio, which allows consistent dosing of CD4+ and CD8+ CAR T-cells to each patient. This ratio is based on in vitro and xenograft data which demonstrated that administering CD4+ and CD8+ CAR T-cells in a defined ratio improves CAR T-cell expansion and persistence, whilst optimizing antitumor efficacy. Furthermore, the incorporation of a 4-1BB co-stimulation domain leads to a more gradual expansion and longer persistence which appears to result in reduced severity and toxicity.³ Lisocabtagene maraleucel is an advanced therapy medicinal product (ATMP) within the definition of a gene therapy medicine. The scientific recommendation for an ATMP classification is issued by the EMA's Committee for Advanced Therapies (CAT).⁴

Lisocabtagene Maraleucel is administered via intravenous (IV) infusion and is currently in a phase I/II clinical trial (NCT03331198, 017001) for treatment of relapsed or refractory CLL or SLL.¹

Key Innovation

First conceptualised in the late 1980s, CAR-T cell therapy has developed rapidly and is considered one of the most promising treatments for hematologic malignancies.⁵ Most patients eventually develop resistance to current therapies (such as BTKis and venetoclax), underscoring the need for effective novel therapies.⁶ Nevertheless, there are currently no CAR-T therapies recommended by NICE for chronic lymphocytic leukaemia or small lymphocytic lymphoma.⁷ If licensed, lisocabtagene maraleucel will act as the first CART therapy treatment option for adult patients with CLL or SLL.

Regulatory & Development Status

Lisocabtagene maraleucel does not currently have Marketing Authorisation in the EU/UK for this indication.

On 28 January 2022, the Committee for Medicinal Products for Human Use (CHMP) adopted a positive opinion, recommending the granting of a marketing authorisation for lisocabtagene maraleucel, intended for the treatment of adult with relapsed or refractory diffuse large B cell lymphoma (DLBCL), primary mediastinal large B-cell lymphoma (PMBCL) and follicular lymphoma grade 3B (FL3B), after at least two previous lines of treatments.⁸

Lisocabtagene maraleucel is currently in phase II clinical development for the treatment of other forms of lymphoma and lymphocytic leukaemia.⁹

Patient Group

Disease Area and Clinical Need

Chronic lymphocytic leukaemia (ICD-10 code: C91.1) is a type of cancer that affects the white blood cells and tends to progress slowly over many years. In CLL, the spongy material found inside some bones (bone

marrow) produces too many white blood cells called lymphocytes, which are not fully developed and do not work properly. Over time this can cause a range of problems, such as an increased risk of picking up infections, persistent tiredness, swollen glands in the neck, armpits or groin, and unusual bleeding or bruising.¹⁰ The term "chronic" in chronic lymphocytic leukaemia comes from the fact that this leukaemia typically progresses more slowly than other types. The term "lymphocytic" in CLL comes from the group of white blood cells (lymphocytes) affected by the disease, which help the body fight infection.¹¹ Relapsed indicates that the disease responded to therapy initially, but after 6 or more months, stopped responding. Refractory disease refers to cancer which doesn't result in a remission (but may be stable) or disease that gets worse within 6 months of the last treatment.¹² CLL and SLL are the same disease, but in CLL cancer cells are found mostly in the blood and bone marrow and in SLL cancer cells are found mostly in the lymph nodes.¹³

Around 3,800 people are diagnosed with CLL in the UK each year. CLL is by far the most common type of chronic leukaemia and is more common in men.¹⁴ There are around 970 CLL deaths in the UK every year (2016-2018). Mortality rates for CLL in the UK are highest in people aged 90+ (2016-2018). Since the early 1990s, CLL incidence rates have increased by a sixth (17%) in the UK.¹⁵ In England, 2020-2021, there were 17,230 finished consultant episodes (FCE) and 16,385 admissions for CLL (ICD-10 code C91.1) which resulted in 10,364 FCE bed days and 13,911 day cases.¹⁶

Recommended Treatment Options

NICE currently recommends the following therapies for the treatment of relapsed or refractory CLL or SLL^{7,12}:

- Idelalisib
- Ibrutinib alone or with bendamustine and rituximab
- Acalabrutinib
- Venetoclax alone or with rituximab
- Rituximab
- Fludarabine

Clinical Trial Information

Trial	<p>NCT03331198, An Open-Label, Phase 1/2 Study of JCAR017 in Subjects with Relapsed or Refractory Chronic Lymphocytic Leukaemia or Small Lymphocytic Lymphoma</p> <p>Phase I/II: Recruiting</p> <p>Location: US</p> <p>Primary completion date: December 5, 2025</p>
Trial Design	Non-randomised, parallel assignment, open label
Population	N = 259; adults 18 years and older; subjects with relapsed or refractory CLL or SLL; treatment-naïve for prior treatment with any gene therapy product; must have failed 2 or 3 lines of prior non gene therapy treatment
Intervention(s)	Phase 2: Lisocabtagene maraleucel via intravenous infusion
Comparator(s)	No comparator
Outcome(s)	<p>Primary outcome measures:</p> <ul style="list-style-type: none"> • Proportion of subjects experiencing adverse events [Time Frame: Through post treatment Day 90]

	<ul style="list-style-type: none"> Proportion of subjects experiencing laboratory abnormalities [Time Frame: Through post treatment Day 90] <p>See trial record for full list of other outcomes</p>
Results (efficacy)	-
Results (safety)	-

Estimated Cost

The estimated cost of lisocabtagene maraleucel is not yet known.

Relevant Guidance

NICE Guidance

- NICE technology appraisal in development. Ibrutinib with Venetoclax for untreated chronic lymphocytic leukaemia or small lymphocytic lymphoma [ID3860]. Expected March 2023.
- NICE technology appraisal in development. Duvelisib for treating relapsed or refractory chronic lymphocytic leukaemia after at least 2 prior treatments [ID1083]. Expected June 2022.
- NICE technology appraisal. Acalabrutinib for treating chronic lymphocytic leukaemia (TA689). April 2021.
- NICE technology appraisal. Venetoclax with rituximab for previously treated chronic lymphocytic leukaemia (TA561). February 2019.
- NICE technology appraisal. Venetoclax for treating chronic lymphocytic leukaemia (TA487). November 2017.
- NICE technology appraisal. Ibrutinib for previously treated chronic lymphocytic leukaemia and untreated chronic lymphocytic leukaemia with 17p deletion or TP53 mutation (TA429). January 2017.
- NICE technology appraisal guidance. Idelalisib for treating chronic lymphocytic leukaemia (TA359). October 2015.
- NICE technology appraisal. Rituximab for the treatment of relapsed or refractory chronic lymphocytic leukaemia (TA193). July 2010.
- NICE technology appraisal guidance. Guidance on the use of fludarabine for B-cell chronic lymphocytic leukaemia (TA29). September 2001.

NHS England (Policy/Commissioning) Guidance

- NHS England. 2013/14 NHS Standard Contract for Cancer: Chemotherapy (Adult). B15/S/a.
- NHS England. 2013/14 NHS Standard Contract for Cancer: Radiotherapy (All Ages). B01/S/a.

Other Guidance

- European Society for Medical Oncology. Chronic Lymphocytic Leukaemia: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. 2020.¹⁷
- William G, Wierda MD, John C et al. Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma, Version 4.2020, NCCN Clinical Practice Guidelines in Oncology. 2020.¹⁸
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Additional Information

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