NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Obecabtagene autoleucel for treating relapsed or refractory B-cell acute lymphoblastic leukaemia ID6347

Draft scope

Draft remit/evaluation objective

To appraise the clinical and cost effectiveness of obecabtagene autoleucel within its marketing authorisation for treating relapsed or refractory B-cell acute lymphoblastic leukaemia.

Background

Acute lymphoblastic leukaemia (ALL) is a cancer of lymphocyte-producing cells. Lymphocytes are white blood cells that are vital for the body's immune system. In ALL there is an excess production of immature lymphocyte-precursor cells, called lymphoblasts or blast cells, in the bone marrow. This affects the production of normal blood cells and there is a reduction in the number of red cells, white cells and platelets in the blood. ALL can be split into B-cell and T-cell types based on immunophenotyping. B-cell ALL can be divided into further subgroups based on the maturity of the cells (precursor B-cell ALL, mature B cell ALL, common ALL and pro B cell ALL); precursor B-cell ALL accounts for around 75% of all cases of ALL. A specific chromosomal abnormality known as the 'Philadelphia chromosome' is present in 20 to 30% of adults with ALL.[1]

ALL is most common in children, adolescents and young adults, with around 65% of cases diagnosed in people aged under 25. A second increase in incidence is observed in people aged over 60 (around 13% of cases). ALL is more common in than women.[2] In England, around 650 new cases of ALL were diagnosed in 2021.[3] The 5-year survival rate following diagnosis of ALL is approximately 90% for children under 15, 65% for people aged between 15 and 39, and 20% for adults aged 40 and over. [1]

The aim of treatment in ALL is to achieve a cure. Treatment for newly diagnosed ALL can take up to 3 years to complete and is generally divided into 3 phases: induction, consolidation and maintenance. During induction, newly diagnosed ALL is generally treated with chemotherapy combinations including prednisolone, vincristine, an anthracycline and asparaginase. Consolidation treatment typically includes intensified chemotherapy, followed by low dose chemotherapy in the maintenance phase. For high risk ALL, stem cell transplantation may also be used as consolidation therapy. A tyrosine kinase inhibitor (such as imatinib or dasatinib) would also be offered to people with Philadelphia-chromosome positive ALL at all phases of treatment.[1]

Around 45% of ALL in adults relapses after or becomes refractory to initial treatment and requires further treatment.[4] There is no universally accepted treatment approach for relapsed or refractory ALL. Treatment may include conventional combination chemotherapy and for most people this would be fludarabine, cytarabine and granulocyte colony-stimulating factor (FLAG) with idarubicin.[5] Off-label clofarabine may be used in young adults. Adults with Philadelphia-chromosome-positive

relapsed or refractory disease can have a tyrosine kinase inhibitor alone or in combination with conventional chemotherapy.

NICE technology appraisal guidance 975 recommends tisagenlecleucel therapy as an option for people 25 years and under for treating B-cell acute lymphoblastic leukaemia that is relapsed after a transplant, relapsed for a second or later time, or refractory.

NICE technology appraisal guidance 893 recommends brexucabtagene autoleucel for use within the Cancer Drugs Fund as an option for treating relapsed or refractory B-cell ALL in people 26 years and over.

NICE technology appraisal guidance 541 recommends inotuzumab ozogamicin as an option for treating relapsed or refractory CD22-positive B-cell precursor ALL in adults.

NICE technology appraisal guidance 451 recommends ponatinib as an option for Philadelphia-chromosome positive ALL in adults with the T315I gene mutation or for whom dasatinib or imatinib cannot be used.

NICE technology appraisal guidance 450 recommends blinatumomab as an option for Philadelphia chromosome-negative relapsed or refractory precursor B-cell ALL in adults.

Other treatment options may include stem cell transplantation if a suitable donor can be found, or best supportive care (including palliative care).

The technology

Obecabtagene autoleucel (brand name unknown, Autolus) does not currently have a marketing authorisation in the UK for treating relapsed or refractory B-cell ALL. It has been studied in a clinical trial in adults aged 18 years and over with relapsed or refractory B-cell ALL.

Intervention(s)	Obecabtagene autoleucel
Population(s)	Adults with relapsed or refractory B-precursor acute lymphoblastic leukaemia

Comparators	• Tisagenlecleucel (for adults aged 25 years and under) • Inotuzumab ozogamicin (CD22-positive B-precursor ALL) • Fludarabine, cytarabine and granulocyte colony stimulating factor (FLAG)-based combination chemotherapy • Clofarabine (young adults) • Blinatumomab (Philadelphia-chromosome-negative ALL) • Tyrosine kinase inhibitor (such as imatinib, dasatinib or ponatinib), alone or in combination with FLAG based combination chemotherapy (Philadelphia-chromosome-positive ALL) • Stem cell transplantation • Best supportive care (including palliative care)
Outcomes	The outcome measures to be considered include: • overall survival • progression-free survival ((including relapse-free and event-free survival) • treatment response rate (including minimal residual disease, haematologic responses and complete remission) • rate of allogeneic stem cell transplant • adverse effects of treatment • health-related quality of life.
Economic analysis	The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year. The reference case stipulates that the time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared. Costs will be considered from an NHS and Personal Social Services perspective. The availability of any commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account.
Other considerations	Guidance will only be issued in accordance with the marketing authorisation. Where the wording of the therapeutic indication does not include specific treatment combinations, guidance will be issued only in the context of the evidence that has underpinned the marketing authorisation granted by the regulator.

Related NICE recommendations	**Related technology appraisals:** Tisagenlecleucel for treating relapsed or refractory B-cell acute lymphoblastic leukaemia in people aged up to 25 years (2024) NICE technology appraisal guidance 975. Brexucabtagene autoleucel for treating relapsed or refractory B-cell acute lymphoblastic leukaemia in people 26 years and over (2023) NICE technology appraisal guidance 893. Inotuzumab ozogamicin for treating relapsed or refractory B-cell acute lymphoblastic leukaemia (2018) NICE technology appraisal guidance 541. Ponatinib for treating chronic myeloid leukaemia and acute lymphoblastic leukaemia (2017) NICE technology appraisal guidance 451. Blinatumomab for previously treated Philadelphia-chromosome-negative acute lymphoblastic leukaemia (2017) NICE technology appraisal guidance 450 **Related NICE guidelines:** Haematological cancers: improving outcomes (2016) NICE guideline NG47. **Related quality standards:** Haematological cancers (2017) NICE quality standard 150.
Related National Policy	The NHS Long Term Plan (2019) NHS Long Term Plan NHS England (2021) Addition of rituximab to first-line standard chemotherapy for CD20 positive B-cell precursor acute lymphoblastic leukaemia (Adults). Clinical commissioning policy. Reference no. [P200901P] (URN: 1748) NHS England (2023) Manual for prescribed specialist services (2023/2024)

Questions for consultation

Where do you consider obecabtagene autoleucel will fit into the existing care pathway for relapsed or refractory B-cell acute lymphoblastic leukaemia?

Is off-label use of clofarabine in young adults part of current care for relapsed or refractory B-cell acute lymphoblastic leukaemia? If so, up to what age would clofarabine be used?

Please select from the following, will obecabtagene autoleucel be:

A. Prescribed in primary care with routine follow-up in primary care
B. Prescribed in secondary care with routine follow-up in primary care
C. Prescribed in secondary care with routine follow-up in secondary care
D. Other (please give details):

For comparators and subsequent treatments, please detail if the setting for prescribing and routine follow-up differs from the intervention.

Would obecabtagene autoleucel be a candidate for managed access?

Do you consider that the use of obecabtagene autoleucel can result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation?

Please identify the nature of the data which you understand to be available to enable the committee to take account of these benefits.

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope:

- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which obecabtagene autoleucel will be licensed;
- could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology;
- could have any adverse impact on people with a particular disability or disabilities.

Please tell us what evidence should be obtained to enable the committee to identify and consider such impacts.

NICE intends to evaluate this technology through its Single Technology Appraisal process. (Information on NICE's health technology evaluation processes is available at https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/nice-technology-appraisal-guidance/changes-to-health-technology-evaluation).

References

1. Cancer Research UK (2021). Acute lymphoblastic leukaemia (ALL). Accessed May 2024.

2. Cancer Research UK (2021). Acute lymphoblastic leukaemia (ALL) statistics. Accessed May 2024.

3. NHS Digital (2023) Cancer registration statistics, 2021. Accessed May 2024.

4. Fielding AK, Richards SM, Chopra R et al. (2007) Outcome of 609 adults after relapse of acute lymphoblastic leukemia (ALL); an MRC UKALL12/ECOG 2993 study. Blood 109(3):944-50.

5. BMJ Best Practice (2024). Acute lymphoblastic leukaemia. Accessed May 2024.