NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Blinatumomab with chemotherapy for consolidation treatment of Philadelphia-chromosome-negative CD19-positive MRD-negative B-precursor acute lymphoblastic leukaemia with no minimal residual disease

Final scope

Remit/evaluation objective

To appraise the clinical and cost effectiveness of blinatumomab with chemotherapy within its marketing authorisation for consolidation treatment of Philadelphia-chromosome-negative CD19-positive B-precursor acute lymphoblastic leukaemia with no minimal residual disease.

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 classified into 3 groups based on immunophenotyping: B-precursor ALL (also known as precursor-B-cell ALL); mature B-cell ALL and T-cell ALL. In adults, around 75-80% of ALL cases are classified as B-precursor ALL.[1] B-precursor ALL is characterised by the presence of cytoplasmic immunoglobulins and CD10, CD19, CD22 and CD79a expression. A specific chromosomal abnormality known as the 'Philadelphia chromosome' is present in 20 to 30% of adults with ALL.[2]

ALL is most common in children, adolescents and young adults, with around 62% of cases diagnosed in people aged under 25.[3] A second increase in incidence is observed in people aged over 60 (around 16% of cases).[3] It is also more common in males (around 6 out of 10 cases) than females.[3] In the UK, around 350 cases of ALL are diagnosed in adults each year.[4]

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. Stem cell transplant is reserved for patients with high-risk disease characteristics, and if a suitable donor can be found. Consolidation treatment typically includes intensified chemotherapy, followed by low-dose chemotherapy in the maintenance phase. 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 (i.e., in addition to induction, consolidation and maintenance therapy). NICE technology appraisal 589 recommends blinatumomab for treating acute lymphoblastic leukaemia in remission with minimal residual disease activity. Other treatment options may include best supportive care (including palliative care).

Around 45% of ALL relapses after, or becomes refractory to initial treatment and requires further treatment.[5] There is no universally accepted treatment approach for relapsed or refractory ALL.[6]

The technology

Blinatumomab (Blincyto, Amgen Ltd) with chemotherapy does not currently have a marketing authorisation in the UK for consolidation treatment of Philadelphia-chromosome-negative CD19-positive B-precursor acute lymphoblastic leukaemia with no measurable residual disease. It has been studied in a clinical trial compared with chemotherapy in people with breakpoint cluster region (BCR)-c-abl oncogene 1, non-receptor tyrosine kinase (ABL)-negative B cell precursor ALL who are minimal residual disease (MRD) negative after induction and intensification chemotherapy.

Blinatumomab, as monotherapy, has a marketing authorisation in the UK for:

- "adults with Philadelphia chromosome negative CD19 positive B-precursor ALL in first or second complete remission with minimal residual disease (MRD) greater than or equal to 0.1%",
- "adults with CD19 positive relapsed or refractory B-precursor acute lymphoblastic leukaemia (ALL)".

Intervention(s)	Blinatumomab with chemotherapy
Population(s)	People with Philadelphia-chromosome-negative CD19-positive MRD-negative B-precursor acute lymphoblastic leukaemia in frontline consolidation
Comparators	Established clinical management without blinatumomab with chemotherapy, which may include chemotherapy (with or without corticosteroids) and stem cell transplant
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 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:** Blinatumomab for treating acute lymphoblastic leukaemia in remission with minimal residual disease activity (2019) NICE technology appraisal guidance 589 Blinatumomab for previously treated Philadelphia-chromosome-negative acute lymphoblastic leukaemia (2017) NICE technology appraisal guidance 450 Pegaspargase for treating acute lymphoblastic leukaemia (2016) NICE technology appraisal guidance 408 **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 (2023) Manual for prescribed specialist services (2023/2024) Chapters 105 and 106

References

1. Leukaemia Foundation. Acute lymphoblastic leukaemia. Accessed June 2024.

2. Cancer Research UK. Research into acute lymphoblastic leukaemia. Accessed June 2024.

3. Cancer Research UK. Acute lymphoblastic leukaemia (ALL) statistics. Accessed June 2024.

4. Leukaemia Care. Acute Lymphoblastic Leukaemia (ALL). Accessed June 2024

5. 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.

6. BMJ Best Practice. Acute lymphocytic leukaemia. Accessed June 2024.