NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE
Health Technology Appraisal

Blinatumomab for acute lymphoblastic leukaemia for people with minimal residual disease activity in remission

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of blinatumomab within its marketing authorisation for treating acute lymphoblastic leukaemia for people with minimal residual disease in remission.

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 numbers of red cells, white cells and platelets in the blood.

ALL is most common in children, adolescents and young adults, with 65% of cases diagnosed in people aged under 25 years[1]. A second increase in incidence is observed in people aged over 60 years[1]. In England, 654 people were diagnosed with ALL[2], and 201 people died from ALL[3], in 2014.

The aim of treatment in ALL is to achieve a cure. Treatment can take up to 3 years to complete and is generally divided into 3 phases; induction phase, consolidation and maintenance. The choice of treatment can depend on the phase. During induction, newly diagnosed ALL is generally treated with chemotherapy combinations including vincristine, an anthracycline, corticosteroids and asparaginase, with or without cyclophosphamide or cytarabine. NICE technology appraisal 408 recommends pegaspargase as part of an antineoplastic combination therapy for untreated, newly diagnosed ALL. During the consolidation phase, intensified chemotherapy is used, which may include high dose methotrexate with mercaptopurine, asparaginase, or a repeat of the induction therapy. During the maintenance phase low dose chemotherapy is used, which typically consists of weekly methotrexate and daily mercaptopurine for an extended period of time to prevent relapse.

Many of the patients that achieve a complete remission will experience a recurrence of disease. Relapse is thought to result from residual leukaemia cells that remain. Minimal disease diagnostics are used to detect these remaining cells and guide treatment response. Treatment depends upon the degree of residual activity and may require more intensified further treatment (that is, commencing induction therapy once again, which includes high dose chemotherapy).

The technology

Blinatumomab (Blincyto, Amgen) is a T-cell engager targeting CD19 and the CD3/T cell receptor. When blinatumomab binds to both the cancer cell and T-cell, the T-cell is recruited and activated to destroy the cancer cell. It is administered intravenously.

It does not have a marketing authorisation for use in people for use in people with ALL in remission with minimal residual disease but has been studied in an open-label single-arm study for the safety and tolerability of blinatumomab.

Blinatumomab has a marketing authorisation in the UK for "adults with Philadelphia chromosome negative relapsed or refractory B-precursor acute lymphoblastic leukaemia (ALL)".

Intervention(s)	Blinatumomab
Population(s)	People with B-cell precursor acute lymphoblastic leukaemia who have minimal residual disease activity while in remission
Comparators	• Retreatment with combination chemotherapy • Monitor for relapse
Outcomes	The outcome measures to be considered include: • overall survival • disease-free survival • relapse-free survival • minimal residual disease response • 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.

Other considerations	If appropriate, the appraisal should include the costs associated with diagnostic testing for these cells in people with acute lymphoblastic leukaemia, while in remission, who would not otherwise have been tested. A sensitivity analysis should be provided without the cost of the diagnostic test. 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 and NICE Pathways	**Related Technology Appraisals** Pegaspargase for treating acute lymphoblastic leukaemia (2016) NICE technology appraisal guidance 408. Published September 2016. Review date October 2019 **Appraisals in development (including suspended appraisals)** Inotuzumab ozogamicin for treating adults with relapsed or refractory acute lymphoblastic leukaemia. NICE technology appraisal [ID893]. Publication date expected September 2017 Blinatumomab for previously treated B-precursor acute lymphoblastic leukaemia. NICE technology appraisal [ID804]. Publication date expected: TBC Erythrocyte encapsulated asparaginase for acute lymphoblastic leukaemia. NICE technology appraisal [ID864]. Suspended October 2016. **Related Guidelines** Suspected cancer: recognition and referral (2015). NICE guideline NG12. Improving outcomes in children and young people with cancer (2005). Cancer Service Guideline. Review proposal date: June 2016 Improving outcomes in haematological cancers' (October 2003) Cancer Service Guideline. Review proposal date: September 2019. **Related Quality Standards** Children and young people with cancer (February 2014) NICE quality standard 55 Review date TBC

	Related NICE Pathways Haematological cancers: improving outcomes NG47 (May 2016) https://www.nice.org.uk/guidance/ng47 Blood and bone marrow cancers' (June 2015) NICE pathway http://pathways.nice.org.uk/pathways/blood-and-bone-marrow-cancers
Related National Policy	**NHS England** NHS England (2013) 2013/14 NHS Standard contract for cancer: Chemotherapy (adult) Section B Part 1 – Service Specifications Ref B15/S/a **National Service Frameworks** Cancer **Other policies** Department of Health (2016) NHS outcomes framework 2016 to 2017 Independent Cancer Taskforce (2015) Achieving world-class cancer outcomes: a strategy for England 2015-2020 Department of Health (2014) The national cancer strategy: 4th annual report Department of Health (2011) Improving outcomes: a strategy for cancer Department of Health (2009) Cancer commissioning guidance Department of Health (2007) Cancer reform strategy

References

1. Cancer Research UK Acute lymphoblastic leukaemia (ALL) incidence by age, Accessed April 2017

2. Cancer Research UK 'Acute lymphoblastic leukaemia (ALL) incidence by sex and UK region'. Accessed April 2017

3. Cancer Research UK 'Acute lymphoblastic leukaemia (ALL) mortality statistics by sex and UK region'. Accessed April 2017