NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal

Blinatumomab for treating Philadelphia-chromosome-negative relapsed or refractory acute lymphoblastic leukaemia

Scope

Remit

To appraise the clinical and cost effectiveness of blinatumomab within its marketing authorisation for previously treated B-precursor 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 numbers 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. B-cell ALL is characterised by the presence of cytoplasmic immunoglobulins and CD10, CD19, CD22 and CD79a expression.

ALL is most common in children, adolescents and young adults, with 65% of cases diagnosed in people aged under 25 years. A second increase in incidence is observed in people aged over 60 years. In England, 536 people were diagnosed with ALL in 2011 and 202 people died from ALL in 2012. Approximately 20–30% of adults with ALL have the Philadelphia chromosome.[1]

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 chemotherapy regimen can depend on the phase and although selection of drugs, dose schedules and treatment duration may differ slightly between different subtypes of ALL, the basic treatment principles remain similar. There is currently no NICE guidance for treating ALL. During induction, newly diagnosed ALL is generally treated with chemotherapy combinations including vincristine, an anthracycline and asparaginase. During the consolidation phase, intensified chemotherapy is used, which may include high dose methotrexate with mercaptopurine, high dose 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. In adults with high risk acute ALL, stem cell

transplantation and chemotherapy are both considered first line treatment options.[2]

Relapse or refractory to initial treatment occurs in approximately 45% of people with newly diagnosed B-cell ALL. The overall survival rate at 5 years is approximately 10%[3]. Although there is currently no standard of care for people with relapsed or refractory ALL, adults are usually treated with a combination chemotherapy regimen of fludarabine, cytarabine and granulocyte colony-stimulating factor, with or without idarubicin, followed by stem cell transplantation where a suitable donor can be found, or best supportive care (including palliative care). Clofarabine is also used outside its marketing authorisation in clinical practice in England through the Cancer Drugs Fund.

The technology

Blinatumomab (Amgen) is a T-cell engager antibody 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.

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

Intervention	Blinatumomab
Population	People with Philadelphia-chromosome-negative relapsed or refractory B-precursor acute lymphoblastic leukaemia
Comparators	• Fludarabine, cytarabine and granulocyte colony-stimulating factor (GCSF) based combination chemotherapy, with or without idarubicin • Clofarabine based combination chemotherapy • Best supportive care (including palliative care)

Outcomes	The outcome measures to be considered include: • overall survival • event-free survival • relapse-free survival • treatment response rates (including minimal residual disease and haematologic responses and complete remission) • time to and duration of 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 the evidence allows the following subgroup will be considered: • people for whom allogeneic stem cell transplantation is considered an appropriate treatment option 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	Appraisals in development (including suspended appraisals) 'Pegaspargase for treating acute lymphoblastic leukaemia'. NICE technology appraisal [ID863]. Publication expected September 2016. 'Ponatinib for treating chronic myeloid leukaemia and acute lymphoblastic leukaemia'. NICE technology

	appraisal [ID671]. Publication expected May 2017. 'Erythrocyte encapsulated asparaginase for treating acute lymphoblastic leukaemia in adults and children after treatment with escherichia coli derived asparaginase' NICE technology appraisal [ID864]. Publication expected June 2017. 'Inotuzumab ozogamicin for treating relapsed or refractory acute lymphoblastic leukaemia' Proposed NICE technology appraisal [ID893]. Publication date to be confirmed. Terminated appraisals: 'Dasatinib for the treatment of acute lymphoblastic leukaemia' (terminated appraisal; 2008). NICE technology appraisal [ID386]. Related Guidelines: 'Suspected cancer: recognition and referral' (2015). NICE guideline NG12. 'Improving outcomes in children and young people with cancer' (2005). Cancer Service Guideline 'Improving outcomes in haematological cancers' (October 2003) Cancer Service Guideline. Related Quality Standards: 'Children and young people with cancer' (February 2014) NICE quality standard 55 Related NICE Pathways: Suspected cancer recognition and referral (2015) NICE pathway Blood and bone marrow cancers (2014) NICE Pathway
Related National Policy	Specialist cancer services for children and young people, Chapter 106, Manual for Prescribed Specialised Services 2013/14 http://www.england.nhs.uk/wp-content/uploads/2014/01/pss-manual.pdf Blood and marrow transplantation services (all ages), Chapter 29, Manual for Prescribed Specialised Services 2013/14 http://www.england.nhs.uk/wp-content/uploads/2014/01/pss-manual.pdf Department of Health, NHS Outcomes Framework 2015/16, Dec 2014. Domains 1 and 2

	https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/385749/NHS_Outcomes_Framework.pdf

References

1 Cancer Research UK (2014) Acute lymphoblastic leukaemia (ALL) statistics, Accessed October 2015

2 Macmillan Cancer Support (2014) Treatment overview for acute lymphoblastic leukaemia, Accessed October 2015

3 Oriol A (2010), Outcome after relapse of acute lymphoblastic leukemia in adult patients included in four consecutive risk-adapted trials by the PETHEMA Study Group. Haematologica Apr 2010, 95 (4) 589–596