NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal

Obinutuzumab in combination with bendamustine for treating rituximab-refractory follicular lymphoma

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of obinutuzumab in combination with bendamustine within its marketing authorisation for treating follicular lymphoma that is refractory to rituximab or a rituximab-containing regimen.

Background

Lymphomas are cancers of the lymphatic system, which is part of the body's immune system. They are divided into Hodgkin's and non-Hodgkin's lymphomas. Non-Hodgkin's lymphoma includes a number of different conditions, which may be classified based on their grade (how fast they grow) or type (the characteristics of the cancer cells). Low-grade, or 'indolent' non-Hodgkin's lymphomas are slow growing, and often have long survival times but low cure rates; follicular lymphoma is one of the most common types of indolent non-Hodgkin's lymphoma.

In 2012, approximately 11,400 people were diagnosed with non-Hodgkin's lymphoma in England,[1] of whom approximately 2,050 had follicular lymphoma.[1] Approximately 87% of people with follicular lymphoma survive for 5 years or more.[2]

Most people with advanced follicular lymphoma will have initial treatment with chemotherapy in combination with rituximab, often followed by maintenance therapy with rituximab. However, most people's lymphoma will relapse after the initial response, and treatment is often characterised by multiple lines of treatment as the disease responds and relapses. Cancers that do not respond to rituximab or relapse soon after finishing treatment are termed 'rituximab refractory'. Treatment options for rituximab-refractory follicular lymphoma include single- or multi-agent chemotherapy (for example, including cyclophosphamide, fludarabine, bendamustine or chlorambucil) and best supportive care.

The technology

Obinutuzumab (Gazyvaro, Roche Products) is a type 2 glycoengineered antibody that binds to the CD20 protein present on B cells, except stem or plasma cells, and causes cell death. It is administered by intravenous infusion.

Obinutuzumab does not currently have a marketing authorisation in the UK for treating non-Hodgkin's lymphoma. It has been studied in combination with bendamustine, followed by obinutuzumab maintenance therapy, compared with bendamustine alone, for treating adults with rituximab-refractory indolent non-Hodgkin's lymphoma.

Intervention(s)	Obinutuzumab in combination with bendamustine, followed by obinutuzumab maintenance therapy
Population(s)	People with follicular lymphoma that is refractory to rituximab or rituximab-containing regimens In this appraisal, 'refractory' is defined as a relapse during, or within 6 months of completing treatment
Comparators	• Chemotherapy regimens without rituximab (such as cyclophosphamide- or fludarabine-containing regimens, bendamustine or chlorambucil) • Best supportive care
Outcomes	The outcome measures to be considered include: • overall survival • progression-free survival • response rates • duration of response/remission • adverse effects of treatment (including immunosuppression and infections) • 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 evidence allows, consideration should be given to subgroups of people whose disease relapses during rituximab induction therapy and those whose disease relapses during, or within 6 months of completing, rituximab maintenance therapy. 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: 'Idelalisib for treating follicular lymphoma that is refractory to 2 prior treatments' (terminated appraisal; 2014). NICE Technology Appraisal 328. 'Bendamustine for the treatment of indolent (low grade) non-Hodgkin's lymphoma that is refractory to rituximab' (terminated appraisal; 2010). NICE Technology Appraisal 206. 'Rituximab for the treatment of relapsed or refractory stage III or IV follicular non-Hodgkin's lymphoma: Review of technology appraisal guidance 37' (2008). NICE Technology Appraisal 137. Static list. Related guidelines: 'Improving outcomes in haematological cancers' (2003) NICE guidance on cancer services. Review in progress, publication date TBC. Guidelines in development: 'Non-Hodgkin's lymphoma: diagnosis and management of non-Hodgkin's lymphoma'. Publication expected July 2016. Related NICE Pathways: Blood and bone marrow cancers (2015) NICE pathway http://pathways.nice.org.uk/
Related National Policy	Department of Health (2011) Improving outcomes: a strategy for cancer Department of Health (2009) Cancer commissioning guidance Department of Health (2007) Cancer reform strategy Department of Health, NHS Outcomes Framework

	2014-2015, Nov 2013. Domain 1. https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/256456/NHS_outcomes.pdf

References

1. Office for National Statistics (2015) Cancer registration statistics, England, 2013. Accessed February 2016.

2. Cancer Research UK (2014) Non-Hodgkin lymphoma survival statistics. Accessed February 2016.