NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal

Nivolumab for treating relapsed or refractory classical Hodgkin lymphoma

Final scope

Final remit/appraisal objective

To appraise the clinical and cost effectiveness of nivolumab within its marketing authorisation for treating relapsed or refractory classical Hodgkin lymphoma.

Background

Hodgkin's lymphoma is a cancer of the lymphatic system. It can be classified into 2 main groups; the classical types, and the nodular lymphocyte predominant type. Classical Hodgkin lymphomas contain the Reed-Sternberg cells (which are cancerous B lymphocyte cells), whereas the nodular lymphocyte predominant type contains other abnormal cells, but not Reed-Sternberg cells. The initial symptom of Hodgkin lymphoma is often swelling of lymph nodes in the neck, armpit or groin. Other symptoms include recurring fever, night sweats, weight loss, cough, breathlessness, abdominal pain, and itching.

Hodgkin lymphoma accounts for around 20% of all diagnosed lymphomas. In England, there were 1634 people diagnosed with Hodgkin lymphoma in 2013[1] and 256 registered deaths from Hodgkin lymphoma in 2012.[2] The age-specific incidence of Hodgkin lymphoma shows two peaks, one in people aged 20–24 years and the second in people aged over 75 years.[1]

Current first-line treatment for Hodgkin lymphoma is chemotherapy alone or chemotherapy combined with radiotherapy. Between 15 and 30% of people with Hodgkin lymphoma do not achieve long-term remission with these therapies.[3] For these people, high-dose chemotherapy followed by autologous stem cell transplant is a potentially curative treatment that is effective in about 50% of people.[3] However, autologous stem cell transplant may not be an option in some circumstances; for example, when the disease is refractory to chemotherapy, or when the person's age or co-morbidities prohibit this intervention.

Brentuximab vedotin is indicated for relapsed or refractory CD30+ Hodgkin lymphoma (CD30 is an integral membrane antigen expressed by some tumours):

- after autologous stem cell transplant, or

- after at least 2 prior therapies when autologous stem cell transplant or multi-agent chemotherapy is not a treatment option (NICE guidance is in development, funded by the Cancer Drugs Fund in the interim).

There is no standard therapy administered after autologous stem cell transplant and brentuximab vedotin. The aim of treatment is generally to attain a sufficient response for allogeneic stem cell transplant. For people in whom allogeneic stem cell transplant is not considered suitable, therapy depends on individual circumstances, and may include chemotherapy such as gemcitabine or bendamustine, or best supportive care. Some chemotherapy regimens are used outside their marketing authorisation.

The technology

Nivolumab (Opdivo, Bristol–Myers Squibb) is a monoclonal antibody that targets a receptor on the surface of lymphocytes known as PD-1. This receptor is part of the immune checkpoint pathway, and blocking its activity may promote an anti-tumour immune response. Nivolumab is given intravenously.

Nivolumab does not currently have a marketing authorisation in the UK for classical Hodgkin Lymphoma. It has been studied in a non-comparative clinical trial alone in adults with previously treated classical Hodgkin lymphoma.

Intervention(s)	Nivolumab
Population(s)	• People with relapsed or refractory classical Hodgkin lymphoma following autologous stem cell transplant and brentuximab vedotin. • People with relapsed or refractory classical Hodgkin lymphoma following at least 2 prior therapies when autologous stem cell transplant is not a treatment option.

Comparators	For people with relapsed or refractory classical Hodgkin lymphoma following autologous stem cell transplant and brentuximab vedotin: • Established clinical management without nivolumab including chemotherapy such as gemcitabine or bendamustine • Best supportive care For people with relapsed or refractory classical Hodgkin lymphoma following at least 2 prior therapies when autologous stem cell transplant is not a treatment option: • Brentuximab vedotin (NICE guidance is in development, funded by the CDF in the interim) • Best supportive care
Outcomes	The outcome measures to be considered include: • overall survival • progression-free survival • response rates • 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, a scenario analysis including allogeneic stem cell transplant as a subsequent treatment after nivolumab or its comparators will be considered. This should reflect the proportion of people who proceed to allogeneic stem cell transplant after each treatment, as well as the costs and quality-adjusted life year benefits of the procedure. 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) 'Brentuximab vedotin for treating CD30-positive Hodgkin lymphoma' NICE technology appraisals guidance [ID722]. Publication expected January 2017. Related Guidelines: 'Improving outcomes in haemato-oncology cancers' (2003). Cancer Service Guidance http://www.nice.org.uk/nicemedia/live/10891/28786/28786.pdf
Related National Policy	Department of Health, NHS Outcomes Framework 2015-2016, Dec 2014. Domains 1 and 2. https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/385749/NHS_Outcomes_Framework.pdf NHS England, National Cancer Drugs Fund List, February 2016. https://www.england.nhs.uk/wp-content/uploads/2016/02/ncdf-list-01-02-16.pdf

References

1 Cancer Research UK (2013) Hodgkin lymphoma incidence statistics. Accessed May 2016.

2 Cancer Research UK (2013) Hodgkin lymphoma mortality statistics. Accessed May 2016.

3 National Institute for Health and Clinical Excellence (2015) Brentuximab vedotin for treating CD30-positive Hodgkin's lymphoma [ID722]. Final scope. Accessed May 2016.