NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal

Polatuzumab vedotin in combination for untreated diffuse large B-cell lymphoma [ID3901]

Final Scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of polatuzumab vedotin with R-CHP (rituximab, cyclophosphamide, doxorubicin, and prednisolone) within its marketing authorisation for untreated diffuse large B-cell lymphoma.

Background

Lymphomas are cancers of the lymphatic system, which is a part of the immune system. Lymphomas are divided into Hodgkin lymphoma and non-Hodgkin lymphoma. Non-Hodgkin lymphomas (NHL) are a diverse group of conditions which are categorised according to the cell type affected (B-cell or T-cell), as well as the clinical features and rate of progression of the disease. The most common B-cell lymphomas are follicular lymphoma which is a slow growing, low grade form of NHL and diffuse large B-cell lymphomas (DLBCL), a fast growing, high grade form of NHL. Some follicular lymphomas transform into high grade DLBCL (transformed high grade follicular lymphoma). The symptoms differ depending on which organ or tissues are affected by the lymphoma. NHL often presents as painless lumps (enlarged lymph nodes) in the neck, armpit or groin but sometimes may start in other parts of the body such as the stomach or bowel (extra-nodal disease). People may also have loss of appetite, tiredness or night sweats.

There are two biologically distinct subtypes of DLBCL, germinal centre B-cell (which arises in secondary lymphoid organs such as lymph node and spleen) and post-germinal centre (also known as activated B-cell lymphoma) which differ in prognosis. They are distinguished by immunohistochemical testing of gene expression profiling.

There were 11,944 people diagnosed with NHL in England in 2018[1]. It is estimated that about 53% of people with NHL have DLBCL, which equates to around 6,330 people diagnosed with DLBCL per year[1]. Most people diagnosed with DLBCL are 65 or over[2].

Overall survival rates at 5 years for DLBCL were 59.8% between 2004-2016[3]. However, diagnosis at early stage and germinal centre DLBCL have a better prognosis[4]. Survival rates at 5 years for large B cell lymphomas were 84.3% and 82.7% for stages I and II and 72.3% and 46.6% for stages III and IV respectively.[3] Current first-line treatment is combination chemotherapy with rituximab. The most widely used first-line chemoimmunotherapy is R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine and prednisolone).

Sometimes etoposide is added to this regimen or doxorubicin is substituted with a different treatment (such as gemcitabine, etoposide or liposomal doxorubicin). In addition, R-ACVBP (rituximab, doxorubicin, vindesine, cyclophosphamide, bleomycin and prednisolone) can be used instead of R-CHOP[5]. NICE guideline NG52 recommends central nervous system-directed prophylaxis for some people.

The technology

Polatuzumab vedotin (Polivy, Roche) is an antibody drug conjugate which is a monoclonal antibody combined with a cytotoxic agent called monomethyl auristatin E (MMAE). It acts by selectively binding to CD79b, a protein which is found on the surface of B-cells, resulting in the death of B-cells. It is administered as an intravenous infusion.

Polatuzumab vedotin with R-CHP does not currently have a marketing authorisation in the UK for untreated DLBCL. It has been studied in clinical trials in which polatuzumab vedotin and R-CHP chemoimmunotherapy was compared to R-CHOP chemoimmunotherapy, in adults with DLBCL who have not received prior treatment.

Intervention(s)	Polatuzumab vedotin with R-CHP (rituximab, cyclophosphamide, doxorubicin, and prednisolone)
Population(s)	Adults with untreated diffuse large B-cell lymphoma
Comparators	Chemoimmunotherapy (including R-CHOP)
Outcomes	The outcome measures to be considered include: • overall survival • progression-free survival • response rate • 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. The availability and cost of biosimilars should be taken into account.
Other considerations	If the evidence allows the following subgroups will be considered. These include: • germinal centre DLBCL, and • post-germinal centre DLBCL 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. The availability and cost of biosimilar products should be taken into account.
Related NICE recommendations and NICE Pathways	Related Guidelines: Non-Hodgkin's lymphoma: diagnosis and management (2016) NICE Guideline NG52 Related Quality Standards: Haematological cancers (2017) NICE Quality Standard 150 Related NICE Pathways: Non-Hodgkin's lymphoma overview (2018) NICE Pathway
Related National Policy	The NHS Long Term Plan, 2019. NHS Long Term Plan NHS England (2018/2019) NHS manual for prescribed specialist services (2018/2019) Chapter 105, specialist cancer services (adult) Department of Health and Social Care, NHS Outcomes Framework 2016-2017: Domains 1 and 2. https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017

References

1. Public Health England - Cancer registration statistics: England 2018 final release – Accessed December 2021

2. Lymphoma association. Diffuse Large B-cell lymphoma. Accessed September 2021.

3. Haematological Malignancy Research Network (HMRN) data (2004-2016) Accessed November 2021.

4. Cho M, Chung Y, Jang S et al. Prognostic impact of germinal center B-cell-like and non-germinal center B-cell-like subtypes of bone marrow involvement in patients with diffuse large B-cell lymphoma treated with R-CHOP, Medicine: November 2018 - Volume 97 - Issue 45

5. Tilly H, Silva M, Vitolo U et al. (2015) Diffuse large B-cell lymphoma (DLBCL): ESMO clinical practice guidelines for diagnosis, treatment and follow-up. Annals of Oncology ;26(Suppl 5):v116-v125.