NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Polatuzumab vedotin with rituximab and bendamustine for treating relapsed or refractory diffuse large B-cell lymphoma

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of polatuzumab vedotin with rituximab and bendamustine within its marketing authorisation for treating adults with relapsed or refractory diffuse large B-cell lymphoma for whom hematopoietic stem cell transplant is not suitable.

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 (extranodal disease). People may also have loss of appetite, tiredness or night sweats.

There were around 12,065 people diagnosed with NHL in England in 2017.[1] It is estimated that about 40% of people with NHL have DLBCL,[2] which would equate to 4,826registrations of DLBCL per year.

Most people diagnosed with DLBCL are 65 or over.[3] Although most patients are cured with first-line chemotherapy, about 10-15% have primary refractory disease and a further 20-30% relapse.[4] Survival rates at 5 years for DLBCL are around 65-70% for stage I and II and around 50% at stages III and IV (patients diagnosed between 2004 and 2011).[5]

The most widely used first-line treatment for DLBCL is R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine and prednisolone). Sometimes etoposide is added to this regimen. NICE guideline NG52 recommends chemotherapy in combination with rituximab for relapsed or refractory disease followed by stem cell transplantation. Chemotherapy regimens commonly used in clinical practice include DHAP (dexamethasone, cytarabine, cisplatin),

GDP (gemcitabine, dexamethasone, cisplatin), ICE (ifosfamide, carboplatin, etoposide) and IVE (ifosfamide, etoposide, epirubicin). For patients who are not fit enough, a wide range of different treatments are available. If stem cell transplantation is not suitable, further chemotherapy or immunotherapy may be used alone. NICE technology appraisal 306 recommends pixantrone monotherapy for people who have multiply relapsed or refractory aggressive non-Hodgkin B-cell lymphoma, when they have received previous treatment with rituximab and are in the third or fourth line of treatment.

The technology

Polatuzumab vedotin (brand name unknown, Roche Products) is an antibody drug conjugate that 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 does not currently have marketing authorisation in the UK for any indication. It has been studied in combination with rituximab and bendamustine in an ongoing randomized open-label clinical trial in adult patients with relapsed or refractory DLBCL. Polatuzumab vedotin in combination with rituximab and bendamustine was compared to rituximab and bendamustine.

Intervention(s)	Polatuzumab vedotin (with rituximab and bendamustine)
Population(s)	Adults with relapsed or refractory diffuse large B-cell lymphoma for whom hematopoietic stem cell transplant is not suitable
Comparators	• Rituximab in combination with one or more chemotherapy agents such as: ○ R-GemOx (rituximab, gemcitabine oxaliplatin), R-Gem (rituximab gemcitabine), R-P-MitCEBO (rituximab, prednisolone, mitoxantrone cyclophosphamide, etoposide bleomycin, vincristine), (R-)DECC (rituximab, dexamethasone, etoposide, chlorambucil, lomustine), BR (bendamustine, rituximab)

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. The availability of any commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account. Costs will be considered from an NHS and Personal Social Services perspective.
Other considerations	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 Technology Appraisals**: 'Pixantrone monotherapy for treating multiply relapsed or refractory aggressive non-Hodgkin's B-cell lymphoma' (2014). NICE Technology Appraisal guidance TA306. Review date to be confirmed. 'Axicabtagene ciloleucel for treating diffuse large B-cell lymphoma and primary mediastinal B-cell lymphoma and after 2 or more systemic therapies' NICE technology appraisal guidance TA559 'Tisagenlecleucel-T for treating relapsed or refractory diffuse large B-cell lymphoma after 2 or more systemic therapies' NICE Technology appraisal guidance TA567

	Related Guidelines: 'Non-Hodgkin's lymphoma: diagnosis and management' (2016) NICE Guideline 52. Review date to be confirmed. 'Haematological cancers: improving outcomes' (2016). NICE Guideline 47. Review date to be confirmed. Non-Hodgkin's lymphoma: rituximab subcutaneous injection (2014) NICE evidence summary of new medicines 46. **Related Quality Standards:** Haematological cancers (2017) NICE quality standard 150. **Related NICE Pathways:** Blood and bone marrow cancers (2016) 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 Department of Health and Social Care, NHS Outcomes Framework 2016-2017: Domains 1-5

References

1. Office for National Statistics. Cancer registration statistics, England. 2019. Accessed May 2019

2. Cancer Research UK. Non-Hodgkin lymphoma 2018. Accessed May 2019

3. Lymphoma association Diffuse B-cell lymphoma Accessed May 2019

4. Chaganti S, Illidge T, Barrington S, McKay P, Linton K, Cwynarski K, et al. Guidelines for the management of diffuse large B-cell lymphoma. British journal of haematology. 2016;174(1):43-56. Available from: https://doi.org/10.1111/bjh.14136

5. Cancer Research UK Non-Hodgkin lymphoma- Survival Accessed May 2019