NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal

Axicabtagene ciloleucel for treating relapsed or refractory low-grade non-Hodgkin lymphoma

Final Scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of axicabtagene ciloleucel within its marketing authorisation for treating relapsed or refractory low-grade non-Hodgkin lymphoma.

Background

Lymphomas are cancers of the lymphatic system, which is part of the body's immune system. They are divided into Hodgkin and non-Hodgkin lymphomas. Non-Hodgkin lymphomas are a heterogeneous group of conditions ranging from 'indolent' (low-grade) to 'aggressive' (high-grade) depending on the rate at which the abnormal lymphocytes divide. Indolent lymphomas are slow growing, with long median survival times but are less likely to be cured by treatment.

Follicular lymphoma is the most common type of indolent non-Hodgkin lymphoma. Patients with follicular lymphoma typically present with painless, swollen lymph nodes in the neck, armpit or groin. Lymphomas are commonly staged I (best prognosis) to IV (worse prognosis). The stage of the lymphoma reflects how many groups of lymph nodes are affected, where they are in the body, and whether other organs such as the bone marrow or liver are affected. Most people present with advanced disease (stage III to IV).[1]

Marginal zone lymphoma is another type of indolent non-Hodgkin lymphoma that develops from B lymphocytes that are normally found at the edge of areas of lymph node tissue. Mucosa associated lymphoid tissue (MALT) lymphoma is the most common type of marginal zone lymphoma and it most commonly affects the stomach. Nodal marginal zone lymphoma starts in the lymph nodes and splenic marginal zone lymphoma starts in the spleen but can also be found in the bloodstream.[2]

In 2017, approximately 12,000 people were diagnosed with non-Hodgkin lymphoma in England, of whom around 18% had follicular lymphoma.[2,3] The 5-year survival rate is between 80 to 90% for people with follicular lymphoma and is between 50 to 80% for marginal zone lymphoma depending on the stage of disease.[4]

For untreated disease:

- NICE technology appraisal guidance 243 recommends rituximab in combination with chemotherapy as an option for untreated symptomatic stage III and IV follicular lymphoma.

- NICE technology appraisal guidance 513 recommends obinutuzumab in combination with chemotherapy as induction treatment followed by

obinutuzumab as maintenance therapy for people who have a Follicular Lymphoma International Prognostic Index of 2 or more.

- For people who do not have symptoms, the NICE clinical guideline for non-Hodgkin's lymphoma recommends that rituximab is given alone, although at the time of writing this scope rituximab monotherapy did not have a marketing authorisation in the UK for untreated non-Hodgkin's lymphoma.

For treated disease:

- People whose disease does not respond to treatment, or relapses after treatment is completed, will usually receive a different combination chemotherapy regimen, with or without rituximab. Stem cell transplantation may also be considered.

- NICE technology appraisal guidance 137 recommends rituximab in combination with chemotherapy or as monotherapy for relapsed stage III or IV follicular non-Hodgkin's lymphoma.

- NICE technology appraisal guidance 226 recommends rituximab maintenance therapy as an option for people whose follicular non-Hodgkin's lymphoma has responded to first-line induction therapy with rituximab in combination with chemotherapy.

- NICE technology appraisal guidance 627 recommends lenalidomide in combination with rituximab as an option for previously treated follicular lymphoma (grade 1 to 3A) in adults.

- NICE technology appraisal guidance 629 recommends obinutuzumab in combination with bendamustine followed by obinutuzumab maintenance as an option for treating follicular lymphoma that did not respond or progressed up to 6 months after treatment with rituximab or a rituximab-containing regimen.

The technology

Axicabtagene ciloleucel (Yescarta, Kite, a Gilead company) is a type of immunotherapy that uses autologous T cells directed against the tumour antigen CD19. It is administered intravenously.

Axicabtagene ciloleucel has a marketing authorisation for treating relapsed or refractory diffuse large B-cell lymphoma and primary mediastinal large B-cell lymphoma, after 2 or more lines of systemic therapy. It does not currently have a marketing authorisation in the UK for treating relapsed or refractory low-grade non-Hodgkin lymphoma. It is currently being studied in a clinical trial in adults with relapsed or refractory follicular lymphoma or marginal zone lymphoma after at least 2 prior treatments.

Intervention	Axicabtagene ciloleucel
Population	Adults with relapsed or refractory non-Hodgkin lymphoma

Comparators	• Rituximab monotherapy • Rituximab in combination with chemotherapy • Obinutuzumab with bendamustine • Lenalidomide with rituximab • Clinical management without axicabtagene ciloleucel including chemotherapy (such as cyclophosphamide, fludarabine, bendamustine or chlorambucil) • 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. The availability of any commercial arrangements for the intervention, comparator technologies and subsequent treatment technologies will be taken into account.
Other considerations	The availability and cost of biosimilar and generic products should be taken into account. 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: 'Obinutuzumab with bendamustine for treating follicular lymphoma after rituximab' (2020). NICE Technology Appraisal 629. 'Lenalidomide with rituximab for previously treated follicular lymphoma' (2020). NICE technology appraisal guidance 627.

	'Idelalisib for treating refractory follicular lymphoma' (2019). NICE technology appraisal guidance 604. 'Obinutuzumab for untreated advanced follicular lymphoma' (2018). NICE Technology Appraisal 513. 'Rituximab for the first-line treatment of stage III-IV follicular lymphoma' (2012). NICE Technology Appraisal 243. Review date August 2014. 'Rituximab for the first-line maintenance treatment of follicular non-Hodgkin's lymphoma' (2011). NICE Technology Appraisal 226. Review date August 2014. 'Rituximab for the treatment of relapsed or refractory stage III or IV follicular non-Hodgkin's lymphoma' (2008). NICE Technology Appraisal 137. Review decision March 2011: static guidance list. Terminated appraisals '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 aggressive non-Hodgkin's lymphoma' (withdrawn appraisal – routinely used outside its licensed indication in clinical practice) (2003). NICE Technology Appraisal 65. Appraisals in development (including suspended appraisals) 'Ibrutinib for treating relapsed or refractory follicular lymphoma' NICE technology appraisal guidance [ID1251]. Publication date to be confirmed. 'Duvelisib for treating relapsed follicular lymphoma after 2 systemic therapies' NICE technology appraisal guidance (suspended) [ID1090]. 'Bortezomib for the treatment of relapsed or refractory follicular non-Hodgkin's lymphoma' NICE technology appraisal guidance (suspended) [ID407]. 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. 'Suspected cancer: recognition and referral' (2015). NICE guideline 12. Reviewed 2021. Related Quality Standards: 'Haematological cancers' (2017) NICE quality standard 150.

	Related NICE Pathways: Non-Hodgkin's lymphoma (Updated 2021) NICE pathway 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 to 5. https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017

References

1 Freedman A (2018) Follicular Lymphoma: 2018 Update on Diagnosis and Management. American Journal of Hematology 93(2): 296-305

2 Cancer Research UK (2014) Different types of non Hodgkin lymphoma. Accessed May 2021.

3 Office for National Statistics (2019) Cancer registration statistics, England: 2017. Accessed May 2021.

4 Cancer Research UK (2004–11) Non Hodgkin lymphoma survival statistics. Accessed May 2021.