NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Mosunetuzumab for treating relapsed or refractory follicular lymphoma

Draft scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of mosunetuzumab within its marketing authorisation for treating relapsed or refractory follicular lymphoma.

Background

Lymphomas are cancers of the lymphatic system, which is part of the immune system and are divided into Hodgkin and non-Hodgkin lymphomas. Non-Hodgkin lymphomas are a diverse group of conditions which can affect either of the two main types of lymphocytes, T lymphocytes or B lymphocytes. Non-Hodgkin lymphomas can be low grade, or indolent, meaning they are slow growing, or high-grade, meaning they grow faster and more aggressively.[1]

Follicular lymphoma is a type of indolent, low grade lymphoma which affects B-lymphocytes. People with this condition typically present with painless lumps (enlarged lymph nodes) in the neck, armpit or groin although there may be additional symptoms such as night sweats and recurrent fevers in some people.[2]

Follicular lymphomas are commonly staged from I (best prognosis) to IV (worse prognosis) and the staging depends on how many groups of lymph nodes are affected, where they are in the body, the size of the areas of lymphoma and whether other organs outside of the lymphatic system such as the bone marrow or liver are affected.[3]

In England in 2018 there were 11,944 diagnoses of non-Hodgkin's lymphoma and 2329 (19%) of those were follicular lymphoma.[4] The five year survival rate for those diagnosed with follicular lymphoma is around 90% for those with stage one and two disease, falling to almost 80% for those with stage three and four disease.[5]

Clinical management for relapsed and refractory follicular lymphoma includes:

- NICE technology appraisal 137 recommends rituximab either alone or in combination with chemotherapy as a treatment option for people with relapsed or refractory stage III or IV follicular non-Hodgkin's lymphoma followed by rituximab monotherapy maintenance for those whose follicular lymphoma responded to initial treatment.

- NICE technology appraisal 629 recommends obinutuzumab with bendamustine followed by obinutuzumab maintenance monotherapy as an option for treating follicular lymphoma that was relapsed after, or refractory to, a rituximab-containing regime

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

- Consolidation with autologous or allogenic stem cell transplantation can also be offered for people with follicular lymphoma, in second or subsequent remission (complete or partial), who meet the eligibility criteria.

The technology

Mosunetuzumab (brand name unknown, Roche) is a bispecific fully humanised monoclonal antibody that has two distinct "Fab" regions, meaning that the antibody can bind two distinct targets. One of these regions is specific for CD20, which is expressed in the majority of B-cell malignancies, and the other is specific for CD3 which is a receptor on T-lymphocytes. By binding both cells the antibody mediates activation of the recruited T-lymphocytes against the CD20 expressing B-cells, resulting in B-cell death and an anti-tumour effect.

Mosunetuzumab does not currently have a marketing authorisation in the UK but is being assessed as both a monotherapy and in combination with atezolizumab in a single arm clinical trial of adults with relapsed or refractory non-Hodgkin's lymphoma, including a subset of patients with follicular lymphoma, or chronic lymphocytic leukaemia after at least one prior treatment. It is administered intravenously.

Intervention(s)	Mosunetuzumab
Population(s)	Adults with relapsed or refractory follicular lymphoma
Comparators	Established clinical management without mosunetuzumab. Treatment choice will depend on previous treatments, and how effective those treatments were. • Obinutuzumab with bendamustine followed by obinutuzumab maintenance. • Lenalidomide with rituximab • Rituximab in combination with chemotherapy • 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 and subsequent treatment technologies will be taken into account. The availability of any managed access arrangement for the intervention 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: '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: 'Idelalisib for treating refractory follicular lymphoma' (2019) NICE Technology Appraisal 604. Review date 2022 'Lenalidomide with rituximab for previously treated follicular lymphoma' (2020) NICE Technology Appraisal 627. Review date 2023 'Obinutuzumab with bendamustine for treating follicular lymphoma after rituximab' (2020) NICE Technology Appraisal 629. Review date 2023

	Terminated appraisals 'Bendamustine for the treatment of indolent (low grade) **non-**Hodgkin's lymphoma that is refractory to rituximab (terminated appraisal)' NICE Technology Appraisal 206. 'Duvelisib for treating relapsed follicular lymphoma after 2 or more systemic therapies (terminated appraisal)' (2021) NICE Technology Appraisal 717. Appraisals in development (including suspended appraisals) 'Ibrutinib for treating relapsed or refractory follicular lymphoma' NICE technology appraisals guidance [ID1251] Publication date to be confirmed 'Axicabtagene ciloleucel for treating relapsed or refractory low-grade non-Hodgkin's lymphoma' NICE technology appraisals guidance [ID1685] Publication date to be confirmed 'Bortezomib for the treatment of relapsed or refractory follicular non-Hodgkin's lymphoma' NICE technology appraisals guidance (Suspended) [ID407] "Ofatumumab (Arzerra) in combination with chemotherapy for follicular lymphoma; second line - refractory to rituximab" NICE technology appraisals guidance (Suspended) [ID1487] 'Tisagenlecleucel for treating follicular lymphoma after 2 or more therapies' Proposed NICE technology appraisals guidance [ID3950] Publication date to be confirmed 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' NICE quality standard 150 Related NICE Pathways: Blood and bone marrow cancers (2021) NICE pathway Non-Hodgkin's Lymphoma (2021) 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 https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017 Independent Cancer Taskforce (2015) Achieving world-class cancer outcomes: a strategy for England 2015-2020

Questions for consultation

Have all relevant comparators for mosunetuzumab been included in the scope?

Which treatments are considered to be established clinical practice in the NHS for relapsed and refractory follicular lymphoma?

If applicable, 'How should best supportive care be defined?How would the use of mosunetuzumab change the subsequent treatments available for managing relapsed or refractory follicular lymphoma, including stem cell transplantation?

Are the outcomes listed appropriate?

How should best supportive care be defined?

Where do you consider mosunetuzumab will fit into the existing NICE pathway, for 'treating follicular lymphoma'?

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope:

- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which mosunetuzumab is licensed;
- could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology;
- could have any adverse impact on people with a particular disability or disabilities.

Please tell us what evidence should be obtained to enable the Committee to identify and consider such impacts.

Do you consider mosunetuzumab to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a 'step-change' in the management of the condition)?

Do you consider that the use of mosunetuzumab can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation?

Please identify the nature of the data which you understand to be available to enable the Appraisal Committee to take account of these benefits.

To help NICE prioritise topics for additional adoption support, do you consider that there will be any barriers to adoption of this technology into practice? If yes, please describe briefly.

NICE intends to appraise this technology through its Single Technology Appraisal (STA) Process. We welcome comments on the appropriateness of appraising this topic through this process. (Information on the Institute's Technology Appraisal processes is available at http://www.nice.org.uk/article/pmg19/chapter/1-Introduction).

References

1 Cancer Research UK 2020 How doctors group non-Hodgkin lymphoma | non-Hodgkin lymphoma | Cancer Research UK – Accessed November 2021

2 Cancer Research UK 2020 - Symptoms | non-Hodgkin lymphoma | Cancer Research UK Accessed November 2021

3 Cancer Research UK 2020 - Stages of non-Hodgkin lymphoma | non-Hodgkin lymphoma | Cancer Research UK Accessed November 2020

4 Public Health England Cancer registration statistics: England 2018 final release - GOV.UK (www.gov.uk) – Accessed November 2021

5 Cancer Research UK 2020 Survival | non-Hodgkin lymphoma | Cancer Research UK – Accessed November 2021