NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Tisagenlecleucel for treating follicular lymphoma after 2 or more therapies

Draft scope

Draft remit/evaluation objective

To appraise the clinical and cost effectiveness of tisagenlecleucel within its marketing authorisation for treating follicular lymphoma after 2 or more therapies.

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 2 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 5-year survival rate for those diagnosed with follicular lymphoma is around 90%.[5] Duration of response to chemoimmunotherapy and survival decreases with each subsequent relapse of follicular lymphoma.[6]

Clinical management for relapsed and refractory follicular lymphoma includes:

- NICE technology appraisal guidance 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.
- NICE technology appraisal guidance 627 recommends lenalidomide with rituximab as an option for previously treated follicular lymphoma (grade 1 to 3A) in adults.
- NICE technology appraisal guidance 629 recommends obinutuzumab 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.

- 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

Tisagenlecleucel (Kymriah, Novartis) does not currently have a marketing authorisation in the UK for treating follicular lymphoma after 2 or more therapies. It is being studied in a single-arm clinical trial in people with refractory or relapsed follicular lymphoma.

Intervention(s)	Tisagenlecleucel
Population(s)	Adults with refractory or relapsed follicular lymphoma
Comparators	Established clinical management without tisagenlecleucel including chemotherapy (such as cyclophosphamide, fludarabine, bendamustine or chlorambucil). 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 • Axicabtagene ciloleucel (subject to NICE evaluation) • Mosunetuzumab (subject to NICE evaluation) • 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 and cost of biosimilar and generic products should be taken into account.
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.
Related NICE recommendations	**Related Technology Appraisals:** 'Obinutuzumab with bendamustine for treating follicular lymphoma after rituximab' (2020). NICE Technology appraisal guidance 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. '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. **Related appraisals in development:** 'Ibrutinib for treating relapsed or refractory follicular lymphoma' NICE Technology appraisal guidance [ID1251]. Publication date to be confirmed. 'Bortezomib for the treatment of relapsed or refractory follicular non-Hodgkin's lymphoma' NICE Technology appraisal guidance (suspended March 2012) [ID407]. 'Axicabtagene ciloleucel for treating relapsed or refractory low-grade non-Hodgkin's lymphoma.' NICE Technology appraisal guidance [ID1685]. Publication date to be confirmed.

	'Mosunetuzumab for treating relapsed or refractory follicular lymphoma.' NICE Technology appraisal guidance [ID3931]. Expected publication date: January 2023 **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 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-outcomesframework-2016-to-2017 Independent Cancer Taskforce (2015) Achieving world-class cancer outcomes: a strategy for England 2015-2020

Questions for consultation

Where do you consider tisagenlecleucel will fit into the existing care pathway for refractory or relapsed follicular lymphoma?

Would tisagenlecleucel be a candidate for managed access?

Do you consider tisagenlecleucel 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 tisagenlecleucel can result in any potential 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 committee to take account of these benefits.

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 tisagenlecleucel will be 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.

NICE intends to evaluate this technology through its Single Technology Appraisal process. We welcome comments on the appropriateness of appraising this topic through this process. (Information on NICE's health technology evaluation processes is available at https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/nice-technology-appraisal-guidance/changes-to-health-technology-evaluation).

References

1. Cancer Research UK. How doctors group non-Hodgkin lymphomas. Accessed March 2022.

2. Cancer Research UK. Symptoms. Accessed March 2022.

3. Cancer Research UK. Stages of non-Hodgkin lymphoma. Accessed March 2022.

4. Public Health England. Cancer registration statistics, England: final release, 2018. Accessed March 2022.

5. Cancer Research UK. Survival. Accessed March 2022.

6. Rivas-Delgado A, Magnano L, Moreno-Velázquez M et al. Response duration and survival shorten after each relapse in patients with follicular lymphoma treated in the rituximab era. British Journal of Haematology. 2018;184(5):753-759.