NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Amivantamab with lazertinib for untreated EGFR mutation-positive advanced non-small-cell lung cancer ID6256

Draft scope

Draft remit/evaluation objective

To appraise the clinical and cost effectiveness of amivantamab with lazertinib within its marketing authorisation as a treatment for untreated EGFR mutation-positive advanced non-small-cell lung cancer (NSCLC).

Background

Lung cancer is the third most common cancer and the most common cause of cancer death in the UK, accounting for 10% of all new cancer cases and 20% of all cancer deaths in 2020.[1] There were around 37,000 new lung cancer cases and 27,000 deaths from lung cancer in England in 2020.[1] Most lung cancers are diagnosed at an advanced stage, when the cancer has spread to lymph nodes and other organs in the chest (locally advanced disease; stage 3) or to other parts of the body (metastatic disease; stage 4).[2] In 2021, 91% (around 31,000) of people diagnosed with lung cancer in England had NSCLC.[2] Around 12 to 14% of people with NSCLC in Europe have mutations in the gene coding the epidermal growth factor receptor (EGFR).[3,4]

The treatment pathway for NSCLC can be divided into interconnected decision points based on the number staging system and line of therapy. Treatment choices are influenced by the presence of biological markers (including programmed cell death 1 ligand PD-L1 status), oncogenic driver genetic alterations, histology (squamous or non-squamous) and previous treatment.

For NSCLC with an EGFR mutation, NICE guidance recommends various tyrosine kinase inhibitors (TKIs) for untreated disease including gefitinib (TA192), erlotinib (TA258), afatinib (TA310), dacomitinib (TA595) and osimertinib (TA654). For NSCLC which has been previously treated with an EGFR TKI, platinum doublet chemotherapy and atezolizumab combination are treatment options (NICE guideline 122 and NICE technology appraisal 584). NICE guidance also recommends osimertinib in EGFR T790M mutation-positive disease (TA653). For previously treated NSCLC without targetable mutations, NICE guidance recommends nivolumab (TA655 and TA713), atezolizumab (TA520) and pembrolizumab (TA428) monotherapies as well as docetaxel with nintedanib (TA347). Docetaxel alone may also be offered.

The technology

Amivantamab (Rybrevant, Janssen-Cilag) with lazertinib (Leclaza, Janssen-Cilag) does not currently have a marketing authorisation in the UK for untreated EGFR mutation positive NSCLC. It is being studied in a phase 3 clinical trial compared with osimertinib alone and lazertinib alone in people with NSCLC that has an exon 19 deletion or an exon 21 L858R substitution mutation.

Appendix B

Amivantamab has a marketing authorisation for the treatment of adults with locally advanced or metastatic NSCLC with activating EGFR exon 20 insertion mutations, whose disease has progressed on or after platinum-based chemotherapy.

Intervention(s)	Amivantamab with lazertinib
Population(s)	People with NSCLC which has an EGFR exon 19 deletion or exon 21 L858R substitution mutation
Subgroups	If the evidence allows, the following subgroups will be considered: • Type of EGFR mutation • Disease stage • Histology • Treatments had at previous stages (surgery, radiotherapy, previous systemic therapies) • Presence of CNS metastases
Comparators	• Osimertinib monotherapy • Dacomitinib • Afatinib • Erlotinib • Gefitinib • Osimertinib with chemotherapy (subject to NICE appraisal)
Outcomes	The outcome measures to be considered include: • overall survival • progression-free survival • response rate • time to treatment discontinuation • time to subsequent therapy • 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. If the technology is likely to provide similar or greater health benefits at similar or lower cost than technologies recommended in published NICE technology appraisal guidance for the same indication, a cost comparison may be carried out. 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:** Osimertinib for untreated EGFR mutation-positive non-small-cell lung cancer (2020) NICE technology appraisal guidance 654 Dacomitinib for untreated EGFR mutation-positive non-small-cell lung cancer (2019) NICE technology appraisal guidance 595 Afatinib for treating epidermal growth factor receptor mutation-positive locally advanced or metastatic non-small-cell lung cancer (2014) NICE technology appraisal guidance 310 Erlotinib for the first-line treatment of locally advanced or metastatic EGFR-TK mutation-positive non-small-cell lung cancer (2012) NICE technology appraisal guidance 258 Gefitinib for the first-line treatment of locally advanced or metastatic non-small-cell lung cancer (2010) NICE technology appraisal guidance 192

	Related NICE guidelines: Lung cancer: diagnosis and management (2019; updated 2023) NICE guideline 122 **Related diagnostics guidance:** EGFR-TK mutation testing in adults with locally advanced or metastatic non-small-cell lung cancer (2013) NICE diagnostics guidance 9. **Related interventional procedures:** Microwave ablation for primary or metastatic cancer in the lung (2022) Interventional procedures guidance 716. Irreversible electroporation for treating primary lung cancer and metastases in the lung (2013) Interventional procedures guidance 441. Percutaneous radiofrequency ablation for primary or secondary lung cancers (2010) NICE interventional procedures guidance 372. **Related quality standards:** Lung cancer in adults (2012; updated 2019) NICE quality standard 17
Related National Policy	Department of Health and Social Care (2016) NHS Outcomes Framework 2016-2017 The NHS Long Term Plan (2019) NHS Long Term Plan The NHS Long Term Plan, 2019. NHS Long Term Plan NHS England (2023) Manual for prescribed specialist services (2023/2024) Chapter 105: Specialist cancer services (adults).

Questions for consultation

Where do you consider amivantamab with lazertinib will fit into the existing care pathway for EGFR mutation positive NSCLC?

Would amivantamab with lazertinib be a candidate for managed access?

Are the suggested comparators appropriate?

Are the suggested subgroups appropriate?

Would the effectiveness of amivantamab with lazertinib be expected to vary depending on whether or not CNS metastases are present?

Would the effectiveness of amivantamab with lazertinib be expected to vary depending on whether or not the patient had newly diagnosed advanced or metastatic disease or disease recurrent after surgery or radiotherapy?

Do you consider that the use of amivantamab with lazertinib 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 amivantamab with lazertinib 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 is considering evaluating this technology through its cost comparison evaluation process.
Please provide 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).

Technologies can be evaluated through the cost-comparison process if they are expected to provide similar or greater health benefits, at a similar or lower cost, compared with technologies that have been previously recommended (as an option) in published NICE guidance for the same indication. Companies can propose cost-comparison topics to NICE at any stage during topic selection and scoping. NICE will route technologies for evaluation through the cost-comparison process if it is agreed during scoping that the process is an appropriate route to establish the clinical and cost effectiveness of the technology.

NICE's health technology evaluations: the manual states the methods to be used where a cost comparison case is made.

- Is the technology likely to be similar in its clinical effectiveness and resource use to any of the comparators? Or in what way is it different to the comparators?
- Will the intervention be used in the same place in the treatment pathway as the comparator(s)? Have there been any major changes to the treatment pathway recently? If so, please describe.

- Will the intervention be used to treat the same population as the comparator(s)?
- Overall is the technology likely to offer similar or improved health benefits compared with the comparators?
- Would it be appropriate to use the cost-comparison methodology for this topic?

References

1. NHS England. Cancer Registration Statistics, England 2020. Accessed March 2024
2. Royal College of Surgeons of England (2023). National Lung Cancer Audit: State of the Nation Report 2023. Accessed March 2024
3. Van Sanden, S., Murton, M., Bobrowska, A et al (2022) Prevalence of Epidermal Growth Factor Receptor Exon 20 Insertion Mutations in Non-small-Cell Lung Cancer in Europe: A Pragmatic Literature Review and Meta-analysis.
4. Zhang, YL., Yuan, JQ., Wang, KF. et al. (2016). The prevalence of EGFR mutation in patients with non-small cell lung cancer: a systematic review and meta-analysis. *Oncotarget, 7*(48), 78985. Accessed April 2023