NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Amivantamab with carboplatin and pemetrexed for untreated EGFR exon 20 insertion mutation-positive advanced non-small-cell lung cancer ID5110

Draft scope

Draft remit/evaluation objective

To appraise the clinical and cost effectiveness of amivantamab in combination with carboplatin and pemetrexed within its marketing authorisation for untreated EGFR exon 20 insertion mutation-positive advanced non-small-cell lung cancer.

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).[4,5] Exon 20 is part of the EGFR gene that can be mutated by an addition to the DNA sequence (an insertion mutation). Mutations in exon 20 occur in 0.7% (around 170) of people diagnosed with NSCLC.[4] However, they are associated with poorer outcomes than other EGFR mutations.[6]

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.

There is no standard treatment pathway for treating exon 20 insertion mutation-positive NSCLC. For people with EGFR-positive NSCLC who have not previously had treatment, NICE guidance recommends the TKIs osimertinib, dacomitinib, afatinib, erlotinib, and gefitinib as treatment options (NICE technology appraisal guidance 654, 595, 310, 258, and 192 respectively). However, they are reported as having limited efficacy when EGFR exon 20 insertions are present.[7] Amivantamab is recommended for EGFR exon 20 positive NSCLC that has been previously treated with platinum-based chemotherapy (TA850). Following disease progression with a TKI, osimertinib is recommended for EGFR T790M mutation-positive disease (NICE technology appraisal 653). Platinum doublet chemotherapy and atezolizumab in combination are also treatment options (NICE guideline 122 and NICE technology appraisal 584).

Other treatment options for untreated NSCLC include immunotherapies such as atezolizumab (NICE technology appraisal guidance 584 and 705) or pembrolizumab (NICE technology appraisal guidance 531, 683 and 770).

The technology

Amivantamab (Rybrevant, Janssen-Cilag) does not currently have a marketing authorisation in the UK for the treatment EGFR exon 20 insertion mutation-positive untreated NSCLC. It has been studied in a phase 3 clinical trial in combination with carboplatin and pemetrexed compared with chemotherapy alone. The trial included people with previously untreated EGFR exon 20 insertion mutation-positive locally advanced or metastatic NSCLC.

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

Intervention	Amivantamab with carboplatin and pemetrexed
Population	Adults with untreated, locally advanced or metastatic NSCLC with an EGFR exon 20 insertion mutation
Subgroups	If the evidence allows, the following subgroups will be considered: • PD-L1 status • Disease stage • Histology
Comparators	• Chemotherapy such as docetaxel, gemcitabine, paclitaxel or vinorelbine in combination with a platinum drug (carboplatin or cisplatin), with or without pemetrexed maintenance treatment. • Pembrolizumab (monotherapy or in combination with chemotherapy) • Atezolizumab • Tyrosine kinase inhibitors (gefitinib, erlotinib, afatinib, dacomitinib and osimertinib) • 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. 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. The availability and cost of biosimilar and generic products should be taken into account. The use of amivantamab is conditional on the presence of an EGFR exon 20 insertion mutation. The economic modelling should include the costs associated with diagnostic testing for EGFR exon 20 insertions in people with locally-advanced or metastatic NSCLC who would not otherwise have been tested. A sensitivity analysis should be provided without the cost of the diagnostic test. See section 4.8 of the guidance development manual (available here: https://www.nice.org.uk/process/pmg36/chapter/introduction-to-health-technology-evaluation).
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:**

	Pembrolizumab with carboplatin and paclitaxel for untreated metastatic squamous non-small-cell lung cancer (2022) NICE technology appraisal guidance 770. Atezolizumab monotherapy for untreated advanced non-small-cell lung cancer (2021) NICE technology guidance 705. Pembrolizumab with pemetrexed and platinum chemotherapy for untreated, metastatic, non-squamous non-small-cell lung cancer (2021) NICE technology guidance 683. Atezolizumab in combination for treating metastatic non-squamous non-small-cell lung cancer (2019) NICE technology guidance 584. Pembrolizumab for untreated PD-L1-positive metastatic non-small-cell lung cancer (2018) NICE technology guidance 531. 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 Amivantamab for treating EGFR exon 20 insertion mutation-positive advanced non-small-cell lung cancer after platinum-based chemotherapy (2022) NICE technology appraisal guidance 850 **Related technology appraisals in development:** Amivantamab with lazertinib for previously untreated locally advanced or metastatic non-small-cell lung cancer TS ID 11842. Publication date to be confirmed. **Related NICE guidelines:** Lung cancer: diagnosis and management (2019; updated March 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 (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 will fit into the existing care pathway for locally advanced or metastatic NSCLC?

Are immunotherapy containing regimens offered to people with untreated EGFR exon 20 insertion mutation-positive locally advanced or metastatic non-small-cell lung cancer in NHS clinical practice? If so, which regimens and what is considered the standard of care?

Would EGFR inhibitors such as gefitinib, erlotinib, afatinib dacomitinib and osimertinib be used in untreated EGFR exon 20 mutation positive disease in NHS clinical practice?

Are there any comparator treatments that are not listed that would be used for untreated EGFR exon 20 mutation positive disease in NHS clinical practice?

Are the suggested subgroups appropriate?

Is testing for EGFR exon 20 insertions done routinely at this point in the treatment pathway (untreated advanced or metastatic disease)?

Would amivantamab be a candidate for managed access?

Do you consider that the use of amivantamab 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 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. (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

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4. 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.
5. 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
6. Oxnard, GR., Lo, PC., Nishino, M. et al. (2013). Natural history and molecular characteristics of lung cancers harboring EGFR exon 20 insertions. *Journal of thoracic oncology, 8*(2), 179–184. Accessed April 2023

7. Hou, J., Li, H., Ma, S. et al. (2022). EGFR exon 20 insertion mutations in advanced non-small-cell lung cancer: current status and perspectives. *Biomarker Research, 10*, 21. Accessed April 2023