NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Alectinib for adjuvant treatment of ALK-positive non-small-cell lung cancer ID6368

Draft scope

Draft remit/evaluation objective

To appraise the clinical and cost effectiveness of alectinib within its marketing authorisation as adjuvant treatment of ALK-positive 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 13% of all new cancer cases and 21% of all cancer deaths between 2017 and 2019.[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). Around 30% of lung cancers are diagnosed at an early stage (stage 1 or 2).[2]

In 2021, 91% (around 31,000) of people diagnosed with lung cancer in England had NSCLC.[2] Of these people, 17% (5,333) had surgical treatment for their cancer.[2] Despite the curative intent of treatment for early-stage lung cancer, survival is poor, with only about 57% people with stage 1, 34% with stage 2 and 13% with stage 3 surviving for 5 years after diagnosis.[3] It is estimated that around 5% of NSCLCs have an ALK fusion genetic alteration, this alteration inhibits processes which stop lung cells dividing and can lead to cancer.[4,5] ALK fusions can occur in type of NSCLC, but are most likely to occur in adenocarcinoma histology. [5]

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. NICE's Technology Appraisal Pathway Pilot scope for treatments for non-small-cell lung cancer outlines in more detail the NSCLC treatment pathway.

NICE guideline 122 (NG122) 'Lung cancer: diagnosis and management' recommends surgery, radiotherapy, chemoradiotherapy or a combination of these for stage 1 to 2 NSCLC. People may be offered a neo-adjuvant (before surgical removal of cancerous tumour) treatment which could be platinum based chemotherapy, or nivolumab with chemotherapy as recommended by NICE TA876. Neoadjuvant chemotherapy has shown equivalent outcomes in terms of survival to adjuvant chemotherapy.[6]

For stage 3 NSCLC, surgery is carried out if the surgeon deems the tumour to be resectable. Before surgery, chemoradiotherapy (chemotherapy with radiotherapy) may be used or surgery may potentially be followed by chemotherapy. If well enough,

people may be offered a cisplatin-based chemotherapy (adjuvant treatment) after surgery.

People who have had surgery may have an adjuvant treatment. NICE TA761 recommends osimertinib in the Cancer Drugs Fund as adjuvant treatment for people whose cancer has an EGFR exon 19 deletion or an exon 21 (L858R) substitution mutation. For people whose cancer does not have an EGFR mutation, platinum chemotherapy may be offered as adjuvant treatment. NICE TA823 recommends atezolizumab in the Cancer Drugs Fund as an option for maintenance treatment after complete tumour resection in adults with stage 2 to 3a NSCLC and adjuvant chemotherapy.

People with confirmed ALK-fusion positive NSCLC also have several treatment options available for untreated advanced and metastatic disease. These include crizotinib (TA406), ceritinib (TA500), alectinib (TA536) and brigatinib (TA670).

The technology

Alectinib (Alecensa, Roche) does not currently have a marketing authorisation in the UK for adjuvant treatment of ALK-fusion positive NSCLC. It is being studied in comparison with platinum based chemotherapy in adults with resected ALK-positive NSCLC.

Alectinib monotherapy is currently licenced for other indications including as first-line treatment of ALK positive advanced NSCLC

Intervention(s)	Alectinib
Population(s)	Adults with ALK-positive NSCLC who have undergone complete surgical resection
Subgroups	If the evidence allows it, the following subgroups will be considered: • Disease stage
Comparators	Established adjuvant clinical management without alectinib, which may include: • Platinum-based chemotherapy • Active monitoring • Pembrolizumab (subject to NICE appraisal) For people whose tumours express PD-L1 with at least a 50% tumour proportion score • **Atezolizumab** after adjuvant cisplatin-based chemotherapy (subject to NICE appraisal)

Outcomes	The outcome measures to be considered include: • event-free survival • disease-free survival • pathological complete response • response rates • overall survival • 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. The use of alectinib is conditional on the presence of an ALK gene fusion. The economic modelling should include the costs associated with the diagnostic testing for ALK gene fusions in people with resected 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:** Nivolumab with chemotherapy for neoadjuvant treatment of resectable non-small-cell lung cancer (2023) NICE technology appraisal guidance 876

	Atezolizumab for adjuvant treatment of resected non-small-cell lung cancer (2022) NICE technology appraisal guidance 823 [In CDF] Osimertinib for adjuvant treatment of EGFR mutation-positive non-small-cell lung cancer after complete tumour resection (2022) TA761 **Related technology appraisals in development:** Pembrolizumab for adjuvant treatment of resected non-small-cell lung cancer [ID3907] Publication date to be confirmed Pembrolizumab for neoadjuvant and adjuvant treatment of resectable stage 2 to 3B non-small-cell lung cancer [ID5094] Publication date to be confirmed Atezolizumab with chemotherapy for neoadjuvant and adjuvant treatment of resectable non-small-cell lung cancer [ID3894] Publication date to be confirmed Nivolumab for adjuvant treatment of resected non-small-cell lung cancer [ID4053] Publication date to be confirmed **Related NICE guidelines:** Lung cancer: diagnosis and management (NG122) **Related quality standards:** Lung cancer in adults (2019) NICE quality standard 17
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: Specialist cancer services (adults).

Questions for consultation

Is the population defined appropriately in the scope?

Is testing for ALK gene fusions considered to be standard practice in the adjuvant setting for NSCLC in the NHS?

Where do you consider alectinib will fit into the existing care pathway for NSCLC?

Have all relevant comparators been included?

For someone with ALK-positive NSCLC, would a clinician generally offer adjuvant alectinib over an adjuvant immunotherapy?

If someone with ALK-positive NSCLC had ***neo-adjuvant*** treatment with an immunotherapy and then surgery would clinicians offer alectinib as ***adjuvant*** treatment? Or would an adjuvant immunotherapy be preferred?

If recommended, would alectinib use depend on whether there was complete or incomplete resection of the locally advanced NSCLC?

Have all relevant subgroups been included in the scope?

If someone had alectinib as an adjuvant treatment, would clinicians offer ALK inhibitors later for advanced or metastatic disease?

Would alectinib be a candidate for managed access?

Do you consider that the use of alectinib 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 alectinib 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

1. Cancer Research UK (2023). Lung cancer statistics. Accessed November 2023
2. Royal College of Surgeons of England (2023). National Lung Cancer Audit: State of the Nation Report 2023 (data tables). Accessed November 2023
3. Office for National Statistics. Cancer Survival in England: adults diagnosed between 2013 and 2017 and followed up to 2018. 2019. Available from: https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/conditionsanddiseases/datasets/cancersurvivalratescancersurvivalinenglandadultsdiagnosed. Accessed October 2023

4. Cancer Research UK (2023) Targeted and immunotherapy treatment for lung cancer. Accessed November 2023
5. Le T, Gerber DE. (2017) ALK alterations and inhibition in lung cancer. Semin Cancer Biol. Accessed November 2023