

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Evaluation

Lorlatinib for untreated ALK-positive advanced non-small-cell lung cancer (Review of TA909) [ID6434]

Final scope

Remit/evaluation objective

To appraise the clinical and cost effectiveness of lorlatinib within its marketing authorisation for ALK-positive advanced non-small cell lung cancer previously not treated with an ALK inhibitor

Background

Lung cancer falls into two main histological categories: around 80 to 85% are non-small-cell lung cancers (NSCLC) and the remainder are small cell lung cancers¹. NSCLC can be further classified into squamous cell carcinoma and non-squamous cell carcinoma. Approximately 70% of NSCLC are of non-squamous histology and can be either large-cell undifferentiated carcinoma or adenocarcinoma². 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).

In 2022, 90% (around 33,200) of people diagnosed with lung cancer in England and Wales had NSCLC³. Of these people, 50% had stage 4 disease³. Lung cancer caused approximately 35,000 deaths in the UK between 2017-2019⁴. 48% of people with lung cancer survive for more than 1 year after diagnosis³. It is estimated that around 2 to 6% of NSCLCs have an ALK fusion genetic alteration. This alteration inhibits processes which stop lung cells dividing and can lead to cancer.^{5,6,7} ALK fusions can occur in any type of NSCLC, but are most likely to occur in adenocarcinoma histology.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. [NICE's Technology Appraisal Pathway Pilot scope for treatments for non-small-cell lung cancer](#) outlines in more detail the NSCLC treatment pathway.

For the majority of people with NSCLC, the aims of treatment are to prolong survival and improve quality of life. For people with ALK-positive advanced NSCLC first line treatment options include crizotinib ([TA406](#)), ceritinib ([TA500](#)), alectinib ([TA536](#)) and brigatinib ([TA670](#)). People with NSCLC of an unknown ALK status may be offered initial treatment with platinum-doublet chemotherapy.

Lorlatinib received a negative recommendation in [TA909](#) evaluating lorlatinib for untreated ALK-positive advanced NSCLC. Based on the [review of TA909](#), this scope is a review of TA909 and focuses on the additional evidence collected from the CROWN trial. It is expected that the additional evidence will address the

uncertainties in TA909, after which NICE will decide whether or not to recommend lorlatinib for routine use in the NHS.

The technology

Lorlatinib (Lorviqua, Pfizer) has a marketing authorisation in the UK for the treatment of ALK-positive advanced NSCLC previously not treated with an ALK inhibitor or whose disease has progressed after prior treatment with an ALK inhibitor in adults. [TA628](#) recommends lorlatinib for previously treated ALK-positive advanced NSCLC which has progressed after alectinib or ceritinib, or after crizotinib and at least 1 other ALK tyrosine kinase inhibitor. Therefore, this evaluation is limited to ALK-positive advanced NSCLC previously untreated with an ALK inhibitor.

Intervention(s)	Lorlatinib
Population(s)	Adults with ALK-positive advanced NSCLC previously not treated with an ALK inhibitor
Comparators	<ul style="list-style-type: none"> • Alectinib • Brigatinib
Outcomes	<p>The outcome measures to be considered include:</p> <ul style="list-style-type: none"> • overall survival • progression free survival • response rates • adverse effects of treatment • health-related quality of life.
Economic analysis	<p>The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year.</p> <p>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.</p> <p>Costs will be considered from an NHS and Personal Social Services perspective.</p> <p>The availability of any commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account.</p>
Other considerations	<p>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.</p>

<p>Related NICE recommendations</p>	<p>Related technology appraisals:</p> <p>Brigatinib for ALK-positive advanced non-small-cell lung cancer that has not been previously treated with an ALK inhibitor (2021). NICE Technology Appraisal 670.</p> <p>Lorlatinib for previously treated ALK-positive advanced non-small-cell lung cancer (2020). NICE Technology Appraisal 628.</p> <p>Alectinib for untreated ALK-positive advanced non-small-cell lung cancer (2018). NICE Technology Appraisal 536.</p> <p>Ceritinib for untreated ALK-positive non-small-cell-lung cancer (2018). NICE Technology Appraisal 500.</p> <p>Crizotinib for untreated anaplastic lymphoma kinase- positive advanced non-small-cell lung cancer (2016). NICE Technology Appraisal 406.</p> <p>Related NICE guidelines:</p> <p>Lung cancer: diagnosis and management (2019). NICE guideline 122. Updated March 2024</p> <p>Related quality standards:</p> <p>Lung cancer in adults (2019). NICE Quality Standard 17.</p>
<p>Related National Policy</p>	<p>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).</p>

References

1. [Types of lung cancer](#). Cancer Research UK. Accessed July 2024.
2. Howlader N, Noone AM, Krapcho M, Miller D, Brest A, Yu M, Ruhl J, Tatalovich Z, Mariotto A, Lewis DR, Chen HS, Feuer EJ, Cronin KA (eds). SEER Cancer Statistics Review, 1975-2016, National Cancer Institute. [Available from: https://seer.cancer.gov/csr/1975_2016/]. Accessed July 2024.
3. [NLCA annual report 2024 \(2022 data\)](#) National Lung Cancer Audit. Accessed July 2024.
4. [Lung cancer mortality statistics \(2022\)](#). Cancer Research UK. Accessed July 2024.
5. Cancer Research UK (2023) [Targeted and immunotherapy treatment for lung cancer](#). Accessed July 2024.

6. Le T, Gerber DE. (2017) [ALK alterations and inhibition in lung cancer](#). Semin Cancer Biol. Accessed July 2024.
7. Schneider JL, Lin JJ, Shaw AT. [ALK-positive lung cancer: a moving target](#). Nat Cancer. Accessed July 2024.