

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal

Ceritinib for untreated anaplastic lymphoma kinase-positive advanced non-small-cell lung cancer

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of ceritinib within its marketing authorisation for untreated, anaplastic lymphoma kinase-positive (ALK-positive) advanced non-small-cell lung cancer.

Background

Lung cancer falls into two main histological categories: non-small-cell lung cancers, which account for 85–90% of all lung cancers¹, and small-cell lung cancers. Non-small-cell lung cancer may be grouped by tumour histology into squamous cell carcinoma, adenocarcinoma and large-cell carcinoma, with the latter 2 being collectively referred to as 'non-squamous' lung cancer.

Anaplastic lymphoma kinase (ALK) fusion genes are chromosomal alterations that occur between the tyrosine kinase portion of the ALK gene and other genes. They are believed to be involved in the growth of tumours. ALK translocation can occur in non-small cell lung cancer of any histology, although it is thought to be most common in tumours with adenocarcinoma histology and is uncommon in tumours with squamous cell carcinoma histology.² People with non-small-cell lung cancer who have an ALK fusion gene are unlikely to have epidermal growth factor receptor (EGFR) mutations. Accordingly, people with the ALK fusion gene are not usually treated with drugs that inhibit EGFR tyrosine kinase such as erlotinib and gefitinib.

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 III) or to other parts of the body (metastatic disease; stage IV). In 2015, approximately 31,700 people were diagnosed with NSCLC in England, of whom 74% had stage III or stage IV disease³. Approximately 5% of people with stage III or IV non-small-cell lung cancer have ALK fusion genes, equating to around 1170 people in England.⁴

NICE technology appraisal guidance 406 recommends crizotinib as an option for untreated ALK-positive non-small-cell lung cancer. NICE clinical guideline 121 recommends platinum-based chemotherapy as a first-line treatment for people with stage III or IV non-small-cell lung cancer and good performance status. Alternatively, people may receive pemetrexed in combination with cisplatin if the histology of the tumour has been confirmed as adenocarcinoma or large-cell carcinoma (NICE technology appraisal guidance 181). For non-

squamous NSCLC that has not progressed immediately following initial therapy with a NICE-recommended platinum-based chemotherapy regimen, maintenance treatment with pemetrexed is recommended as an option (NICE technology appraisal guidance 190 and 402).

The technology

Ceritinib (Zykadia, Novartis) selectively inhibits the ALK receptor tyrosine kinase. This has been found to induce the death of cancer cells harbouring ALK fusion genes. Ceritinib is administered orally.

Ceritinib does not currently have a marketing authorisation in the UK for untreated ALK-positive advanced non-small cell lung cancer. It is being studied in clinical trials in adults with untreated, anaplastic ALK-positive advanced non-squamous non-small cell lung cancer, compared with pemetrexed in combination with either cisplatin or carboplatin followed by pemetrexed monotherapy.

Ceritinib has a marketing authorisation in the UK for ALK-positive advanced non-small cell lung cancer previously treated with crizotinib. This indication is covered by NICE Technology Appraisal 395.

Intervention(s)	Ceritinib
Population(s)	People with untreated, anaplastic lymphoma kinase-positive (ALK-positive) advanced non-small cell lung cancer
Comparators	<ul style="list-style-type: none"> • Crizotinib • Pemetrexed in combination with a platinum drug (carboplatin or cisplatin) (for people with adenocarcinoma or large cell carcinoma only) <ul style="list-style-type: none"> ○ with or without pemetrexed maintenance treatment (following cisplatin-containing regimens only)
Outcomes	<p>The outcome measures to be considered include:</p> <ul style="list-style-type: none"> • overall survival • progression-free survival • response rate • adverse effects of treatment • health-related quality of life.

<p>Economic analysis</p>	<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 patient access schemes for the intervention or comparator technologies will be taken into account.</p>
<p>Other considerations</p>	<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 and NICE Pathways</p>	<p>Related Technology Appraisals:</p> <p>Ceritinib for previously treated anaplastic-lymphoma-kinase-positive non-small-cell lung cancer (2016) NICE Technology Appraisal 395. Review date: June 2019</p> <p>Crizotinib for untreated anaplastic lymphoma kinase-positive advanced non-small-cell lung cancer (2016) NICE Technology Appraisal 406. Review date: September 2019</p> <p>Pemetrexed for the first-line treatment of non-small-cell lung cancer (2009) NICE Technology Appraisal 181 Guidance on static list</p> <p>Pemetrexed maintenance treatment for non-squamous non-small-cell lung cancer after pemetrexed and cisplatin (2016) NICE Technology Appraisal 402. Review proposal date August 2019</p> <p>Pemetrexed for the maintenance treatment of non-small-cell lung cancer (2010) NICE Technology Appraisal 190. On static list</p> <p>Related Guidelines:</p> <p>Lung cancer: diagnosis and management. (2011) NICE guideline 121. Review date TBC.</p> <p>Related Quality Standards:</p> <p>Lung cancer in adults (2012) NICE quality standard 17</p>

	<p>Related NICE Pathways:</p> <p>Lung Cancer (2012) NICE pathway</p>
Related National Policy	<p>National Service Frameworks</p> <p>Cancer</p> <p>Department of Health</p> <p>Department of Health (2013) NHS Outcomes Framework 2014–2015</p> <p>Department of Health (2011) Improving outcomes: a strategy for cancer</p> <p>Department of Health (2009) Cancer commissioning guidance</p> <p>Department of Health (2007) Cancer reform strategy</p> <p>Department of Health, NHS Outcomes Framework 2014-2015, Nov 2013. Domains 1, 2, 4 and 5. https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/256456/NHS_outcomes.pdf</p> <p>NHS England</p> <p>NHS England (2014) Manual for Prescribed Specialised Services 2013/14. Chapter 105: Specialist cancer services (adults) http://www.england.nhs.uk/wp-content/uploads/2014/01/pss-manual.pdf</p>

References

- 1 Royal College of Physicians (2015) National Lung Cancer Audit annual report 2015 London. Healthcare Quality Improvement Partnership.
- 2 Scagliotti G, Stahel RA, Rosell R et al. (2012) ALK translocation and crizotinib in non-small cell lung cancer: An evolving paradigm in oncology drug development. European Journal of Cancer 48: 961-973
- 3 Health and Social Care Information Centre (2017) [National Lung Cancer Audit annual report 2016 \(for the audit period 2015\)](#)
- 4 Cancer Research UK (2014) [Biological therapy for lung cancer](#). Accessed May 2017