NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal

Alectinib for previously treated anaplastic lymphoma kinase-positive non-small-cell lung cancer

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of alectinib within its marketing authorisation for previously treated anaplastic lymphoma kinase-positive (ALK-positive) non-small-cell lung cancer.

Background

Lung cancer falls into two main histological categories: around 85–90% are non-small-cell lung cancers and the remainder are 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. Some non-small-cell lung cancers are associated with chromosomal alterations described as anaplastic lymphoma kinase (ALK) fusion genes. ALK fusion genes 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.[1]

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.

In England, 36,828 people were diagnosed with lung cancer in 2013.[2] At the time of diagnosis, about 20% of people have locally advanced disease (stage III; the cancer may have grown into the surrounding tissues and there may be cancer cells in the lymph nodes) and 50% have metastatic disease (stage IV; the cancer has spread to another part of the body).[3] It is estimated that approximately 5% of people with stage III or IV non-small-cell lung cancer have ALK fusion genes, equating to around 925 patients in England.[4,5]

For most people with non-small-cell lung cancer, the aim of treatment is to improve survival, control the disease and improve quality of life. 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. In addition, NICE technology appraisal guidance 181 and 190 recommend pemetrexed as an option for the first-line treatment and

maintenance treatment of locally advanced or metastatic non-squamous non-small-cell lung cancer. If second-line treatment is appropriate for people in whom relapse has occurred after previous chemotherapy, docetaxel monotherapy should be considered (NICE clinical guideline 121). Crizotinib is not recommended in NICE technology appraisal guidance 296 for adults with previously treated ALK-positive advanced non-small-cell lung cancer, but crizotinib is available through the Cancer Drugs Fund for the second- or subsequent-line treatment of ALK-positive advanced or metastatic non-small-cell lung cancer after first-line treatment with combination chemotherapy. Ceritinib (NICE technology appraisal guidance 395) is recommended as an option for ALK-positive NSCLC previously treated with crizotinib.

The technology

Alectinib (brand name unknown, Roche Products) selectively inhibits the ALK receptor tyrosine kinase. This has been found to induce the death of cancer cells harbouring ALK fusion genes. It is administered orally.

Alectinib does not currently have a marketing authorisation in the UK for ALK-positive advanced non-small-cell lung cancer. It has been studied in single-arm clinical trials as monotherapy in people with ALK-positive metastatic or locally advanced non-small-cell lung cancer which has progressed after treatment with crizotinib. It is also being studied as monotherapy in people with ALK-positive advanced non-small-cell lung cancer which has progressed after treatment with platinum-based chemotherapy and crizotinib; the comparator in this trial is docetaxel or pemetrexed.

Intervention	Alectinib
Population	People with anaplastic lymphoma kinase-positive (ALK-positive) advanced non-small-cell lung cancer previously treated with crizotinib
Comparators	After prior crizotinib only (subject to ongoing NICE appraisal) • Platinum doublet chemotherapy (including cisplatin plus pemetrexed) • Ceritinib After prior platinum-based chemotherapy and crizotinib • Best supportive care • Docetaxel • Ceritinib

Outcomes	The outcome measures to be considered include: • overall survival • progression-free survival • response rate • 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.
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 and NICE Pathways	Related Technology Appraisals: 'Ceritinib for previously treated anaplastic-lymphoma-kinase-positive non-small-cell lung cancer' (2016) NICE Technology Appraisal 395. Review date: June 2019 'Crizotinib for previously treated non-small-cell lung cancer associated with an anaplastic lymphoma kinase fusion gene' (2013) NICE Technology Appraisal 296 Subject to ongoing NICE CDF transition review, expected date of publication February 2017 Technology Appraisal in preparation: 'Crizotinib for untreated anaplastic lymphoma kinase-positive advanced non-small-cell lung cancer' ID865. Anticipated date of publication September 2016 Related Guidelines: Lung cancer: diagnosis and management. (2011) NICE guideline 121 Review date TBC. Related Quality Standards:

	'Lung cancer for adults' (2012) NICE quality standard 17 Related NICE Pathways: Lung Cancer (2012) NICE pathway
Related National Policy	**National Service Frameworks** Cancer **Department of Health** Department of Health (2013) NHS Outcomes Framework 2014–2015 Department of Health (2011) Improving outcomes: a strategy for cancer Department of Health (2009) Cancer commissioning guidance Department of Health (2007) Cancer reform strategy 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 **NHS England** 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

References

1 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

2 National Cancer Intelligence Network (2015) Cancer breakdown by stage 2013. Accessed November 2015

3 Cancer Research UK (2015) Lung cancer statistics. Accessed October 2015

4 National Institute for Health and Clinical Excellence (2015) Ceritinib for previously treated anaplastic lymphoma kinase-positive non-small-cell lung cancer. Final scope. Accessed March 2015

5 Cancer Research UK (2014) Biological therapy for lung cancer. Accessed October 2015