

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal

Brigatinib for treating ALK-positive non-small-cell lung cancer after crizotinib

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of brigatinib within its marketing authorisation for treating advanced ALK-positive non-small-cell lung cancer after treatment with crizotinib.

Background

Lung cancer falls into two main histological categories: non-small-cell lung cancers (NSCLC), which account for 88% of all lung cancers¹, and small-cell lung cancers. NSCLC 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 NSCLC of any histology, although it is thought to be most common in tumours (almost exclusively) with adenocarcinoma histology (that is, non-squamous histology) which represent 36% of NSCLC patients and is uncommon in tumours with squamous cell carcinoma histology.^{1,2} People with NSCLC who have an ALK fusion gene are unlikely to have epidermal growth factor receptor (EGFR) mutations. Accordingly, people with the ALK fusion gene do not usually receive drugs that inhibit EGFR tyrosine kinase, such as erlotinib, gefitinib and afatinib.

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 disease.³ Approximately 5% of people with stage III or IV non-squamous (adenocarcinoma) NSCLC have ALK fusion genes, equating to around 1170 people in England & Wales.⁴

For the majority of people with NSCLC, the aims of treatment are to prolong survival and improve quality of life. Treatment choices are influenced by the presence of biological markers (such as mutations in EGFR-TK, ALK or PD-L1 status, histology (squamous or non-squamous) and previous treatment experience. NICE technology appraisal guidance 395 recommends ceritinib

as a treatment option for treating advanced anaplastic lymphoma kinase positive non-small-cell lung cancer in adults who have previously had crizotinib.

The technology

Brigatinib (Alunbrig, Takeda UK) is an anti-neoplastic agent. Brigatinib acts as an ALK antagonist, EGFR antagonist and ROS1 inhibitor. It is administered orally.

Brigatinib does not currently have a marketing authorisation in the UK for treating ALK-positive advanced non-small-cell lung cancer. A randomised phase II study is currently evaluating the efficacy and safety of two different dosing regimens of brigatinib in adults with advanced ALK+ NSCLC whose disease has progressed after treatment with crizotinib. Brigatinib has also been studied in a phase 1/2 safety study in adults with ALK-rearranged non-small-cell lung cancer.

Intervention(s)	Brigatinib
Population(s)	People with anaplastic lymphoma kinase (ALK)-positive advanced non-small cell lung cancer (NSCLC) previously treated with crizotinib
Comparators	<ul style="list-style-type: none"> • ceritinib
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.

<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 guidance 395. Review date: TBC.</p> <p>Related Guidelines:</p> <p>Lung cancer: diagnosis and management (2011) NICE guidelines CG121. Reviewed 2016, next review January 2019.</p> <p>Related Quality Standards:</p> <p>Quality standard for lung cancer. (2012) NICE Quality Standard 17. Reviewed 2016, next review August 2017.</p> <p>Related NICE Pathways:</p> <p>Lung cancer (2017) NICE</p>

Related National Policy	<p>National Service Frameworks 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 (2017) [National Lung Cancer Audit Report 2016 \(for the audit period 2015\)](#). Accessed October 2017
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. Office for National Statistics (May 2017) [Cancer Statistics Registrations, England: 2015](#). Accessed October 2017
4. Cancer Research UK (2014) [Biological therapy for lung cancer](#). Accessed October 2017