

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal

Brigatinib for ALK-positive advanced non-small-cell lung cancer that has not been previously treated with an ALK inhibitor

Final scope

Remit/appraisal objective

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

Background

Lung cancer falls into two main groups: around 87% 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 III) or to other parts of the body (metastatic disease; stage IV). In 2017, 39,205 people were diagnosed with NSCLC in England & Wales, and around 65% had stage IIIB or stage IV disease³.

Lung cancer caused over 28,000 deaths in England in 2017⁴. Thirty two percent of people with lung cancer survive for more than 1 year after diagnosis⁵.

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 (almost exclusively) in tumours with adenocarcinoma histology. Approximately 3–7% of all lung tumours contain ALK mutations⁶.

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. People with confirmed ALK-positive NSCLC are likely to be offered initial treatment with ALK-targeted treatment. NICE recommends crizotinib (TA406), ceritinib (TA500) and alectinib (TA536) as treatment options for adults with untreated ALK-positive advanced NSCLC. People with

NSCLC of an unknown ALK status may be offered initial treatment with platinum-doublet chemotherapy.

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 has been granted positive opinion by the Committee for Medicinal Products for Human Use, as “monotherapy for the treatment of adult patients with anaplastic lymphoma kinase (ALK) positive advanced non-small cell lung cancer (NSCLC) previously not treated with an ALK inhibitor”.

Intervention(s)	Brigatinib
Population(s)	Adults with ALK-positive advanced NSCLC that has not been previously treated with an ALK inhibitor
Comparators	<ul style="list-style-type: none">• Alectinib• Ceritinib• Crizotinib
Outcomes	The outcome measures to be considered include: <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>If the technology is likely to provide similar or greater health benefits at similar or lower cost than technologies recommended in published NICE technology appraisal guidance for the same indication, a cost-comparison may be carried out.</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>
<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>Alectinib for untreated ALK-positive advanced non-small-cell lung cancer (2018). NICE Technology Appraisal 536. Review date: August 2021.</p> <p>Ceritinib for untreated ALK-positive non-small-cell lung cancer (2018). NICE Technology Appraisal 500. Review date: January 2021.</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>Brigatinib for treating ALK-positive advanced non-small-cell lung cancer after crizotinib (2019). NICE Technology Appraisal 571. Review date: 2022.</p> <p>Appraisals in development:</p> <p>Lorlatinib for treating ALK-positive advanced non-small-cell lung cancer [ID1338]. Publication expected March 2020.</p>

	<p>Related Guidelines:</p> <p>Lung cancer: diagnosis and management (2019) NICE Guideline NG122. Reviewed June 2019.</p> <p>Related Quality Standards:</p> <p>Quality standard for lung cancer. (2012) NICE Quality Standard 17. Reviewed December 2019.</p> <p>Related NICE Pathways:</p> <p>Lung cancer (2020) NICE pathway http://pathways.nice.org.uk/</p>
<p>Related National Policy</p>	<p>The NHS Long Term Plan, 2019. NHS Long Term Plan</p> <p>NHS England (2018/2019) NHS manual for prescribed specialist services (2018/2019)</p> <p>Department of Health and Social Care, NHS Outcomes Framework 2016-2017 https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017</p>

References

- 1 [Lung cancer stages, types and grades](#). Cancer Research UK. Accessed January 2020.
- 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 January 2020.
- 3 [National Lung Cancer Audit: Annual report 2018 \(for the audit period 2017\)](#) (2019). Royal College of Physicians. Accessed January 2020.
- 4 [Lung cancer mortality statistics \(2016\)](#). Cancer Research UK. Accessed January 2020.
- 5 [Lung cancer survival statistics \(2010-11\)](#). Cancer Research UK. Accessed January 2020.
- 6 Zappa C, Mousa S (2016). [Non-small cell lung cancer: current treatment and future advances](#). Translational Lung Cancer Research. Accessed January 2020.