NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Brigatinib for untreated ALK-positive metastatic non-small-cell lung cancer

Draft scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of brigatinib within its marketing authorisation for untreated ALK-positive metastatic non-small-cell lung cancer.

Background

Lung cancer falls into 2 histological categories: around 88% are classified as non-small cell lung cancer (NSCLC), with the remaining patients classified as small cell lung cancer.[1] NSCLC may be further 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]

In 2016, there were 38,381 (20,560 males and 17,821 females) cases of lung cancer registered in England[3]. Approximately 3% of people with NSCLC have ALK fusion genes[4] equating to an incidence of approximately 1000 people in England per year.

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 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 does not currently have a marketing authorisation in the UK for untreated ALK-positive NSCLC. It has been studied in clinical trials, compared with crizotinib, in adults with ALK-positive NSCLC that has not been previously treated.

Intervention(s)	Brigatinib
Population(s)	Adults with untreated anaplastic lymphoma kinase (ALK)-positive non-small cell lung cancer (NSCLC)
Comparators	• Alectinib • Ceritinib • Crizotinib
Outcomes	The outcome measures to be considered include: • overall survival • progression-free survival • response rates • 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. 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. 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. The availability of any commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account.

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: Alectinib for untreated ALK-positive advanced non-small-cell lung cancer (2018). NICE Technology Appraisal 536. Review date: August 2021. Ceritinib for untreated ALK-positive non-small-cell-lung cancer (2018). NICE Technology Appraisal 500. Review date: January 2021. Crizotinib for untreated anaplastic lymphoma kinase-positive advanced non-small-cell lung cancer (2016). NICE Technology Appraisal 406. Review date: September 2019. Appraisals in development: Brigatinib for treating ALK-positive non-small-cell lung cancer after crizotinib [ID1328]. Publication expected: December 2018. Related Guidelines: Lung cancer: diagnosis and management (2011) NICE Clinical Guideline CG121. Review date: January 2019. Related Quality Standards: Quality standard for lung cancer. (2012) NICE Quality Standard 17. Reviewed 2016, next review August 2017. Related NICE Pathways: Lung cancer (2017) NICE
Related National Policy	National Service Frameworks: Cancer research and treatment 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

Questions for consultation

Have all relevant comparators for brigatinib been included in the scope?

Which treatments are considered to be established clinical practice in the NHS for untreated ALK-positive metastatic NSCLC?

Are the outcomes listed appropriate?

Are there any subgroups of people in whom brigatinib is expected to be more clinically effective and cost effective or other groups that should be examined separately?

Where do you consider brigatinib will fit into the existing NICE pathway, Lung cancer?

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope:

- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which brigatinib will be licensed;
- could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology;
- could have any adverse impact on people with a particular disability or disabilities.

Please tell us what evidence should be obtained to enable the Committee to identify and consider such impacts.

Do you consider brigatinib to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a 'step-change' in the management of the condition)?

Do you consider that the use of brigatinib can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation?

Please identify the nature of the data which you understand to be available to enable the Appraisal Committee to take account of these benefits.

To help NICE prioritise topics for additional adoption support, do you consider that there will be any barriers to adoption of this technology into practice? If yes, please describe briefly.

NICE intends to appraise this technology through its Single Technology Appraisal (STA) Process. We welcome comments on the appropriateness of appraising this topic through this process. (Information on the Institute's Technology Appraisal processes is available at http://www.nice.org.uk/article/pmg19/chapter/1-Introduction).

NICE has published an addendum to its guide to the methods of technology appraisal (available at https://www.nice.org.uk/Media/Default/About/what-we-do/NICE-guidance/NICE-technology-appraisals/methods-guide-addendum-cost-comparison.pdf), which states the methods to be used where a cost comparison case is made.

- Would it be appropriate to use the cost comparison methodology for this topic?
- Is the new technology likely to be similar in its clinical efficacy and resource use to any of the comparators?
- Is the primary outcome that was measured in the trial or used to drive the model for the comparator(s) still clinically relevant?
- Is there any substantial new evidence for the comparator technologies that has not been considered? Are there any important ongoing trials reporting in the next year?

References

1 Royal college of physicians (2018). National Lung Cancer Audit: Annual report 2017. Accessed May 2018.

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 (2018). Cancer registration statistics, England: first release, 2016. Accessed May 2018.

4 The Clinical Lung Cancer Genome Project (CLCGP) and Network Genomic Medicine (NGM) (2013). A Genomics-Based Classification of Human Lung Tumors. Science Translational Medicine 5: 209

