NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal

Lorlatinib for untreated ALK-positive advanced non-small-cell lung cancer [ID3896]

Final scope

Final remit/appraisal objective

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

Background

Lung cancer falls into two main groups: around 80 to 85% are non-small-cell lung cancers (NSCLC) and the remainder are small cell lung cancers[1]. 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 adenocarcinoma[2]. 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 2018, 39,754 people were diagnosed with NSCLC in England & Wales. Of these people, 49% had stage IV disease and 12% had stage IIIB/C[3].

Lung cancer caused over 35,000 deaths in the UK between 2016-2018[4]. Forty-five percent of people with lung cancer survive for more than 1 year after diagnosis[5].

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 mutations[6].

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, ROS-1 or BRAF, or levels of PD-L1 expression), 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), alectinib (TA536) and brigatinib (TA670) 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

Lorlatinib (Lorviqua, Pfizer) inhibits the ALK and ROS1 receptor tyrosine kinases, acting against a range of ALK resistant mutations. By inhibiting ALK phosphorylation

and ROS1 activity, lorlatinib inhibits the downstream signalling, inducing cell death, which results in the inhibition of tumour cell growth. It is taken orally.

Lorlatinib does not currently have a marketing authorisation in the UK for untreated ALK-positive NSCLC. It has been studied in a clinical trial in adults with untreated ALK-positive NSCLC compared with crizotinib. Lorlatinib as monotherapy has conditional marketing authorisation for the treatment of adults with ALK-positive advanced NSCLC that has been previously treated by other ALK-positive advanced tyrosine kinase inhibitors, including alectinib, ceritinib and crizotinib.

Intervention(s)	Lorlatinib
Population(s)	Adults with untreated ALK-positive advanced NSCLC
Comparators	• Alectinib • Brigatinib • 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. The availability of any managed access arrangement for the intervention 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:** Brigatinib for ALK-positive advanced non-small-cell lung cancer that has not been previously treated with an ALK inhibitor (2021). NICE Technology Appraisal 670. Review date: 2024. 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. **Terminated appraisals** None **Appraisals in development (including suspended appraisals)** None **Proposed appraisals** None **Related Guidelines:** Lung cancer: diagnosis and management (2019). NICE guideline 122. **Related Quality Standards:** Lung cancer in adults (2019). NICE Quality Standard 17. **Related NICE Pathways:** Lung cancer. Updated 2021. NICE pathway.
Related National Policy	The NHS Long Term Plan, 2019. NHS Long Term Plan NHS England (2018/2019) NHS manual for prescribed specialist services (2018/2019). Chapters 18 and 105. Department of Health and Social Care, NHS Outcomes Framework 2016-2017: Domains 1, 2 and 4. https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017

References

1 Types of lung cancer. Cancer Research UK. Accessed February 2021.

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 February 2021.

3 National Lung Cancer Audit annual report (for the audit period 2018) (2020). Royal College of Physicians. Accessed February 2021.

4 Lung cancer mortality statistics (2018). Cancer Research UK. Accessed February 2021.

5 Lung cancer survival statistics (2013 - 2017). Cancer Research UK. Accessed February 2021.

6 Zappa C, Mousa S (2016). Non-small cell lung cancer: current treatment and future advances. Translational Lung Cancer Research. Accessed February 2021.