NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Crizotinib for treating ROS1-positive advanced non-small-cell lung cancer (MA review of TA529)

Draft scope

Draft remit/evaluation objective

To appraise the clinical and cost effectiveness of crizotinib within its marketing authorisation for treating ROS1-positive advanced non-small cell lung cancer (NSCLC).

Background

Lung cancer falls into 2 main histological categories: around 80 to 90% are classified as NSCLC, with most remaining patients classified as small cell lung cancer.[1,2] NSCLC may be further classified 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. Most lung cancers are diagnosed at an advanced stage,[1] 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).

ROS1 is a rare type of mutation in which chromosomal rearrangement leads to fusion of a portion of ROS1, where resulting fusion kinases are constitutively activated and drive cellular transformation.[3] These rearrangements are more commonly found in patients who have never smoked and who have histologic features of adenocarcinoma, meaning there is a significant overlap with patients who have anaplastic lymphoma kinase (ALK)-positive NSCLC.[3] However, ROS1 tends to be mutually exclusive to ALK and other known oncogenic drivers such as EGFR, KRAS, HER-2, RET and MET aberrations.[3]

In 2021, approximately 31,000 people were diagnosed with NSCLC in England.[1] Of those with known staging, 22% had stage III and 48% had stage IV.[1] ROS1 rearrangements occur in around 1 to 2% of patients with NSCLC.[3,4]

NICE's Lung cancer: diagnosis and management guideline (NG122) recommends entrectinib (TA643) or crizotinib (TA529; available on the Cancer Drugs Fund) as treatment for ROS1-positive advanced NSCLC. Upon disease progression, the guideline recommends treatment with platinum doublet chemotherapy, or pemetrexed and cisplatin (TA181) or carboplatin, or a combination of atezolizumab, bevacizumab, carboplatin, and paclitaxel (TA584).

The technology

Crizotinib (Xalkori, Pfizer) has a marketing authorisation in the UK for the treatment of adults with ROS1-positive advanced non-small cell lung cancer.

Intervention(s)	Crizotinib
Population(s)	Adults with ROS1-positive advanced non-small cell lung cancer
Comparators	Entrectinib
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 use of crizotinib is conditional on ROS1+ status. The economic modelling should include the costs associated with diagnostic testing for ROS1 status in people with advanced non-small-cell lung cancer who would not otherwise have been tested. A sensitivity analysis should be provided without the cost of the diagnostic test. See section 4.8 of the guidance development manual (available here: https://www.nice.org.uk/process/pmg36/chapter/introduction-to-health-technology-evaluation).
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	**Related technology appraisals:** Crizotinib for treating ROS1-positive advanced non-small-cell lung cancer (2018) NICE technology appraisal guidance 529 Entrectinib for treating ROS1-positive advanced non-small-cell lung cancer (2020) NICE technology appraisal guidance 643. **Related technology appraisals in development:** Repotrectinib for treating ROS1-positive advanced non-small-cell lung cancer. NICE technology appraisal guidance [ID 6277] Publication date to be confirmed. **Related NICE guidelines:** Lung cancer: diagnosis and management (2023) NICE guideline 122 **Related quality standards:** Lung cancer in adults (2012). NICE quality standard 17
Related National Policy	The NHS Long Term Plan (2019) NHS Long Term Plan NHS England (2018) NHS manual for prescribed specialist services (2018/2019)

Questions for consultation

Is entrectinib the most appropriate comparator?

Where do you consider crizotinib will fit into the existing care pathway for ROS1-positive advanced NSCLC?

Would crizotinib ever be used before, after, or as an alternative to, entrectinib?

In current NHS practice, is testing for ROS1 genetic rearrangement routinely performed for people with advanced NSCLC?

At what point in the pathway is testing for ROS1 genetic rearrangement usually carried out?

Do you consider that the use of crizotinib can result in any potential 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 committee to take account of these benefits.

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 crizotinib is 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.

NICE is considering evaluating this technology through its cost comparison evaluation process.

Please provide comments on the appropriateness of appraising this topic through this process.

(Information on NICE's health technology evaluation processes is available at https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/nice-technology-appraisal-guidance/changes-to-health-technology-evaluation).

Technologies can be evaluated through the cost-comparison process if they are expected to provide similar or greater health benefits, at a similar or lower cost, compared with technologies that have been previously recommended (as an option) in published NICE guidance for the same indication. Companies can propose cost-comparison topics to NICE at any stage during topic selection and scoping. NICE will route technologies for evaluation through the cost-comparison process if it is agreed during scoping that the process is an appropriate route to establish the clinical and cost effectiveness of the technology.

NICE's health technology evaluations: the manual states the methods to be used where a cost comparison case is made.

- Is the technology likely to be similar in its clinical effectiveness and resource use to any of the comparators? Or in what way is it different to the comparators?

- Will the intervention be used in the same place in the treatment pathway as the comparator(s)? Have there been any major changes to the treatment pathway recently? If so, please describe.

- Will the intervention be used to treat the same population as the comparator(s)?

- Overall is the technology likely to offer similar or improved health benefits compared with the comparators?

- Would it be appropriate to use the cost-comparison methodology for this topic?

References

1. National Lung Cancer Audit (2023) NHS provider results: NLCA State of the Nation Report 2023. Accessed November 2023.

2. Cancer Research UK (2022) Types of lung cancer. Accessed November 2023.

3. D'Angelo A, Sobhani N, Chapman R et al. (2020) Focus on ROS1-Positive Non-Small Cell Lung Cancer (NSCLC): Crizotinib, Resistance Mechanisms and the Newer Generation of Targeted Therapies. Cancers 12(11):3293.

4. American Lung Association (2022) ROS1 and Lung Cancer. Accessed November 2023.