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)

Final scope

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 locally in the chest (locally advanced disease; stage IIIA), more widely in the chest (advanced disease; stage IIIB and IIIC), or to other parts of the body (metastatic disease; stage IV).

ROS1 is a rare type of gene alteration 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, having a similar patient profile to those who have anaplastic lymphoma kinase (ALK)-positive NSCLC.[3] 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.
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)

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.