NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Selpercatinib for previously treated RET fusion-positive advanced non-small-cell lung cancer (MA review of TA760) [ID6293]

Draft scope

Draft remit/evaluation objective

To appraise the clinical and cost effectiveness of selpercatinib within its marketing authorisation for treating previously treated RET fusion-positive advanced non-small-cell lung cancer.

Background

Lung cancer falls into two main histological categories: around 85 – 90% 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, and around 61% had stage IIIB or stage IV disease[3]. Rearranged during transfection (RET) fusion-positive tumours occur in 1-2% of NSCLC and are more commonly found in people who are younger than 60 years, former light smokers or those who have never smoked[4].

Around a third of people with lung cancer survive for more than 1 year after diagnosis, however this is reduced to a fifth of people diagnosed at stage IV[3]. At advanced stage (III and IV) NSCLC treatment aims to control the cancer for as long as possible and help with symptoms. Treatment generally includes chemotherapy, targeted drugs, radiotherapy and symptom control treatment. Treatment choices are influenced by the presence of biological markers (such as mutations in epidermal growth factor receptor-tyrosine kinase [EGFR-TK], anaplastic-lymphoma-kinase [ALK] or PD-L1 status), histology (squamous or non-squamous) and previous treatment experience. There are specific NICE treatment pathways for cancers positive for EGFR-TK, ALK or ROS-1 gene mutations. Testing for RET fusion status is not routinely carried out as standard of care in the UK. People with unconfirmed RET fusion-positive advanced NSCLC would therefore follow the standard NSCLC treatment pathway.

For locally advanced, metastatic or locally recurrent non-small-cell lung cancer of adenocarcinoma histology that has progressed after first-line chemotherapy NICE technology appraisal 347 recommends nintedanib in combination with docetaxel.

For locally advanced or metastatic PD-L1-positive non-small-cell lung cancer in adults who have had at least one chemotherapy (and targeted treatment if they have an epidermal growth factor receptor [EGFR]- or anaplastic lymphoma kinase [ALK]-positive tumour) NICE technology appraisal 428 recommends pembrolizumab.

For locally advanced or metastatic non-small-cell lung cancer who have had chemotherapy (and targeted treatment if they have an EGFR- or ALK-positive tumour) NICE technology appraisal guidance 520 recommends atezolizumab.

For locally advanced or metastatic squamous non-small-cell lung cancer who have had chemotherapy who have not previously been treated with a PD-L1 inhibitor NICE technology appraisal 655 recommends nivolumab.

For locally advanced or metastatic PD-L1 positive non-squamous non-small-cell lung cancer who have had chemotherapy who have not previously been treated with a PD-L1 inhibitor NICE technology appraisal 713 recommends nivolumab.

The technology

Selpercatinib (Retsevmo, Eli Lilly) has a marketing authorisation in the UK for treating people with RET fusion-positive advanced non-small-cell lung cancer that is previously untreated with a RET inhibitor.

Intervention(s)	Selpercatinib
Population(s)	People with RET fusion-positive advanced non-small-cell lung cancer that has been previously treated but has not been treated with a RET inhibitor.
Subgroups	If the evidence allows the following subgroups will be considered: • tumour histology (squamous or non-squamous), and • level of PD-L1 expression
Comparators	For people with squamous cancer previously treated with platinum doublet chemotherapy: • atezolizumab • docetaxel • nivolumab For people with PD-L1 positive squamous cancer previously treated with platinum doublet chemotherapy: • pembrolizumab For people with squamous cancer previously treated with pembrolizumab with carboplatin and paclitaxel: • docetaxel For people with squamous cancer previously treated with pembrolizumab or atezolizumab monotherapy: • platinum doublet chemotherapy For people with non-squamous cancer previously treated with platinum doublet chemotherapy or pemetrexed and carboplatin or cisplatin: • atezolizumab

	• docetaxel • docetaxel and nintedanib For people with PD-L1 positive non-squamous cancer previously treated with platinum doublet chemotherapy or pemetrexed and carboplatin or cisplatin: • nivolumab • pembrolizumab For people with non-squamous cancer previously treated with pembrolizumab with pemetrexed and platinum chemotherapy or atezolizumab with bevacizumab, carboplatin and paclitaxel: • docetaxel • docetaxel and nintedanib For people with non-squamous cancer previously treated with pembrolizumab or atezolizumab monotherapy: • docetaxel • docetaxel and nintedanib • pemetrexed and carboplatin • pemetrexed and cisplatin • platinum doublet chemotherapy
Outcomes	The outcome measures to be considered include: • overall survival • progression free survival • response rate • time to treatment discontinuation • 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. 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 selpercatinib in NSCLC is conditional on the presence of RET gene fusion. The economic modelling should include the costs associated with diagnostic testing for

	RET 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:** Nintedanib for previously treated locally advanced, metastatic, or locally recurrent non-small-cell lung cancer (2015) NICE technology appraisal guidance 347. Pembrolizumab for treating PD-L1-positive non-small-cell lung cancer after chemotherapy (2017) NICE technology appraisal guidance 428. Atezolizumab for treating locally advanced or metastatic non-small-cell lung cancer after chemotherapy (2018) NICE technology appraisal guidance 520. Nivolumab for advanced squamous non-small-cell lung cancer after chemotherapy (2020) NICE technology appraisal guidance 655. Nivolumab for advanced non-squamous non-small-cell lung cancer after chemotherapy (2021) NICE technology appraisal guidance 713. Selpercatinib for untreated RET fusion-positive advanced non-small-cell lung cancer (2023) NICE technology appraisal 911. **Related technology appraisals in development:** Treatments for non-small-cell lung cancer. NICE technology appraisal guidance [ID6234] Publication expected September 2024 **Related NICE guidelines:** Lung cancer: diagnosis and management (2023) NICE guideline NG122. **Related quality standards:** Lung cancer in adults (2012, updated 2019) NICE quality standard 17
Related National Policy	NHS England (2023) Prescribed specialised services manual (version 6) Chapter 105. Specialist cancer services (adults)

	NHS England (2021) Proton beam therapy for lung cancer (Adults). Clinical commissioning policy. Reference no. 201201P NHS England (2019) The NHS long term plan NHS England (2013) Stereotactic ablative body radiotherapy for non-small-cell lung cancer (Adult). Clinical commissioning policy. Reference no. NHSCB/B01/P/a

Questions for consultation

Under what circumstances would RET gene fusion be tested for?

Is the proportion of people with RET gene fusion in the background (1-2% of NSCLC cases) accurate for NHS clinical practice?

Where do you consider selpercatinib will fit into the existing care pathway for RET positive non-small-cell lung cancer?

Do you consider that the use of selpercatinib 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 selpercatinib 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 intends to evaluate this technology through its Single Technology Appraisal 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).

References

[1] Lung cancer incidence by morphology. Cancer Research UK. Accessed March 2022

[2] Howlader N, Noone AM, Krapcho M, Garshell J, Miller D, Altekruse SF, et al. SEER Cancer Statistics Review, 1975-2012, National Cancer Institute. 2015 [Available from: https://seer.cancer.gov/csr/1975_2012/

[3] National Lung Cancer Audit: Annual report 2021 (for the audit period 2018) (2021). Royal College of Physicians. Accessed March 2022

[4] Falchook, G et al. 2016. Effect of the RET Inhibitor Vandetanib in a Patient With RET Fusion–Positive Metastatic Non–Small-Cell Lung Cancer. Journal of Clinical Oncology 34:15