NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Pembrolizumab with pemetrexed and platinum-based chemotherapy for previously treated EGFR-positive metastatic non-small-cell lung cancer

Draft scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of pembrolizumab with pemetrexed and platinum-based chemotherapy within its marketing authorisation for previously treated EGFR-positive non-small-cell lung cancer.

Background

Lung cancer is the third most common cancer and the most common cause of cancer death in the UK, accounting for 13% of all new cancer cases and 21% of all cancer deaths in 2017.[1] There are around 48,000 new lung cancer cases and 35,000 deaths from lung cancer in the UK every year. Around 85% of lung cancers are non-small-cell lung cancers (NSCLC).[2]

The majority of 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), and usually cannot be surgically removed. In 2017, 88% (34,591) of people diagnosed with lung cancer had NSCLC in England, Wales, Jersey and Guernsey[3]. For the majority of people with NSCLC, the aims of therapy are to prolong survival and improve quality of life. 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.

An estimated 10% to 35% of people with NSCLC have mutations to the protein epidermal growth factor receptor (EGFR).[4]

For people whose locally advanced or metastatic disease tests positive for the activating EGFR-TK mutation and who have not previously had treatment, NICE guidance recommends the tyrosine kinase inhibitors (TKIs) osimertinib, dacomitinib, afatinib, erlotinib, and gefitinib as treatment options (NICE technology appraisal guidance 654, 595, 310, 258, and 192 respectively).

Following disease progression with a TKI, osimertinib is available for EGFR T790M mutation-positive disease (NICE technology appraisal 653). Otherwise, atezolizumab in combination and pemetrexed with carboplatin or other platinum doublet chemotherapy are treatment options (NICE technology appraisal 584 and NICE guideline 121).

The technology

Pembrolizumab (Keytruda, Merck Sharp & Dohme) is a humanised, antiprogrammed cell death 1 (PD-1) antibody involved in the blockade of immune suppression and the subsequent reactivation of anergic T-cells. It is administered intravenously.

Pembrolizumab with pemetrexed and platinum-based chemotherapy does not currently have a marketing authorisation in the UK for previously treated EGFR-positive metastatic NSCLC. It is currently being studied in a clinical trial compared with placebo, pemetrexed and platinum-based chemotherapy in patients with stage 4 EGFR-positive NSCLC after prior treatment with an EGFR-TKI.

Intervention(s)	Pembrolizumab with pemetrexed and platinum-based chemotherapy
Population(s)	Adults with EGFR-positive metastatic NSCLC after prior treatment with an EGFR-TKI
Comparators	Established clinical management without pembrolizumab including but not limited to: • atezolizumab plus bevacizumab, carboplatin and paclitaxel • pemetrexed with platinum-based chemotherapy (such as carboplatin or cisplatin)
Outcomes	The outcome measures to be considered include: • overall survival • disease-free survival • 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. 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 pembrolizumab is conditional on the presence of an EGFR mutation. The economic modelling should include the costs associated with diagnostic testing for EGFR in people with NSCLC who would not otherwise have been tested. A sensitivity analysis should be provided without the cost of the diagnostic test. See section 5.9 of the Guide to the Methods of Technology Appraisals.
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:** Osimertinib for treating EGFR T790M mutation-positive advanced non-small-cell lung cancer (2020) NICE technology appraisal guidance 653. Review date 2023. Atezolizumab in combination for treating metastatic non-squamous non-small-cell lung cancer (2019) NICE technology appraisal guidance 584. Review date 2022. **Appraisals in development (including suspended appraisals)** Cimavax for treating wild-type EGFR-positive non-small-cell lung cancer NICE technology appraisals guidance [ID1259]. Publication date to be confirmed **Related Guidelines:** Lung cancer: diagnosis and management (2019) NICE guideline 122

	Related Quality Standards: Lung cancer in adults (2012; updated 2019) Quality standard 17 **Related NICE Pathways:** Treating non-small-cell lung cancer (2020) NICE pathway
Related National Policy	**National Service Frameworks:** Cancer **Department of Health:** Department of Health (2014) The national cancer strategy: 4th annual report Department of Health (2011) Improving outcomes: a strategy for cancer Department of Health (2009) Cancer commissioning guidance Department of Health (2007) Cancer reform strategy The NHS Long Term Plan, 2019. NHS Long Term Plan NHS England (2018/2019) NHS manual for prescribed specialist services (2018/2019) Chapter 105: Specialist cancer services (adults) Department of Health and Social Care, NHS Outcomes Framework 2016-2017 (published 2016): Domains 1, 2, 4, 5. https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017 **Other policies** Independent Cancer Taskforce (2015) Achieving world-class cancer outcomes: a strategy for England 2015-2020

Questions for consultation

Have all relevant comparators for pembrolizumab with pemetrexed and platinum-based chemotherapy been included in the scope?

Are the outcomes listed appropriate?

Are there any subgroups of people in whom pembrolizumab with pemetrexed and platinum-based chemotherapy is expected to be more clinically effective and cost effective or other groups that should be examined separately?

Where do you consider pembrolizumab with pemetrexed and platinum-based chemotherapy will fit into the existing NICE pathway, Treating non-small-cell 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 pembrolizumab 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 pembrolizumab with pemetrexed and platinum-based chemotherapy 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 pembrolizumab with pemetrexed and platinum-based chemotherapy 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 technology/ies that has not been considered? Are there any important ongoing trials reporting in the next year?

References

1. Lung cancer incidence. Cancer Research UK. Accessed January 2021.

2. Types of lung cancer. Cancer Research UK. Accessed January 2021.

3. NLCA annual report 2018. Accessed January 2021.

4. Osimertinib for EGFR-positive non-small cell lung cancer – adjuvant. NIHR Innovation Observatory Health Technology Briefing. Accessed January 2021.