NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Proposed Health Technology Appraisal

Pembrolizumab for treating advanced or recurrent PD-L1 positive non-small-cell lung cancer after progression with platinum-based chemotherapy

Draft scope (pre-referral)

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of pembrolizumab within its marketing authorisation for treating advanced or recurrent PD-L1 positive non-small-cell lung cancer after progression with platinum-based chemotherapy.

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. NSCLC can be further classified into 3 histological sub-types of large-cell undifferentiated carcinoma, squamous cell carcinoma and adenocarcinoma. 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 2013, approximately 28,500 people were diagnosed with NSCLC in England and Wales, of whom 13% had stage IIIA, 10% had stage IIIB and 46% had stage IV disease.[1]

Cancer cells expressing an immunologic marker called programmed cell death 1 ligand (PD-L1) are believed to suppress certain immune responses and cause increased tumor aggressiveness. The proportion of NSCLC that is PD-L1 positive in England is unknown.

Lung cancer caused approximately 28,000 deaths in England in 2012.[2] The median survival of people with lung cancer (all stages) is approximately 6 months; 35% of people with lung cancer survive for more than 1 year after diagnosis.

For the majority of people with NSCLC, the aims of treatment are to prolong survival and improve quality of life. Treatment choices may be influenced by the presence of biological markers (such as mutations in EGFR-TK, ALK or PD-L1 status), histology (squamous or non-squamous) and previous treatment experience. NICE clinical guideline 121 (CG121) recommends platinum-based chemotherapy as an option for people with previously untreated stage III or IV NSCLC and good performance status. For people with locally advanced or metastatic NSCLC whose disease has progressed after chemotherapy, NICE recommends docetaxel monotherapy, afatinib and erlotinib as options in some circumstances (CG121, technology appraisal 162

and technology appraisal 310 respectively). In clinical practice, NSCLC tumours that progress after treatment with EGFR-targeted therapies may be treated with platinum in combination with gemcitabine, vinorelbine, pemetrexed or a taxane. Best supportive care may be considered for some people for whom chemotherapy is unsuitable or may not be tolerated.

The technology

Pembrolizumab (Keytruda, Merck Sharp & Dohme) is a humanised, anti-programmed 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 does not have a marketing authorisation in the UK for treating non-small cell lung cancer. It has been studied in clinical trials, in adults with NSCLC that is PD-L1 positive, whose disease has recurred after receiving platinum-containing doublet chemotherapy, compared with docetaxel.

Intervention(s)	Pembrolizumab
Population(s)	People with advanced non-small-cell lung cancer that is PD-L1 positive, whose disease has recurred after platinum-containing doublet chemotherapy.
Comparators	• Docetaxel • Best supportive care
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. 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.

Other considerations	If the evidence allows, consideration will be given to subgroups based on cancer histology and biological markers (PD-L1, EGFR, ALK). If appropriate, the appraisal should include consideration of the costs and implications of additional testing for biological markers, but will not make recommendations on specific diagnostic tests or devices. 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: Afatinib for treating epidermal growth factor receptor mutation-positive locally advanced or metastatic non-small-cell lung cancer (2014). NICE technology appraisal guidance 310. Review Proposal Date Apr 2017. Crizotinib for previously treated non-small-cell lung cancer associated with an anaplastic lymphoma kinase fusion gene (2013). NICE technology appraisal guidance 296. Review Proposal Date May 2016. Gefitinib for the second-line treatment of locally advanced or metastatic non-small-cell lung cancer (terminated appraisal) (2009). NICE technology appraisal guidance 175. Review in progress. Erlotinib for the treatment of non-small-cell lung cancer (2008). NICE technology appraisal guidance 162. Review in progress. Pemetrexed for the treatment of non-small-cell lung cancer (2007). NICE technology appraisal guidance 124. Static list. Erlotinib and gefitinib for treating non-small-cell lung cancer that has progressed following prior chemotherapy (Review of TA162 and TA175). NICE technology appraisal in preparation [ID620]. Expected date of publication TBC. Nintedanib for treating previously treated metastatic

	non-small-cell lung cancer. NICE technology appraisal in preparation [ID438]. Expected date of publication May 2015. Related Guidelines: The diagnosis and treatment of lung cancer (2011). NICE clinical guideline 121. Review date June 2015. Related Quality Standards: 'Quality standard for lung cancer (2012). NICE quality standard 17. http://www.nice.org.uk/guidance/qualitystandards/qualitystandards.jsp Related NICE Pathways: Lung cancer. Pathway created: Mar 2012. http://pathways.nice.org.uk/pathways/lung-cancer
Related National Policy	Department of Health, Improving Outcomes: A strategy for cancer, third annual report, Dec 2013 https://www.gov.uk/government/publications/the-national-cancer-strategy-3rd-annual-report--2 NHS England, Manual for prescribed specialised services, chapter 105: specialist cancer services (adults), Jan 2014. http://www.england.nhs.uk/wp-content/uploads/2014/01/pss-manual.pdf Department of Health, NHS Outcomes Framework 2013-2014, Nov 2013. https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/256456/NHS_outcomes.pdf Department of Health, Cancer commissioning guidance, Dec 2009. http://webarchive.nationalarchives.gov.uk/20130107105354/http:/www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_110115

Questions for consultation

What is the size of the relevant population in England who are likely to be treated with pembrolizumab?

How is PD-L1 status tested? Are validated tests readily available? Is it tested routinely in current clinical practice?

Have all relevant comparators for pembrolizumab been included in the scope?

- Which treatments are considered to be established clinical practice in the NHS for advanced or recurrent PD-L1 positive non-small-cell lung cancer after progression with platinum-based chemotherapy?
- How should best supportive care be defined?
- Is docetaxel a relevant comparator?

Are the subgroups suggested in 'other considerations appropriate?

- Are there any other subgroups of people in whom pembrolizumab is expected to be more clinically effective and cost effective or other groups that should be examined separately?
- Should any other biological markers be considered separately?

Where do you consider pembrolizumab will fit into the existing NICE pathway, 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 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 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.

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)

References

1. National Lung Cancer Audit: 2013 Patient Cohort. Published 2014 [accessed March 2015]

2. Cancer Research UK (2013) Lung cancer survival and mortality statistics. [accessed March 2015]