

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal

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

Final scope

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 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. 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, nintedanib, afatinib and erlotinib as options in some circumstances (CG121, technology

appraisal 347, 310 and technology appraisal 374 respectively). In clinical practice, ALK-positive NSCLC tumours that progress after treatment with platinum doublet therapy may be treated with a targeted therapy such as crizotinib (not recommended by NICE but available via the Cancer Drugs Fund at the time of issuing the scope). EGFR-TK positive NSCLC tumours that progress after treatment with targeted therapy may be treated with a platinum agent 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)	<p>People with advanced non-small-cell lung cancer that is PD-L1 positive:</p> <ul style="list-style-type: none"> • whose disease has progressed after platinum-containing doublet chemotherapy. • whose disease has progressed on both platinum-containing doublet chemotherapy and targeted therapy for EGFR or ALK positive tumours.
Comparators	<ul style="list-style-type: none"> • Docetaxel monotherapy • Nintedanib with docetaxel (for people with adenocarcinoma histology) • Ceritinib (only for patients with ALK positive mutation status, subject to ongoing NICE appraisal) • Nivolumab (subject to ongoing NICE appraisal) • Ramucirumab with docetaxel (subject to ongoing NICE appraisal) • Best supportive care

Outcomes	<p>The outcome measures to be considered include:</p> <ul style="list-style-type: none"> • overall survival • progression-free survival • response rates • adverse effects of treatment • health-related quality of life.
Economic analysis	<p>The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year.</p> <p>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.</p> <p>Costs will be considered from an NHS and Personal Social Services perspective.</p> <p>The availability of any patient access schemes for the intervention or comparator technologies should be taken into account.</p>
Other considerations	<p>If the evidence allows, consideration will be given to subgroups based on cancer histology and biological markers (PD-L1 and EGFR).</p> <p>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.</p> <p>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.</p>
Related NICE recommendations and NICE Pathways	<p>Related Technology Appraisals:</p> <p>‘Nintedanib for previously treated locally advanced, metastatic, or locally recurrent non-small-cell lung cancer’ (2015). NICE technology appraisal 347. Review date July 2018.</p> <p>Appraisals in development:</p> <p>‘Ceritinib for previously treated anaplastic lymphoma kinase positive non-small-cell lung cancer’. NICE</p>

	<p>technology appraisal guidance [ID729]. Expected date of publication TBC.</p> <p>‘Nivolumab for previously treated locally advanced or metastatic squamous non-small-cell lung cancer’. NICE technology appraisal guidance [ID811]. Expected date of publication May 2016.</p> <p>‘Nivolumab for previously treated locally advanced or metastatic non-squamous non-small-cell lung cancer’. NICE technology appraisal guidance [ID900]. Expected date of publication September 2016</p> <p>‘Ramucirumab for previously treated locally advanced or metastatic non-small-cell lung cancer’. NICE technology appraisal [ID838]. Expected date of publication August 2016.</p> <p>Related Guidelines: The diagnosis and treatment of lung cancer (2011). NICE clinical guideline 121. Review date June 2015.</p> <p>Related Quality Standards: ‘Quality standard for lung cancer (2012). NICE quality standard 17. http://www.nice.org.uk/guidance/qualitystandards/qualitystandards.jsp</p> <p>Related NICE Pathways: Lung cancer. Pathway created: Mar 2012. http://pathways.nice.org.uk/pathways/lung-cancer</p>
Related National Policy	<p>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</p> <p>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</p> <p>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</p> <p>Department of Health, Cancer commissioning guidance, Dec 2009. http://webarchive.nationalarchives.gov.uk/20130107105</p>

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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]