NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal

Pembrolizumab with carboplatin and paclitaxel or nab-paclitaxel for untreated metastatic squamous non-small-cell lung cancer [ID1306]

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of pembrolizumab in combination with carboplatin and paclitaxel or nab-paclitaxel within its marketing authorisation for untreated metastatic squamous 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. 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 2016, around 33,000 people were diagnosed with NSCLC in England.[1] Around 12% had stage IIIA, 8% had stage IIIB and 53% had stage IV disease[1]. The prognosis for people with non-small-cell lung cancer is generally poor. For people with stage III and stage IV disease respectively, around 43% and 16% survive for 1 year or longer.[1]

For the majority of people with NSCLC, the aims of treatment 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.

NICE clinical guideline 121 (CG121 'Lung cancer') recommends platinum-based chemotherapy (that is, cisplatin or carboplatin and either docetaxel, gemcitabine, paclitaxel, or vinorelbine) as an option for people with previously untreated stage III or IV NSCLC and good performance status. NICE technology appraisal guidance 531 recommends pembrolizumab monotherapy as an option for untreated PD-L1-positive metastatic NSCLC if the tumour expresses PD-L1 with at least 50% tumour proportion score and has no EGFR- or ALK-positive mutations.

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 untreated metastatic squamous NSCLC when used in combination with carboplatin and paclitaxel or nab-paclitaxel. It has been studied in a clinical trial in combination with carboplatin and investigator's choice of paclitaxel or nab-paclitaxel, compared with carboplatin and investigator's choice of paclitaxel or nab-paclitaxel alone, in adults with metastatic squamous NSCLC who have not had chemotherapy for metastatic disease.

Pembrolizumab monotherapy has a marketing authorisation in the UK for:

- first line treatment of metastatic NSCLC for tumours that express PD-L1 with at least 50% tumour proportion score with no EGFR or ALK positive tumour mutations
- treating locally advanced or metastatic NSCLC for tumours that express PD-L1 with at least 1% tumour proportion score after at least one prior chemotherapy regimen.

Interventions	Pembrolizumab in combination with: • carboplatin and paclitaxel • carboplatin and nab-paclitaxel
Population	Adults with untreated metastatic squamous non-small-cell lung cancer (NSCLC)
Comparators	• Chemotherapy (docetaxel, gemcitabine, paclitaxel or vinorelbine) in combination with a platinum drug (carboplatin or cisplatin) • Pembrolizumab monotherapy (for people with tumours that express PD-L1 with at least 50% tumour proportion score with no EGFR- or ALK-positive tumour mutations only)
Outcomes	The outcome measures to be considered include: • overall survival • progression-free survival • response rates • duration of response • 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 access agreements for the intervention or comparator technologies will be taken into account. If appropriate, the economic modelling should include the costs associated with diagnostic testing for biological markers (for example PD-L1) 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	If evidence allows, consideration will be given to subgroups based on the biological marker PD-L1. 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** 'Pembrolizumab for untreated PD-L1-positive metastatic non-small-cell lung cancer' (2018). NICE technology appraisal 531. Review date July 2021. 'Necitumumab for untreated advanced or metastatic squamous non-small-cell lung cancer' (2016) NICE technology appraisal 411. Review date September 2019. **Related Technology Appraisals in development**

	(including suspended appraisals) 'Nivolumab with ipilimumab for untreated non-small-cell lung cancer that has a high tumour mutational burden' NICE technology appraisals guidance [ID1187]. Expected publication May 2019. 'Nivolumab in combination with platinum-doublet chemotherapy for untreated PD-L1-negative non-small-cell lung cancer' NICE technology appraisals guidance [ID1135]. Publication date to be confirmed. 'Pembrolizumab for untreated PD-L1 positive non-small-cell lung cancer with at least 1% tumour proportion score' NICE technology appraisals guidance [ID1247]. Publication date to be confirmed. 'Nivolumab monotherapy for non-small-cell lung cancer' NICE technology appraisals guidance [ID1088]. Suspended. **Terminated appraisals** Paclitaxel as albumin-bound nanoparticles with carboplatin for untreated non-small-cell lung cancer (terminated appraisal) (2015) NICE technology appraisals guidance 362. **Related Guidelines** Lung Cancer: The diagnosis and treatment of lung cancer (2011). NICE guideline 121. Review in progress. **Guidelines in development** 'Lung cancer: diagnosis and management (update)'. Publication expected February 2019. **Related Quality Standards** Quality standard for lung cancer (2012). NICE quality standard 17 https://www.nice.org.uk/guidance/qs17 **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, fourth annual report, Dec 2014 https://www.gov.uk/government/publications/the-national-cancer-strategy-4th-annual-report NHS England, Manual for prescribed specialised services, chapter 105: specialist cancer services (adults), May 2016.

	https://www.england.nhs.uk/commissioning/wp-content/uploads/sites/12/2016/06/pss-manual-may16.pdf Department of Health, NHS Outcomes Framework 2016-20167, April 2016. https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017 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

References

1 National lung cancer audit 2017 (2018). Royal college of Physicians. Accessed May 2018.