NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Pembrolizumab for adjuvant treatment of resected non-small-cell lung cancer

Draft scope

Draft remit/evaluation objective

To appraise the clinical and cost effectiveness of pembrolizumab within its marketing authorisation for adjuvant treatment of resected 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 2018.[1] There are around 39,340 new lung cancer cases and 27,682 deaths from lung cancer in the England every year. Up to 85% of lung cancers are non-small-cell lung cancers (NSCLC).[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). Less than 30% of lung cancers are diagnosed at an early stage (stage 1 or 2).

NICE guideline Lung cancer: diagnosis and management recommends surgery, radiotherapy, chemoradiotherapy or a combination of these for early stage disease.[3] Around 18% of people with NSCLC had surgical resection with curative intent in England and Wales in 2017.[4] If well enough, people may be offered a cisplatin-based chemotherapy (adjuvant treatment) after surgery.[3] People are actively monitored for cancer recurrence. If the cancer comes back, treatment options and prognosis depend on the site of the recurrence. Despite the curative intent of treatment for early-stage lung cancer, survival is poor, with only about 57% people with stage I, 34% with stage II and 13% with stage III surviving for 5 years after diagnosis.[1] NICE technology appraisal guidance TA761 recommends osimertinib for use within the Cancer Drugs Fund as adjuvant treatment after complete tumour resection in adults with stage IB to IIIA NSCLC whose tumours have epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 (L858R) substitution mutations.

It is estimated that over half of all NSCLCs express the programmed cell death ligand-1 (PD-L1) biomarker.[5] Cancer cells expressing PD-L1 are believed to suppress certain immune responses and cause increased tumor aggressiveness.

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 monotherapy does not currently have a marketing authorisation in the UK for adjuvant treatment of resected NSCLC. It is currently being studied in a clinical trial compared with placebo in people with Union for International Cancer

Control (UICC) v7 stage II to IIIA (and stage IB with a tumour size of 4 cm or greater) NSCLC after complete surgical resection with or without standard adjuvant therapy.

Intervention(s)	Pembrolizumab (as an adjuvant treatment)
Population(s)	Adults with NSCLC who have undergone surgical resection with or without adjuvant chemotherapy
Subgroups	If evidence allows, results by disease stage and level of PD-L1 expression will be considered
Comparators	Established clinical management without pembrolizumab: • Active monitoring • Cisplatin-based chemotherapy • Atezolizumab after adjuvant cisplatin-based chemotherapy (subject to NICE appraisal)
Outcomes	The outcome measures to be considered include: • overall survival • disease-free survival • response rate • 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.

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:** Osimertinib for adjuvant treatment of EGFR mutation-positive non-small-cell lung cancer after complete tumour resection (2022). NICE technology appraisals guidance 761. Pembrolizumab with carboplatin and paclitaxel for untreated metastatic squamous non-small-cell lung cancer (2022). NICE technology appraisal guidance 770. Pembrolizumab with pemetrexed and platinum chemotherapy for untreated, metastatic, non-squamous non-small-cell lung cancer (2021). NICE technology appraisal guidance 683. Pembrolizumab for untreated PD-L1-positive metastatic non-small-cell lung cancer (2018). NICE technology appraisal guidance 531. Pembrolizumab for treating PD-L1-positive non-small-cell lung cancer after chemotherapy (2017). NICE technology appraisal guidance 428. **Related appraisals in development (including suspended appraisals):** Atezolizumab for adjuvant treatment of resected non-small-cell lung cancer [ID3852]. NICE technology appraisal guidance. Publication expected July 2022. Pembrolizumab with pemetrexed and platinum-based chemotherapy for previously TKI-treated EGFR-positive metastatic non-squamous non-small-cell lung cancer [ID3873]. NICE technology appraisal guidance. Publication date to be confirmed. Pembrolizumab with lenvatinib for untreated PD-L1-positive metastatic non-small-cell lung cancer [ID3809]. NICE technology appraisal guidance (*suspended*). Pembrolizumab with ipilimumab for treating PD-L1-positive advanced non-small-cell lung cancer [ID3861]. NICE technology appraisal guidance (*suspended*). Pembrolizumab for untreated PD-L1 positive non-small-cell lung cancer with at least 1% tumour proportion score [ID1247]. NICE technology appraisal guidance (*suspended*). **Related Guidelines:** Lung cancer: diagnosis and management (2019). NICE guideline NG122.

	Related Interventional Procedures Microwave ablation for treating primary lung cancer and metastases in the lung (2013). NICE interventional procedures guidance 469. **Related Quality Standards:** Lung cancer in adults (2019). NICE quality standard 17
Related National Policy	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).

Questions for consultation

Have all relevant comparators for pembrolizumab for adjuvant treatment of fully resected non-small-cell lung cancer with and without adjuvant treatment been included in the scope?

Are all people with fully resected UICC v7 stage II to IIIA (and stage IB with a tumour size of 4 cm or greater) suitable for adjuvant therapy?

How should 'established clinical management without pembrolizumab' be defined?

What considerations are made in determining whether pembrolizumab is used before or after adjuvant chemotherapy?

Is there a routine test to detect the biomarker PD-L1 in resected samples?

Are the outcomes listed appropriate?

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

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 evaluate this technology through its Single Technology Appraisal process. We welcome comments on the appropriateness of appraising this topic through this 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).

NICE's health technology evaluations: the manual 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 statistics. Cancer Research UK. Accessed March 2022
2. Types of lung cancer. Cancer Research UK. Accessed March 2022
3. Lung cancer: diagnosis and management. (2019) NICE guideline 122
4. National Lung Cancer Audit: Annual report 2018 (for the audit period 2017) (2020). Royal College of Physicians. Accessed March 2022.
5. Skov, B., Rørvig, S., Jensen, T. et al. (2020) The prevalence of programmed death ligand-1 (PD-L1) expression in non-small cell lung cancer in an unselected, consecutive population. Mod Pathol 33, 109–117