NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

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

Final scope

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 between 2016 and 2018.[1] Lung cancer falls into 2 main histological categories: around 80–85% are non-small-cell lung cancers (NSCLC) and the remainder are small cell lung cancers.[2] NSCLC can be further classified into 3 histological sub-types of large-cell undifferentiated carcinoma, squamous cell carcinoma and adenocarcinoma.

In 2021, 91% (31,374) of people diagnosed with lung cancer in England had NSCLC.[3] Despite the curative intent of treatment for early-stage lung cancer, survival is poor, with only about 57% people with stage 1, 34% with stage 2 and 13% with stage 3 surviving for 5 years after diagnosis.[4] 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 which results in a weaker anti-tumour response.[5, 6]

The NICE guideline for lung cancer: diagnosis and management recommends surgery, radiotherapy, chemoradiotherapy or a combination of these for early stage disease. Of these people, 17% (5,333) had surgical treatment for their cancer.[3]

NICE technology appraisal guidance TA876 recommends nivolumab with chemotherapy as a neo-adjuvant (before surgery) treatment for resectable NSCLC. If well enough, people may be offered a cisplatin-based chemotherapy adjuvant (after surgery) treatment.

NICE technology appraisal guidance TA761 recommends osimertinib for use within the Cancer Drugs Fund (CDF) as adjuvant treatment after complete tumour resection in adults with stage 1B to 3A NSCLC whose tumours have epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 (L858R) substitution mutations. NICE technology appraisal guidance TA823 recommends atezolizumab for use within the CDF for adjuvant treatment of resected non-small-cell lung cancer.

The technology

Pembrolizumab (Keytruda, Merck Sharp & Dohme) has a marketing authorisation in the UK as adjuvant treatment for adult patients with NSCLC who are at high risk of recurrence following complete resection and platinum-based chemotherapy. It is currently being studied in a clinical trial compared with placebo in people with Union for International Cancer Control (UICC) v7 stage 2 to 3A (and stage 1B with a tumour

size of 4 cm or greater) NSCLC after complete surgical resection with or without standard adjuvant therapy.

Intervention(s)	Pembrolizumab
Population(s)	Adults with NSCLC who have undergone complete surgical resection with or without adjuvant chemotherapy
Subgroups	If evidence allows the following subgroups will be considered: • by disease stage • by level of PD-L1 expression
Comparators	• Established clinical management without pembrolizumab (that is, active monitoring) • Platinum doublet chemotherapy • Durvalumab (subject to NICE appraisal) For people whose tumours express PD-L1 with at least a 50% tumour proportion score • Atezolizumab after adjuvant platinum-based chemotherapy (subject to NICE appraisal) For people whose tumours have an EGFR genetic alteration • Osimertinib (subject to NICE appraisal)
Outcomes	The outcome measures to be considered include: • disease-free survival • event-free survival • overall survival • 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:** Nivolumab with chemotherapy for neoadjuvant treatment of resectable non-small-cell lung cancer (2023). NICE technology appraisals guidance 87 Atezolizumab for adjuvant treatment of resected non-small-cell lung cancer (2022). NICE technology appraisal guidance 823. Osimertinib for adjuvant treatment of EGFR mutation-positive non-small-cell lung cancer after complete tumour resection (2022). NICE technology appraisals guidance 761. **Related technology appraisals in development:** Osimertinib for adjuvant treatment of EGFR mutation-positive non-small-cell lung cancer after complete tumour resection NICE Technology Appraisals guidance [ID5120]. Publication date to be confirmed. Pembrolizumab as neoadjuvant (with chemotherapy) and adjuvant (as monotherapy) treatment for resectable non-small-cell lung cancer. NICE Technology Appraisals guidance [ID5094]. Publication date to be confirmed Durvalumab with chemotherapy for neoadjuvant and adjuvant treatment of resectable non-small-cell lung cancer NICE

	Technology Appraisals guidance [ID6220]. Publication date to be confirmed Atezolizumab with chemotherapy for neoadjuvant and adjuvant treatment of resectable non-small-cell lung cancer [ID3894] Publication date to be confirmed Durvalumab for adjuvant treatment of resectable non-small-cell lung cancer NICE Technology Appraisals guidance ID1263. Publication date to be confirmed **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 (2023) Manual for prescribed specialist services (2023/2024)

References

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2. Types of lung cancer. Cancer Research UK. Accessed January 2024
3. Royal College of Surgeons of England (2023). National Lung Cancer Audit: State of the Nation Report 2023. Accessed November 2023
4. Office for National Statistics. Cancer Survival in England: adults diagnosed between 2013 and 2017 and followed up to 2018. 2019. Available from: https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/conditionsanddiseases/datasets/cancersurvivalratescancersurvivalinenglandadultsdiagnosed. Accessed October 2023
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
6. Han Y, Liu D, Li L. PD-1/PD-L1 pathway: current researches in cancer. Am J Cancer Res. 2020 Mar 1;10(3):727-742. PMID: 32266087; PMCID: PMC7136921.