NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE
Health Technology Evaluation

Nivolumab as neoadjuvant (with chemotherapy) and adjuvant (as monotherapy) treatment for resectable non-small-cell lung cancer [ID6310]

Final scope

Remit/evaluation objective

To appraise the clinical and cost effectiveness of nivolumab with chemotherapy and nivolumab monotherapy within its marketing authorisation for neoadjuvant and adjuvant treatment of resectable non-small-cell lung cancer (NSCLC).

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 2017 and 2019.[1] 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 3) or to other parts of the body (metastatic disease; stage 4). Around 30% of lung cancers are diagnosed at an early stage (stage 1 or 2).[2]

In 2022, 90% (around 33,000) of people diagnosed with lung cancer in England had NSCLC.[2] Of these people, 18% (around 6,600) had surgical treatment for their cancer.[2] 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.[3] It is estimated that over half of all NSCLCs express the programmed cell death ligand-1 (PD-L1) biomarker.[4] Cancer cells expressing PD-L1 are believed to suppress certain immune responses which results in a weaker anti-tumour response.[4,5]

The treatment pathway for NSCLC can be divided into interconnected decision points based on the number staging system and line of therapy. Treatment choices are influenced by the presence of biological markers (including programmed cell death 1 ligand PD-L1 status), oncogenic driver genetic alterations, histology (squamous or non-squamous) and previous treatment. NICE's Technology Appraisal Pathway Pilot scope for treatments for non-small-cell lung cancer outlines in more detail the NSCLC treatment pathway.

NICE guideline 122 (NG122) 'Lung cancer: diagnosis and management' recommends surgery, radiotherapy, chemoradiotherapy or a combination of these for stage 1 to 2 NSCLC. People may be offered a neo-adjuvant (before surgical removal of cancerous tumour) treatment which could be platinum-based chemotherapy, or nivolumab with chemotherapy as recommended by NICE TA876. Neoadjuvant chemotherapy has shown equivalent outcomes in terms of survival to adjuvant chemotherapy.[6]

For stage 3 NSCLC, surgery is carried out if the surgeon deems the tumour to be resectable. Before surgery, chemoradiotherapy (chemotherapy with radiotherapy) may be used or surgery may potentially be followed by chemotherapy. If well enough, people may be offered a cisplatin-based chemotherapy (adjuvant treatment) after surgery.

People who have had surgery may have an adjuvant treatment. NICE TA761 recommends osimertinib in the Cancer Drugs Fund as adjuvant treatment for people whose cancer has an EGFR exon 19 deletion or an exon 21 (L858R) substitution mutation. For people whose cancer does not have an EGFR mutation, platinum chemotherapy may be offered as adjuvant treatment. NICE TA823 recommends atezolizumab in the Cancer Drugs Fund as an option for maintenance treatment after complete tumour resection in adults with stage 2 to 3a NSCLC and adjuvant chemotherapy.

The technology

Nivolumab (Opdivo, Bristol-Myers Squibb) with chemotherapy then nivolumab monotherapy does not currently have a marketing authorisation in the UK for neoadjuvant and then adjuvant treatment of resectable NSCLC. It is being studied in clinical trials as a neo-adjuvant treatment with platinum-based chemotherapy followed by surgery and then adjuvant treatment as monotherapy compared with platinum-based chemotherapy as a neo-adjuvant treatment followed by surgery and adjuvant placebo in those with locally advanced NSCLC.

Nivolumab is currently licenced for several indications including but not limited to:

- neoadjuvant treatment (in combination with platinum-based chemotherapy) of resectable (tumours ≤4cm or node positive) non-small-cell lung cancer in adults.
- as monotherapy for treatment of locally advanced or metastatic NSCLC after prior chemotherapy in adults
- the first-line treatment in combination with ipilimumab and 2 cycles of platinum-based chemotherapy of metastatic non-small cell lung cancer in adults whose tumours have no sensitising EGFR mutation or ALK translocation.

Intervention(s)	Nivolumab with chemotherapy for neoadjuvant treatment then nivolumab monotherapy for adjuvant treatment
Population(s)	People with resectable non-small-cell lung cancer (NSCLC)
Subgroups	If the evidence allows subgroups will be considered based on: • Whether nivolumab is used before and after surgery • PD-L1 tumour proportion score • Disease stage • Presence of biological or genetic markers • Histology (squamous versus non-squamous)

Comparators	Established clinical management without nivolumab, which may include • Neoadjuvant nivolumab with chemotherapy • Neoadjuvant chemoradiotherapy • Platinum-based chemotherapy • Active monitoring • Pembrolizumab • Durvalumab • Alectinib (for people with ALK-positive NSCLC) • Osimertinib (subject to NICE appraisal) For people whose tumours express PD-L1 with at least a 50% tumour proportion score • Atezolizumab after adjuvant cisplatin-based chemotherapy (subject to NICE appraisal)
Outcomes	The outcome measures to be considered include: • event-free survival • disease-free survival • pathological complete response • response rates • 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. 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. The availability and cost of biosimilar and generic products should 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:** Durvalumab with chemotherapy before surgery (neoadjuvant) then alone after surgery (adjuvant) for treating resectable non-small-cell lung cancer (2025) NICE technology appraisal guidance 1030 Pembrolizumab with chemotherapy before surgery (neoadjuvant) then alone after surgery (adjuvant) for treating resectable non-small-cell lung cancer (2024) NICE technology appraisal guidance 1017 **Related NICE guidelines:** Lung cancer: diagnosis and management (NG122) **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).

References

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