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

Draft scope

Draft 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 2021, 91% (around 31,000) of people diagnosed with lung cancer in England had NSCLC.[2] Of these people, 17% (5,333) 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 in combination with platinum based chemotherapy compared with platinum based chemotherapy as a neo-adjuvant and adjuvant therapy 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

Comparators	Established clinical management without nivolumab, which may include • Neoadjuvant nivolumab with chemotherapy • Neoadjuvant chemoradiotherapy • Platinum-based chemotherapy • Active monitoring • Pembrolizumab (subject to NICE appraisal) • Durvalumab (subject to NICE appraisal) • Alectinib (for people with ALK-positive NSCLC and 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:** Nivolumab with chemotherapy for neoadjuvant treatment of resectable non-small-cell lung cancer (2023) NICE technology appraisal guidance 876 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) TA761 **Related technology appraisals in development:** Pembrolizumab for adjuvant treatment of resected non-small-cell lung cancer [ID3907] Publication date to be confirmed Pembrolizumab for neoadjuvant and adjuvant treatment of resectable stage 2 to 3B non-small-cell lung cancer [ID5094] 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 Nivolumab for adjuvant treatment of resected non-small-cell lung cancer [ID4053] 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 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).

Questions for consultation

Where do you consider nivolumab with chemotherapy (as neo-adjuvant) and then nivolumab monotherapy (as adjuvant) will fit into the existing care pathway for locally advanced NSCLC?

Are the subgroups suggested appropriate?

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

Would nivolumab with chemotherapy (as neo-adjuvant) and then nivolumab monotherapy (as adjuvant) be a candidate for managed access?

Do you consider that the use of nivolumab with chemotherapy (as neo-adjuvant) and then nivolumab monotherapy (as adjuvant) can result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation?

Would nivolumab with chemotherapy (as neo-adjuvant) and then nivolumab monotherapy (as adjuvant) only be used in people whose NSCLC was PD-L1 positive?

Would all patients with resectable NSCLC that receive neoadjuvant treatment with nivolumab continue to receive adjuvant treatment? Are there any clinical features post-surgery that may make patients less likely to benefit from adjuvant treatment?

Are there any patients with resectable NSCLC who would not have a neo-adjuvant treatment but who would have an adjuvant treatment after surgery? If so, what might the reasons be for this and which treatments would they have?

If a patient in current practice had nivolumab with chemotherapy as a neo-adjuvant treatment, would they have any chemotherapy regimens as an adjuvant treatment?

Please identify the nature of the data which you understand to be available to enable the committee to take account of these benefits.

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 nivolumab with chemotherapy (as neo-adjuvant) and then nivolumab monotherapy (as adjuvant) 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.

NICE intends to evaluate this technology through its Single Technology Appraisal 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).

References

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