

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Nivolumab in combination with platinum-doublet chemotherapy for untreated non-small-cell lung cancer

Draft scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of nivolumab in combination with platinum-doublet chemotherapy within its marketing authorisation for untreated 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 cancers¹. NSCLC can be further classified into squamous cell carcinoma and non-squamous cell carcinoma. Approximately 70% of NSCLC are of non-squamous histology and can be either large-cell undifferentiated carcinoma or adenocarcinoma². 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, approximately 32,500 people were diagnosed with NSCLC in England, and around 61% had stage IIIB or stage IV disease³.

Lung cancer caused over 35,620 deaths in England in 2016⁴. Thirty two percent of people with lung cancer survive for more than 1 year after diagnosis⁵.

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 programmed cell death 1 ligand [PD-L1] status), histology (squamous or non-squamous) and previous treatment experience. Platinum-based chemotherapy (that is, cisplatin or carboplatin and either gemcitabine, or vinorelbine) may be used as an option for people with untreated stage III or IV NSCLC and good performance status. Alternatively, people may receive pemetrexed in combination with cisplatin if the histology of the tumour has been confirmed as adenocarcinoma or large-cell carcinoma (NICE technology appraisal guidance 181). For non-squamous NSCLC that has not progressed immediately following initial therapy with a NICE-recommended platinum-based chemotherapy regimen, maintenance treatment with pemetrexed is recommended as an option (NICE technology appraisal guidance 190 and 402). For people with non-squamous NSCLC whose PD-L1 tumour proportion

score is between 0% and 49%, atezolizumab in combination with bevacizumab, carboplatin and paclitaxel is currently recommended as an option for use (NICE technology appraisal guidance 584). Pembrolizumab monotherapy is currently recommended for use as an option for people whose tumours express PD-L1 with at least a 50% tumour proportion score and have no EGFR- or ALK-positive mutations (NICE technology appraisal guidance 531).

The technology

Nivolumab (Opdivo, Bristol-Myers Squibb) is a human IgG4 monoclonal antibody targeting the programmed cell death1 receptor (PD-1). Blocking PD-1 may activate T-cell responses and promote an anti-tumour immune response. Nivolumab is administered intravenously.

Nivolumab in combination with platinum doublet chemotherapy does not currently have a marketing authorisation in the UK for previously untreated non-small-cell lung cancer. Nivolumab is being studied in a clinical trial in adults with stage IV or recurrent untreated NSCLC as a monotherapy, in combination with ipilimumab and in combination with platinum-doublet chemotherapy compared with platinum-doublet chemotherapy alone.

Nivolumab has a marketing authorisation in the UK for treating locally advanced or metastatic non-small-cell lung cancer after prior chemotherapy in adults.

Intervention(s)	Nivolumab in combination with platinum-doublet chemotherapy
Population(s)	Adults with untreated stage IV or recurrent NSCLC, who do not have epidermal growth factor receptor or anaplastic lymphoma kinase-positive mutations.

Comparators	<p>For people whose PD-L1 tumour proportion score is at least 50%:</p> <ul style="list-style-type: none"> • Pembrolizumab monotherapy <p>For people with non-squamous NSCLC whose PD-L1 tumour proportion score is between 0% and 49%:</p> <ul style="list-style-type: none"> • Atezolizumab in combination with bevacizumab, carboplatin and paclitaxel • Platinum doublet chemotherapy, with or without pemetrexed maintenance therapy • Pemetrexed in combination with carboplatin, with or without pemetrexed maintenance therapy <p>For people with squamous NSCLC whose PD-L1 tumour proportion score is between 0% and 49%:</p> <ul style="list-style-type: none"> • Gemcitabine or vinorelbine in combination with a platinum drug (carboplatin or cisplatin)
Outcomes	<p>The outcome measures to be considered include:</p> <ul style="list-style-type: none"> • overall survival • progression-free survival • response rate • adverse effects of treatment • health-related quality of life
Economic analysis	<p>The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year.</p> <p>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.</p> <p>Costs will be considered from an NHS and Personal Social Services perspective.</p> <p>The availability of any commercial arrangements for the intervention, comparator or subsequent technologies will be taken into account.</p>

<p>Other considerations</p>	<p>If the evidence allows, subgroup analysis by tumour histology (squamous or non-squamous), tumour stage and by biological markers (for example, PD-L1 expression) will be considered.</p> <p>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.</p>
<p>Related NICE recommendations and NICE Pathways</p>	<p>Related Technology Appraisals:</p> <p>Atezolizumab in combination for treating advanced non-squamous non-small-cell lung cancer (2019). NICE technology appraisal guidance (TA584). Review date June 2022.</p> <p>Pemetrexed for the first-line treatment of non-small-cell lung cancer (2009). NICE technology appraisal 181. Static guidance list.</p> <p>Pemetrexed for the maintenance treatment of non-small-cell lung cancer (2010) NICE technology appraisals guidance (TA190). Static guidance list.</p> <p>Pemetrexed maintenance treatment for non-squamous non-small-cell lung cancer after pemetrexed and cisplatin (2016) NICE technology appraisal guidance (TA402). Review date April 2019</p> <p>Pembrolizumab for untreated PD-L1-positive metastatic non-small-cell lung cancer (2018). NICE technology appraisal guidance (TA531). Review date July 2021</p> <p>Pembrolizumab with pemetrexed and platinum-based chemotherapy for untreated non-small-cell lung cancer (2019) NICE technology appraisals guidance 557.</p> <p>Appraisals in development (including suspended appraisals):</p> <p>Avelumab for untreated PD-L1 positive non-small-cell lung cancer. NICE technology appraisal guidance [ID1261]. Publication date to be confirmed.</p> <p>Atezolizumab with carboplatin and nab-paclitaxel for untreated advanced non-squamous non-small-cell lung</p>

	<p>cancer. NICE technology appraisal guidance [ID1513]. Suspended.</p> <p>Durvalumab for untreated EGFR-negative, ALK-negative non-small-cell lung cancer. NICE technology appraisal guidance [ID1331]. Publication date to be confirmed.</p> <p>Durvalumab with tremelimumab for untreated non-small-cell lung cancer with no EGFR- or ALK-positive mutations. NICE technology appraisal guidance [ID1143]. Publication expected January 2020.</p> <p>Nivolumab monotherapy for non-small-cell lung cancer. NICE technology appraisals guidance [ID1088].Suspended.</p> <p>Nivolumab in combination with ipilimumab for untreated PD-L1-positive non-small-cell lung cancer. NICE technology appraisal [ID1187]. Publication date to be confirmed.</p> <p>Pembrolizumab for untreated PD-L1-positive non-small-cell lung cancer with at least 1% tumour proportion score. NICE technology appraisal guidance [ID1247]. Suspended.</p> <p>Pembrolizumab with carboplatin and paclitaxel for untreated squamous non-small-cell lung cancer NICE technology appraisal guidance [ID1306]. Publication expected July 2019</p> <p>Veliparib with carboplatin and paclitaxel for untreated non-squamous non-small-cell lung cancer. NICE technology appraisal guidance [ID1277]. Publication date to be confirmed.</p> <p>Related Guidelines:</p> <p>Lung cancer: diagnosis and management (2019). NICE guideline NG122.</p> <p>Related Interventional Procedures:</p> <p>Microwave ablation for treating primary lung cancer and metastases in the lung (2013). NICE interventional procedures guidance 469</p> <p>Related Quality Standards:</p> <p>Lung cancer in adults (2019). NICE quality standard 17</p>
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	<p>Related NICE Pathways:</p> <p>Lung cancer (2019) NICE pathway</p>
<p>Related National Policy</p>	<p>The NHS Long Term Plan, 2019. NHS Long Term Plan NHS England (2018/2019) NHS manual for prescribed specialist services (2018/2019)</p> <p>Department of Health and Social Care, NHS Outcomes Framework 2016-2017: Domain 1. https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017</p>

Questions for consultation

Have all relevant comparators for nivolumab in combination with platinum-doublet chemotherapy for untreated non-small-cell lung cancer been included in the scope?

Are the outcomes listed appropriate?

Are the subgroups suggested in 'other considerations 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?

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 incidence by morphology](#). Cancer Research UK. Accessed July 2019.

2 Howlader N, Noone AM, Krapcho M, Garshell J, Miller D, Altekruse SF, et al. SEER Cancer Statistics Review, 1975-2012, National Cancer Institute. 2015 [Available from: https://seer.cancer.gov/csr/1975_2012/]. Accessed July 2019.

3 [National Lung Cancer Audit: Annual report 2017 \(for the audit period 2016\)](#) (2018). Royal College of Physicians. Accessed July 2019.

4 [Lung cancer mortality statistics \(2016\)](#). Cancer Research UK. Accessed July 2019.

5 [Lung cancer survival statistics \(2010-11\)](#). Cancer Research UK. Accessed July 2019.