NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Durvalumab for untreated metastatic non-small-cell lung cancer with no EGFR- or ALK-positive mutations

Draft scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of durvalumab within its marketing authorisation for untreated metastatic non-small-cell lung cancer with no EGFR- or ALK-positive mutations.

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 cancers. NSCLC can be further classified into 3 histological sub-types of large-cell undifferentiated carcinoma, squamous cell carcinoma and adenocarcinoma. 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, of whom 53% had stage IV disease[1]. Around a third of people with lung cancer survive for more than 1 year after diagnosis[2], however this is reduced to a fifth of people diagnosed at stage IV[3].

For the majority of people with NSCLC, the aims of therapy are to prolong survival and improve quality of life. Treatment choices may be influenced by the presence of biological markers (such as the checkpoint inhibitor programmed death-ligand 1 [PD-L1] and mutations in epidermal growth factor receptor-tyrosine kinase [EGFR-TK] or anaplastic-lymphoma-kinase [ALK], or), histology (squamous or non-squamous) and previous treatment experience.

NICE clinical guideline 121 (CG121 'Lung cancer') recommends platinum-combination chemotherapy (that is, cisplatin or carboplatin, and either docetaxel, gemcitabine, paclitaxel, or vinorelbine) as an option for people with previously 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 people who are unable to tolerate a platinum combination, the clinical guideline recommends single-agent chemotherapy with docetaxel, gemcitabine, paclitaxel, or vinorelbine. NICE technology appraisal guidance 531 recommends pembrolizumab monotherapy as an option for untreated PD-L1-positive metastatic NSCLC if the tumour expresses PD-L1 with at least 50% tumour proportion score and has no EGFR- or ALK-positive mutations.

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 NICE technology appraisal guidance 402).

The technology

Durvalumab (Imfinzi, AstraZeneca) is a human monoclonal antibody directed against programmed cell death ligand-1 (PD-L1). Durvalumab blocks PD-L1 interaction with both PD-1 and CD80 on T cells, countering the tumour's immune-evading tactics and activating the patient's immune system to attack the cancer. It is administered intravenously.

Durvalumab does not currently have a marketing authorisation for untreated metastatic non-small-cell lung cancer with no EGFR- or ALK-positive mutations. It has been studied in randomised clinical trials compared with platinum-based chemotherapy in adults with untreated metastatic NSCLC with no sensitizing EGFR mutation or ALK rearrangement.

Intervention	Durvalumab
Population	Adults with untreated metastatic NSCLC with no EGFR- or ALK-positive mutations

Comparators	• Pemetrexed in combination with a platinum drug (carboplatin or cisplatin) (for people with adenocarcinoma or large-cell carcinoma only)
	  ○ with (following cisplatin-containing regimens only) or without pemetrexed maintenance treatment
	• Chemotherapy (docetaxel, gemcitabine, paclitaxel or vinorelbine) in combination with a platinum drug (carboplatin or cisplatin)
	  ○ with (for people with non-squamous NSCLC only) or without pemetrexed maintenance treatment
	• Single agent chemotherapy (docetaxel, gemcitabine, paclitaxel, or vinorelbine) (for people for whom platinum combination therapy is not appropriate)
	• Pembrolizumab monotherapy (for people with tumours that express PD-L1 with at least 50% tumour proportion score with no EGFR- or ALK-positive tumour mutations only)

Outcomes	The outcome measures to be considered include:

	• overall survival • progression-free survival • response rates • 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 patient access schemes for the intervention or comparator technologies will be taken into account. If appropriate, the economic modelling should include the costs associated with diagnostic testing for biological markers or mutations (EGFR and ALK) in people with NSCLC who would not otherwise have been tested. A sensitivity analysis should be provided without the cost of the diagnostic test. See section 5.9 of the Guide to the Methods of Technology Appraisals.
Other considerations	If the evidence allows, consideration will be given to subgroups based on cancer histology and biological markers (PD-L1). 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 and NICE Pathways	**Related Technology Appraisals** 'Pembrolizumab for untreated PD-L1-positive metastatic non-small-cell lung cancer' (2018). NICE Technology Appraisal 531. Review date July 2021. 'Necitumumab for untreated advanced or metastatic squamous non-small-cell lung cancer' (2016) NICE technology appraisal 411. Review date September 2019. 'Pemetrexed maintenance treatment for non-squamous

	non-small-cell lung cancer after pemetrexed and cisplatin' (2016). NICE Technology Appraisal 402. Review date August 2019. 'Pemetrexed for the maintenance treatment of non-small-cell lung cancer' (2010). NICE Technology Appraisal 190. Static guidance list. 'Pemetrexed for the first-line treatment of non-small-cell lung cancer' (2009). NICE Technology Appraisal 181. Static guidance list. **Appraisals in development (including suspended appraisals)** 'Pembrolizumab with pemetrexed and platinum-based chemotherapy for untreated non-small-cell lung cancer' NICE technology appraisals guidance [ID1173]. Publication expected March 2019. 'Nivolumab in combination with ipilimumab for untreated non-small-cell lung cancer that has a high tumour mutational burden' NICE technology appraisals guidance [ID1187]. Expected publication May 2019. 'Pembrolizumab for untreated PD-L1-positive non-small-cell lung cancer with at least 1% tumour proportion score' NICE technology appraisals guidance [ID1247]. Publication date to be confirmed. 'Durvalumab with tremelimumab for untreated non-small-cell lung cancer with no EGFR- or ALK-positive mutations' NICE technology appraisals guidance [ID1143]. Expected publication January 2019. 'Nivolumab in combination with platinum-doublet chemotherapy for untreated PD-L1-negative non-small-cell lung cancer' NICE technology appraisals guidance [ID1135]. Publication date to be confirmed. 'Pembrolizumab with carboplatin and paclitaxel for untreated squamous non-small-cell lung cancer' NICE technology appraisals guidance [ID1306]. Publication date to be confirmed. 'Nivolumab monotherapy for non-small-cell lung cancer' NICE technology appraisals guidance [ID1088]. Suspended. **Related Guidelines** 'Lung cancer: diagnosis and management' (2011). NICE clinical guideline 121. Review in progress. **Guidelines in development** 'Lung cancer: diagnosis and management (update)'.

	Publication expected February 2019. **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' (2012). NICE quality standard 17. **Related NICE Pathways** Lung cancer (2017) NICE pathway.
Related National Policy	NHS England (2017) Manual for prescribed specialised services. Chapter 105: Specialist cancer services (adults). Department of Health (2016) NHS Outcomes Framework 2016-2017. Domains 1, 2, 4 and 5. NHS England (2016) Implementing the cancer taskforce recommendations: Commissioning person centred care for people affected by cancer Department of Health (2014) Improving outcomes: a strategy for cancer. Fourth annual report

Questions for consultation

Have all relevant comparators for durvalumab been included in the scope? Which treatments are considered to be established clinical practice in the NHS for untreated metastatic non-small-cell lung cancer with no EGFR- or ALK-positive mutations?

Are the outcomes listed appropriate?

Are the subgroups suggested in 'other considerations appropriate? Are there any other subgroups of people in whom durvalumab is expected to be more clinically effective and cost effective or other groups that should be examined separately?

Where do you consider durvalumab will fit into the existing NICE pathway for lung cancer?

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 durvalumab 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 durvalumab 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 durvalumab 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.

To help NICE prioritise topics for additional adoption support, do you consider that there will be any barriers to adoption of this technology into practice? If yes, please describe briefly.

NICE intends to appraise this technology through its Single Technology Appraisal (STA) Process. We welcome comments on the appropriateness of appraising this topic through this process. (Information on the Institute's Technology Appraisal processes is available at http://www.nice.org.uk/article/pmg19/chapter/1-Introduction).

References

[1] Royal College of Physicians National Lung Cancer Audit annual report 2017 (for the audit period 2016). Accessed August 2018.
[2] Royal College of Physicians National Lung Cancer Audit annual report 2017 (for the audit period 2016). Accessed August 2018.
[3] Cancer Research UK Lung cancer survival statistics (2014 data). Accessed August 2018.

