NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Durvalumab for maintenance treatment of unresectable non-small cell lung cancer whose disease has not progressed after platinum-based chemoradiation therapy

Draft scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of durvalumab within its marketing authorisation for the maintenance treatment of unresectable non-small-cell lung cancer after platinum-based chemoradiation therapy.

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).

Cancer cells expressing an immunologic marker called programmed cell death 1 ligand (PD-L1) are believed to suppress certain immune responses and cause increased tumor aggressiveness. The proportion of NSCLC that is PD-L1 positive in England is unknown.

In 2014 approximately 37,453 people were diagnosed with NSCLC in England and there were 28,849 NSCLC deaths.[1] Approximately 30% of men and 35% of women survive lung cancer for at least one year after diagnosis.[1]

For the majority of people with NSCLC, the aims of treatment are to prolong survival and improve quality of life. Treatment choices may be influenced by the presence of biological markers (such as mutations in EGFR-TK, ALK or PD-L1 status), histology (squamous or non-squamous) and previous treatment experience. NICE clinical guideline 121 (CG121) recommends platinum-based chemotherapy as an option for people with previously untreated stage III or IV NSCLC and good performance status. NICE technology appraisal 190 (TA190) recommends pemetrexed as an option for the maintenance treatment of people with locally advanced or metastatic non-small-cell lung cancer other than predominantly squamous cell histology if disease has not progressed immediately following platinum-based chemotherapy in combination with gemcitabine, paclitaxel or docetaxel. NICE technology appraisal 402 (TA402) recommends pemetrexed as an option for

the maintenance treatment of locally advanced or metastatic non‑squamous non‑small‑cell lung cancer in adults when their disease has not progressed immediately after 4 cycles of pemetrexed and cisplatin induction therapy and their Eastern Cooperative Oncology Group (ECOG) performance status is 0 or 1 at the start of maintenance treatment.

The technology

Durvalumab (Imfinzi, AstraZeneca) is an investigational human monoclonal antibody directed against programmed 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.

Durvalumab does not currently have a marketing authorisation for treating unresectable non-small-cell lung cancer after platinum-based chemoradiation. It has studied in clinical trials as monotherapy in people with locally advanced, unresectable non-small cell lung cancer (Stage III) whose disease has not progressed following at least 2 cycles of platinum-based chemotherapy with concurrent radiation therapy.

Intervention(s)	Durvalumab
Population(s)	Adults with locally advanced, unresectable non-small cell lung cancer whose disease has not progressed after platinum-based chemotherapy with concurrent radiation therapy
Comparators	• Pemetrexed • Best supportive care
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.
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 and NICE Pathways	Related Technology Appraisals: Pemetrexed maintenance treatment for non-squamous non-small-cell lung cancer after pemetrexed and cisplatin (2016). NICE technology appraisal guidance 402. Review Date August 2019. Pemetrexed for the maintenance treatment of non-small-cell lung cancer (2010). NICE technology appraisal guidance 190. Added to the static list Dec 2014 Related Guidelines: The diagnosis and treatment of lung cancer (2011). NICE clinical guideline 121. Review date TBC. Related Quality Standards: 'Quality standard for lung cancer (2012). NICE quality standard 17. http://www.nice.org.uk/guidance/qualitystandards/qualitystandards.jsp Related NICE Pathways: Lung cancer. Pathway created: Mar 2012. http://pathways.nice.org.uk/pathways/lung-cancer
Related National Policy	NHS England (2016) Manual for Prescribed Specialised Services 2016/17. See section 105 – specialist cancer services, pp 228-. NHS England (2015) Non-small-cell lung cancer.

	National chemotherapy algorithm. This is commercial in confidence NHS England. 2013/14 NHS Standard Contract for Radiotherapy (All ages). B01/S/a NHS England. 2013/14 NHS Standard Contract for Chemotherapy (All ages). B15/S/a NHS England (April 2013). Clinical Commissioning Policy: Stereotactic Ablative Body Radiotherapy for Non-Small-Cell Lung Cancer (Adult). NHSCB/B01/P/a Department of Health (2016) NHS outcomes framework 2016 to 2017 Independent Cancer Taskforce (2015) Achieving world-class cancer outcomes: a strategy for England 2015-2020 Department of Health (2014) The national cancer strategy: 4th annual report Department of Health (2011) Improving outcomes: a strategy for cancer Department of Health (2009) Cancer commissioning guidance Department of Health (2007) Cancer reform strategy

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 unresectable non-small-cell lung cancer in the maintenance setting?

How should best supportive care be defined?'

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? http://pathways.nice.org.uk/pathways/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 is/are/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).

NICE has published an addendum to its guide to the methods of technology appraisal (available at https://www.nice.org.uk/Media/Default/About/what-we-do/NICE-guidance/NICE-technology-appraisals/methods-guide-addendum-cost-comparison.pdf), which states the methods to be used where a cost

comparison case is made. We welcome comments on the appropriateness and suitability of the cost comparison methodology to this topic.

- Is the new technology likely to be similar in its clinical efficacy and resource use to any of the comparators?

- Is the primary outcome that was measured in the trial or used to drive the model for the comparator(s) still clinically relevant?

- Is there any substantial new evidence for the comparator technologies that has not been considered? Are there any important ongoing trials reporting in the next year?

References

1. Cancer Research UK (2014) Lung cancer statistics. Accessed August 2017