NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Nivolumab with chemotherapy for neoadjuvant treatment of early non-small-cell lung cancer

Draft scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of nivolumab with chemotherapy within its marketing authorisation for treatment of early non-small cell lung cancer.

Background

Lung cancer falls into 2 main histological categories: 85-90% are non-small-cell lung cancers (NSCLC) and 10-15% are small-cell lung cancers[1]. Most lung cancers are diagnosed at an advanced stage, when the cancer has spread to lymph nodes and other organs in the chest. Around 20% of patients with NSCLC present with early-stage disease at initial diagnosis[2].

Lung cancer can be classified by stage according to how large the cancer is and where it has spread[3]:

- In stage I, the cancer is small and has not spread to the lymph nodes or other distant organs (stage I can be divided into IA, where the cancer is less than 3cm in size and IB, where the cancer is between 3-4cm in size)
- In Stage IIA, the cancer is between 4-5cm in size but there are no cancer cells in any lymph nodes
- In stage IIB, the cancer is up to 5cm in size and has spread into nearby lymph nodes or
    - the cancer is between 5cm and 7cm but has not spread into any lymph nodes or
    - there is more than one area of cancer in one lobe of the lung or
    - the cancer has spread into structures close to the lung
- In stage III, the cancer is in more than one lobe of the lung, or it has spread to lymph nodes or nearby structures in the chest (Stage III can be divided into IIIA, IIIB and IIIC)
- In stage IV, the cancer has spread to another part of the lungs or to other parts of the body

In 2017, 39,205 people were diagnosed with NSCLC in England and Wales[4]. In England between 2013 to 2017 the age-standardised net cancer survival rate at 5-years for stage I, II and III were 56.6%, 34.1% and 12.6% respectively[5].

Treatment for NSCLC differs by stage[6]. For stage I and II NSCLC, the main treatment option is surgery, consisting of either a lobectomy (removal of part

of the lung) or a pneumonectomy (removal of all of the lung), potentially followed by chemotherapy (adjuvant) or radiotherapy.

For patients that are not well enough to undergo surgery, treatment consists of either radiotherapy or radiofrequency ablation. For people with stage I–II NSCLC that are suitable for surgery, neoadjuvant chemotherapy is not currently recommended by NICE guideline NG122 outside a clinical trial. As neoadjuvant chemotherapy has shown equivalent outcomes in terms of survival to adjuvant chemotherapy[6].

For stage III NSCLC, surgery is carried out if the surgeon deems the tumour to be excisable. Before surgery, chemoradiotherapy may be given (chemotherapy with radiotherapy) or surgery may potentially be followed by chemotherapy[7]. If surgery is not possible, patients may undergo treatments including chemotherapy or radiotherapy which may be followed by immunotherapy.

The technology

Nivolumab (Opdivo, Bristol-Myers Squibb) is a fully humanised IgG4 monoclonal antibody which targets and blocks the programmed cell death-1 receptor (PD-1), to promote an anti-tumour immune response. It is administered intravenously.

Nivolumab with chemotherapy does not currently have a marketing authorisation in the UK for the neoadjuvant treatment of early stage NSCLC. It has been studied in clinical trials with chemotherapy in early stage (stages IB to IIIB) operable NSCLC.

Intervention(s)	Nivolumab with chemotherapy
Population(s)	Early stage IB-IIIB operable NSCLC
Comparators	Established clinical management without nivolumab with chemotherapy
Outcomes	The outcome measures to be considered include: • progression-free survival • overall survival • response rate • 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 of any managed access arrangement for the intervention will be taken into account.
Other considerations	If evidence allows, results by disease stage will be considered 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: None Terminated appraisals: None Appraisals in development (including suspended appraisals) None Related Guidelines: 'Lung cancer: diagnosis and management' (2019). NICE guideline NG122. Related Quality Standards: 'Lung cancer in adults' (2019). NICE quality standard 1 Related NICE Pathways: 'Lung cancer' (2019) NICE pathway
Related National Policy	The NHS Long Term Plan, 2019. NHS Long Term Plan NHS England (2018) Manual for prescribed specialised

	services 2018/19 Chapter 105: Specialist cancer services (adults). Department of Health and Social Care, NHS Outcomes Framework 2016-2017: Domains 1,2 and 4. https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017

Questions for consultation

Have all relevant comparators for nivolumab with chemotherapy been included in the scope?

Which treatments are considered to be established clinical practice in the NHS for early stage (stages IB to IIIB) operable NSCLC? How does this differ by stage?

Which treatments are considered to be established clinical practice in the NHS following surgery in early stage (stages IB to IIIB) operable NSCLC?

Are the outcomes listed appropriate?

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

Where do you consider nivolumab with chemotherapy will fit into the existing NICE pathway 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 the treatment 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 nivolumab with chemotherapy 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 nivolumab with chemotherapy 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.

References

1. Lung cancer incidence by morphology. Cancer Research UK. Accessed February 2021
2. Blandin Knight S, Crosbie PA, Balata H, et al. Progress and prospects of early detection in lung cancer. Open Biol. 2017;7(9):170070.
3. Lung cancer staging. Cancer Research UK
4. Lung cancer mortality statistics (2016). Cancer Research UK. (accessed July 2020)
5. Office for National Statistics. Cancer Survival in England: adults diagnosed between 2013 and 2017 and followed up to 2018. 2019. Available from: https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/conditionsanddiseases/datasets/cancersurvivalratescancersurvivalinenglandadultsdiagnosed [accessed February 2021].
6. European Society for Medical Oncology (ESMO). Early and locally advanced non-small-cell lung cancer (NSCLC): ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Annals of Oncology. 2017;28(Supplement 4):iv1–iv21. Available from: https://www.esmo.org/Guidelines/Lung-and-Chest-Tumours/ (accessed February 2021)
7. Stage 3 lung cancer. Cancer Research UK, (accessed February 2021)

