NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal

Nivolumab for maintenance treatment of extensive-stage small-cell lung cancer after chemotherapy

Draft scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of nivolumab within its marketing authorisation for maintenance treatment of extensive-stage small-cell lung cancer after chemotherapy.

Background

Lung cancer falls into two main histological categories: non-small-cell lung cancers and small-cell lung cancers. Small-cell lung cancer (SCLC) is a type of lung cancer that grows rapidly and spreads quickly to other parts of the body. SCLC can be classified as limited disease (cancer has not spread beyond one lung or nearby lymph nodes) or extensive-stage disease (the cancer has spread beyond one lung)[1]. Common symptoms of SCLC include weight loss, malaise, bone pain, breathlessness and haemoptysis.

In 2016 there were 38,381 people diagnosed with lung cancer registered in England[2]. Around 12% of lung cancer diagnoses are SCLC[3]. The prognosis for patients with SCLC is poor, with a 5-year survival rate of 5%[4]. An estimated 66% of those with SCLC will receive platinum-based combination chemotherapy as a first therapy[5].

The aims of therapy for people with extensive-stage disease are to prolong survival and improve quality of life[3]. The NICE lung cancer clinical guideline 121 recommends that all patients with untreated extensive stage SCLC should be offered platinum-based combination chemotherapy, for a maximum of six cycles. The disease response and drug toxicity should be assessed before each cycle. In clinical practice, patients may receive etoposide in combination with a platinum therapy, or where etoposide is contraindicated, patients may receive irinotecan in combination with cisplatin or gemcitabine in combination with carboplatin (in patients with poor prognosis). Radiotherapy may be given concurrently with chemotherapy or as part of palliative care. Additional cycles of chemotherapy (called maintenance chemotherapy) to prevent or delay the cancer's return are recommended by NICE guideline CG121 only in the context of a clinical trial.

The technology

Nivolumab (Opdivo, Bristol-Myers Squibb) is a fully humanised IgG4 monoclonal antibody which targets and blocks the programmed cell death-1

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receptor (PD-1), to promote an anti-tumour immune response. It is administered intravenously. Nivolumab does not currently have a marketing authorisation in the UK for SCLC.

Nivolumab has been studied in a phase III clinical trial, as a monotherapy and in combination with ipilimumb compared with placebo in adults with extensive SCLC after completion of 1 systemic therapy (that is as a maintenance therapy).

Intervention(s)	Nivolumab monotherapy and/or nivolumab in combination with ipilimumab
Population(s)	Adults with extensive-stage small-cell lung cancer that is stable or responding after chemotherapy
Comparators	Established clinical management without nivolumab
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.
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	**Related Technology Appraisals:**

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recommendations and NICE Pathways	Topotecan for the treatment of relapsed small-cell lung cancer (2009). NICE Technology Appraisal 184. Placed on the static list in 2013. Suspended/discontinued Nivolumab with ipilimumab for previously treated extensive stage small-cell lung cancer ID1228. NICE technology appraisal guidance. Publication date to be confirmed. *Suspended 31/08/2018: Following an update from the company, NICE has decided to suspend this appraisal on its current work programme.* **Related Guidelines:** Lung cancer: diagnosis and treatment (2011). NICE guideline 121. Reviewed March 2016. Review decision: guideline to be updated. **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 (2016) NICE pathway** http://pathways.nice.org.uk/
Related National Policy	**NHS England:** NHS England (May 2017) Manual for prescribed specialised services 2017/18, Chapter 105: Specialist cancer services (adults) and Chapter 18: Adult thoracic surgery services. NHS England (2017/19) Standard contract for cancer: chemotherapy (adult) **Department of Health:** Department of Health (2011) Improving Outcomes: A Strategy for Cancer Department of Health (2016) NHS Outcomes Framework 2016-2017. Domains 1 and 2.

Questions for consultation

Is the intervention defined appropriately? In particular, is nivolumab expected to be used as a monotherapy or in combination with ipilimumab for maintenance treatment of extensive-stage SCLC?

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Is the population defined appropriately?

Is the comparator defined appropriately? In particular

- Which treatments are considered to be established clinical practice in the NHS for extensive-stage small-cell lung cancer (after completion of first line chemotherapy?
- Is best supportive care an appropriate comparator, if so, how should best supportive care be defined?

Are the outcomes listed appropriate?

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

Where do you consider nivolumab 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 nivolumab 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 that nivolumab 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 can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation?

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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. Kalemkerian GP, Schneider BJ. Advances in Small Cell Lung Cancer. Hematol Oncol Clin North Am. 2017; 31(1):143-156 (Accessed September 2018)
2. Office for National Statistics (2016) Cancer registration statistics. (Accessed September 2018)
3. Cancer Research UK, Lung cancer (Accessed September 2018)
4. Alvarado-Luna G, Morales-Espinosa D. Treatment for small cell lung cancer, where are we now?—a review. Transl Lung Cancer Res 2016;5(1):26-38 (Accessed September 2018)
5. Khakwani A, Rich AL, Tata LJ et al. Small-Cell Lung Cancer in England: Trends in Survival and Chemotherapy Using the National Lung Cancer Audit. PLOS ONE. 2014. 9 (2) e89426 (Accessed September 2018)
6. European Society for Medical Oncology. (2013). Small-cell lung cancer: ESMO Clinical Practice Guidelines. (Accessed September 2018)

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