NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Durvalumab in combination for untreated extensive stage small-cell lung cancer

Draft scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of durvalumab within its marketing authorisation for treating extensive stage small-cell lung cancer.

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 that is contained in a single area that can be treated with radiotherapy for example, one lung or nearby lymph nodes) or extensive-stage disease (cancer that has spread beyond a single area that can be treated with radiotherapy for example, to the other lung or to other parts of the body)[1]. Common symptoms of SCLC include weight loss, malaise, bone pain, breathlessness and haemoptysis.

In 2017 there were 38,906 cases of lung cancer registered in England[2]. Around 12% of lung cancer cases are SCLC[3]. The prognosis for patients with extensive-stage SCLC is poor, with a 5-year survival rate of 10%[4]. An estimated 66% of those with extensive-stage 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 guideline 122 for Lung cancer: diagnosis and management 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)[6]. Thoracic radiotherapy with prophylactic cranial irradiation can be offered after chemotherapy if there has been a partial or complete response to chemotherapy within the thorax and at distant sites.

However, for 95 to 100% of people with extensive-stage SCLC treated with first line platinum-based combination chemotherapy, the disease will not respond to treatment or will eventually relapse. 40% of people whose disease relapses or does not respond will have second line chemotherapy. Radiotherapy can be offered for the palliation of local symptoms.

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 in combination with platinum-based chemotherapy regimens with or without tremelimumab does not currently have a marketing authorisation in the UK for small-cell lung cancer. Durvalumab with platinum based chemotherapy with or without tremelimumab has been studied in a clinical trial in people with untreated extensive stage small-cell lung cancer compared with platinum based chemotherapy alone.

Intervention(s)	Durvalumab in combination with platinum-based chemotherapy regimens with or without tremelimumab
Population	Adults with untreated extensive-stage small-cell lung cancer
Comparators	• Established clinical management without durvalumab (including but not limited to platinum-based chemotherapy regimens) • Atezolizumab (subject to ongoing NICE appraisal)
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 commercial arrangements for the intervention, comparator and subsequent treatment 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 recommendations	**Related Technology Appraisals:**

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. **Appraisals in development (including suspended appraisals)** Atezolizumab with carboplatin and etoposide for untreated extensive-stage small-cell lung cancer [ID1504]. Publication expected December 2019. **Related Guidelines:** Lung cancer: diagnosis and treatment (2019). NICE guideline 122. March 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 (2019) NICE pathway** https://pathways.nice.org.uk/pathways/lung-cancer
Related National Policy	The NHS Long Term Plan, 2019. NHS Long Term Plan NHS England (2018/2019) NHS manual for prescribed specialist services (2018/2019). 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 and Social Care, NHS Outcomes Framework 2016-2017: Domains 1 and 2. https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017

Questions for consultation

What treatments are currently used in clinical practice for untreated extensive-stage small-cell lung cancer?

Have all relevant comparators for durvalumab in combination with platinum-based chemotherapy regimens with or without tremelimumab been included in the scope?

Are the outcomes listed appropriate?

Are there any subgroups of people in whom durvalumab in combination with platinum-based chemotherapy regimens with or without tremelimumab is expected to be more clinically effective and cost effective or other groups that should be examined separately?

Where do you consider durvalumab in combination with platinum-based chemotherapy regimens with or without tremelimumab 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 durvalumab in combination with platinum-based chemotherapy regimens with or without tremelimumab 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 in combination with platinum-based chemotherapy regimens with or without tremelimumab 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 in combination with platinum-based chemotherapy regimens with or without tremelimumab 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. Kalemkerian GP, Schneider BJ. Advances in Small Cell Lung Cancer. Hematol Oncol Clin North Am. 2017; 31(1):143-156 (Accessed July 2019)

2. Office for National Statistics (2017) Cancer registration statistics. (Accessed July 2019)
3. Cancer Research UK, Lung cancer (Accessed July 2019)
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 July 2019)
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 July 2019)
6. European Society for Medical Oncology. (2013). Small-cell lung cancer: ESMO Clinical Practice Guidelines. (Accessed July 2019)

