NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Atezolizumab for untreated non-squamous non-small-cell lung cancer

Draft scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of atezolizumab within its marketing authorisation for untreated non-squamous non-small-cell lung cancer.

Background

Lung cancer falls into two main histological categories: 88.5% are non-small-cell lung cancers (NSCLC) and 10% are small-cell lung cancers[1]. NSCLC can be further classified into squamous cell carcinoma and non-squamous cell carcinoma. Non-squamous cell carcinoma can be either large-cell undifferentiated carcinoma or adenocarcinoma. About 22% of lung cancers are squamous cell carcinomas[1]. 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, and around 61% had stage IIIB or stage IV disease[1].

Lung cancer caused over 28,800 deaths in England in 2014[2]. Thirty two percent of people with lung cancer survive for more than 1 year after diagnosis[3].

For the majority of people with NSCLC, the aims of treatment are to prolong survival and improve quality of life. Treatment choices are influenced by the presence of biological markers (such as mutations in epidermal growth factor receptor-tyrosine kinase [EGFR-TK], anaplastic-lymphoma-kinase [ALK] or PD-L1 status), histology (squamous or non-squamous) and previous treatment experience. NICE clinical guideline 121 recommends platinum-based chemotherapy (that is, cisplatin or carboplatin and either docetaxel, gemcitabine, paclitaxel, or vinorelbine) as an option for people with 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 untreated, advanced, non-squamous NSCLC that is epidermal growth factor receptor tyrosine kinase (EGFR-TK) mutation-positive, people may receive:

- afatinib (NICE technology appraisal 310)

- erlotinib (NICE technology appraisal 258) or
- gefitinib (NICE technology appraisal 192).

For untreated, advanced, non-squamous NSCLC that is anaplastic lymphoma kinase (ALK)-positive, people may receive:

- ceritinib (NICE technology appraisal 500) or
- crizotinib (NICE technology appraisal 406).

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 402).

Pembrolizumab is currently recommended within the Cancer Drugs Fund as a treatment option for untreated PD-L1-positve metastatic NSCLC if the tumour expresses PD-L1 with at least 50% tumour proportion score (NICE technology appraisal guidance 447). The company that manufactures pembrolizumab was required to collect data from the KEYNOTE-024 trial in line with the managed access agreement. This guidance is currently under review in the NICE Cancer Drugs Fund review process.

The technology

Atezolizumab (Tecentriq, Roche) is a humanised, anti-programmed cell death ligand-1 (PD-L1) monoclonal antibody involved in the blockade of immune suppression and the subsequent reactivation of anergic T-cells. It is administered intravenously.

Atezolizumab does not currently have a marketing authorisation in the UK for untreated NSCLC. It has been studied in phase 3 clinical trials as monotherapy and in combination with a platinum drug (carboplatin or cisplatin) and paclitaxel (with or without bevacizumab) or pemetrexed, compared with a platinum drug and either pemetrexed or paclitaxel and bevacizumab, in people with metastatic, non-squamous NSCLC who had not had chemotherapy.

Intervention(s)	Atezolizumab as monotherapy or with a platinum-based drug plus paclitaxel (with or without bevacizumab) or pemetrexed
Population(s)	Adults with advanced, untreated non-squamous NSCLC.

Comparators	• Chemotherapy (docetaxel, gemcitabine, paclitaxel or vinorelbine) in combination with a platinum drug (carboplatin or cisplatin)
	  ○ with or without pemetrexed maintenance treatment
	• Pemetrexed with a platinum drug (carboplatin or cisplatin) (for adenocarcinoma or large cell carcinoma only)
	  ○ with (following cisplatin-containing regimens only) or without pemetrexed maintenance treatment
	For tumours expressing PD-L1 [with at least a 50% tumour proportion score] and no EGFR or ALK-positive mutations)
	• Pembrolizumab (NICE guidance is in development, funded by the Cancer Drugs Fund in the interim)
	For ALK-positive advanced NSCLC
	• Afatinib
	• Erlotinib
	• Gefitinib
	For EGFR-TK-positive advanced NSCLC
	• Ceritinib
	• Crizotinib

Outcomes	The outcome measures to be considered include: • overall survival • progression-free 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. If the technology is likely to provide similar or greater health benefits at similar or lower cost than technologies recommended in published NICE technology appraisal guidance for the same indication, a cost-comparison may be carried out. 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. If evidence allows, subgroup analysis by level of PD-L1 expression will be considered. The availability of any patient access schemes for the intervention or comparator technologies will be taken into account.
Other considerations	If the evidence allows, consideration will be given to subgroups based on the PD-L1 biological marker. 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: Afatinib for treating epidermal growth factor receptor mutation-positive locally advanced or metastatic non-small-cell lung cancer (2014) NICE technology appraisal 310. Ceritinib for untreated ALK-positive non-small-cell lung cancer (2018) NICE technology appraisal 500. Review date January 2021. Crizotinib for untreated anaplastic lymphoma kinase-positive advanced non-small-cell lung cancer (2016) NICE technology appraisal 406. Review date September 2019. Erlotinib for the first-line treatment of locally advanced or metastatic EGFR-TK mutation-positive non-small-cell lung cancer (2012) NICE technology appraisal 258.

	Static guidance list. Gefitinib for the first-line treatment of locally advanced or metastatic non-small-cell lung cancer (2010) NICE technology appraisal 192. Static guidance list. Pembrolizumab for untreated PD-L1-positive metastatic non-small-cell lung cancer (2017) NICE technology appraisal 447. Review in progress. Pemetrexed for the first-line treatment of non-small-cell lung cancer (2009) NICE technology appraisal 181. Static guidance list. Pemetrexed for the maintenance treatment of non-small-cell lung cancer (2010) NICE technology appraisals guidance 190. Static guidance list. Pemetrexed maintenance treatment for non-squamous non-small-cell lung cancer after pemetrexed and cisplatin (2016) NICE technology appraisal guidance 402. Review date April 2019. Terminated appraisals Bevacizumab for treating EGFR mutation-positive non-small-cell lung cancer (terminated appraisal) (2017) NICE technology appraisal 436 Bevacizumab for the treatment of non-small-cell lung cancer (terminated appraisal) (2008) NICE technology appraisal 148 Appraisals in development (including suspended appraisals): Alectinib for untreated anaplastic lymphoma kinase-positive advanced non-small-cell lung cancer. NICE technology appraisal guidance [ID925]. Expected publication August 2018. Atezolizumab for treating non-small-cell lung cancer after platinum-based chemotherapy. NICE technology appraisal guidance [ID970]. Publication date to be confirmed. Avelumab for untreated PD-L1 positive non-small-cell lung cancer. NICE technology appraisal guidance [ID1261]. Publication date to be confirmed. Cimavax for treating wild-type EGFR-positive non-small-cell lung cancer. NICE technology appraisal guidance [ID1259]. Publication date to be confirmed.

	Crizotinib for treating ROS1-positive advanced non-small-cell lung cancer. NICE technology appraisal guidance [ID1098]. Publication expected May 2018. Dabrafenib with trametinib for treating advanced, metastatic BRAF V600E mutation-positive non-small-cell lung cancer. NICE technology appraisal guidance [ID929]. Publication date to be confirmed. Durvalumab with tremelimumab for untreated non-small-cell lung cancer with no EGFR- or ALK-positive mutations. NICE technology appraisal guidance [ID1143]. Publication expected January 2019. Nivolumab in combination with ipilimumab for untreated PD-L1-positive non-small-cell lung cancer. NICE technology appraisal guidance [ID1187]. Publication date to be confirmed. Nivolumab in combination with platinum-doublet chemotherapy for untreated PD-L1-negative non-small-cell lung cancer. NICE technology appraisal guidance [ID1135]. Publication date to be confirmed. Nivolumab monotherapy for non-small-cell lung cancer. NICE technology appraisal guidance [ID1088]. Suspended. Osimertinib for untreated EGFR-positive non-small-cell lung cancer. NICE technology appraisal guidance [ID1302]. Publication expected January 2019. Pembrolizumab for untreated PD-L1 positive metastatic non-small-cell lung cancer (CDF review of TA447). NICE technology appraisal guidance [ID1349]. Publication expected July 2018. Pembrolizumab for untreated PD-L1 positive non-small-cell lung cancer with at least 1% tumour proportion score. NICE technology appraisal guidance [ID1247]. Publication date to be confirmed. Pembrolizumab with pemetrexed and platinum-based chemotherapy for untreated non-small-cell lung cancer. NICE technology appraisal guidance [ID1173]. Publication date to be confirmed. Veliparib with carboplatin and paclitaxel for untreated non-squamous non-small-cell lung cancer. NICE technology appraisal guidance [ID1277]. Publication date to be confirmed. Related Guidelines: Lung cancer: diagnosis and management (2011). NICE

	guideline CG121. Review in progress. Guidelines in development Lung cancer: diagnosis and management (update). Publication expected March 2019 Related quality standards: Lung cancer in adults (2012). NICE quality standard 17. Related NICE Pathways: Lung cancer (2018) NICE pathway
Related National Policy	NHS England (2017) Manual for prescribed specialised services 2017/18 Chapter 105: Specialist cancer services (adults). Department of Health, NHS Outcomes Framework 2016-2017 (published 2016): Domain 1.

Questions for consultation

Have all relevant comparators for atezolizumab been included in the scope? Which treatments are considered to be established clinical practice in the NHS for advanced, untreated, non-squamous NSCLC?

Are the outcomes listed appropriate?

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

Is testing for PD-L1 expression routine in the NHS for untreated, non-squamous NSCLC?

Where do you consider atezolizumab 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 atezolizumab 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 atezolizumab 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 atezolizumab 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.

- Would it be appropriate to use the cost comparison methodology for 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 comparators 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 National Lung Cancer Audit: Annual report 2017 (for the audit period 2016) (2018). Royal College of Physicians. Accessed March 2018.

2 Lung cancer mortality statistics (2014). Cancer Research UK. Accessed March 2018.

3 Lung cancer survival statistics (2010-11). Cancer Research UK. Accessed March 2018.