NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Atezolizumab monotherapy for untreated advanced non-small-cell lung cancer

Draft scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of atezolizumab monotherapy within its marketing authorisation for untreated advanced 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]. NSCLC can be further classified into squamous cell carcinoma and non-squamous cell carcinoma. Approximately 70% of NSCLC are of non-squamous histology and can be either large-cell undifferentiated carcinoma or adenocarcinoma[2]. 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[3].
Lung cancer caused over 35,620 deaths in England in 2016[4]. Thirty two percent of people with lung cancer survive for more than 1 year after diagnosis[5].

For the majority of people with NSCLC, the aim 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 combination chemotherapy (that is, cisplatin or carboplatin, and either docetaxel, gemcitabine, paclitaxel, or vinorelbine) as an option for people with previously 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 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).
For untreated, metastatic, non-squamous NSCLC people may have atezolizumab in combination (NICE technology appraisal guidance 557) if the tumours express PD-L1 with a tumour proportion score between 0% and 49%.

People whose tumours express PD-L1 (with at least a 50% tumour proportion score) and have no epidermal growth factor receptor or anaplastic lymphoma kinase-positive mutations may receive pembrolizumab (NICE technology appraisal guidance 531).

NICE technology appraisal guidance 557 recommended pembrolizumab, with pemetrexed and platinum chemotherapy with a managed access agreement through the Cancer Drugs Fund for people whose tumours have no epidermal growth factor receptor (EGFR)- or anaplastic lymphoma kinase (ALK)-positive mutations.

For 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).

NICE technology guidance 531 recommended pembrolizumab as an option for untreated PD-L1-positive metastatic NSCLC in adults whose tumours express PD-L1 (with at least a 50% tumour proportion score) and have no epidermal growth factor receptor- or anaplastic lymphoma kinase-positive mutations.

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 monotherapy for untreated metastatic NSCLC does not currently have a marketing authorisation in the UK. It has been studied in a clinical trial which compared atezolizumab monotherapy with platinum chemotherapy and either gemcitabine or pemetrexed in adults with untreated non-squamous or squamous metastatic NSCLC.

Intervention(s)	Atezolizumab
Population(s)	Adults with non-squamous or squamous untreated metastatic NSCLC with PD-L1 tumour expression and without EGFR- or ALK-positive mutations
Comparators	For non-squamous NSCLC: • Pemetrexed in combination with a platinum drug (carboplatin or cisplatin) (for people with adenocarcinoma or large-cell carcinoma only) ○ with (following cisplatin-containing regimens only) or without pemetrexed maintenance treatment

	• Chemotherapy (docetaxel, gemcitabine, paclitaxel or vinorelbine) in combination with a platinum drug (carboplatin or cisplatin) ○ with or without pemetrexed maintenance treatment • Pembrolizumab (for people whose tumours express PD-L1 with at least a 50% tumour proportion score) • Atezolizumab plus bevacizumab, carboplatin and paclitaxel (for people whose tumours express PD-L1 with a tumour proportion score between 0% and 49%) For squamous NSCLC: • Platinum-based chemotherapy (cisplatin or carboplatin and either docetaxel, gemcitabine, paclitaxel, or vinorelbine) • Pembrolizumab (for people whose tumours express PD-L1 with at least a 50% tumour proportion score)
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. 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 the use of atezolizumab is conditional on any relevant diagnostic tests which would not have otherwise been

	tested for, the economic modelling should include the costs associated with the relevant diagnostic tests. A sensitivity analysis should be provided without the cost of the diagnostic tests. See section 5.9 of the Guide to the Methods of Technology Appraisals'. The availability of any patient access schemes for the intervention or comparator technologies will be taken into account.
Other considerations	If evidence allows, subgroup analysis by: • Level of PD-L1 expression • Squamous and non-squamous status 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:** Atezolizumab in combination for treating metastatic non-squamous non-small-cell lung cancer (2019) NICE technology appraisals guidance 584. Pembrolizumab with pemetrexed and platinum-based chemotherapy for untreated non-squamous non-small-cell lung cancer (2019) NICE technology appraisals guidance 557. Pembrolizumab for untreated PD-L1-positive metastatic non-small-cell lung cancer (2018) NICE technology appraisals guidance 531. Review date July 2021. 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. Nintedanib for previously treated locally advanced, metastatic, or locally recurrent non-small-cell lung cancer (2015) NICE technology appraisal guidance 347. Pemetrexed for the maintenance treatment of non-small-cell lung cancer (2010) NICE technology appraisals guidance 190. Static guidance list. Pemetrexed for the first-line treatment of non-small-cell lung cancer (2009) NICE technology appraisal 181.

	Static guidance list. **Appraisals in development (including suspended appraisals):** Atezolizumab with carboplatin or cisplatin and pemetrexed for untreated advanced non-squamous non-small-cell lung cancer NICE Technology Appraisal Guidance [ID1495] 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. Durvalumab with tremelimumab for untreated non-small-cell lung cancer with no EGFR- or ALK-positive mutations. NICE technology appraisal guidance [ID1143]. Suspended. Nivolumab in combination with ipilimumab for untreated PD-L1-positive non-small-cell lung cancer. NICE technology appraisal guidance [ID1187]. Suspended. Nivolumab in combination with platinum-doublet chemotherapy for untreated PD-L1-negative non-small-cell lung cancer. NICE technology appraisal guidance [ID1135]. Suspended. Nivolumab with ipilimumab and chemotherapy for untreated advanced non-small-cell lung cancer NICE technology guidance [ID1566] Publication to be confirmed Nivolumab monotherapy for non-small-cell lung cancer. NICE technology appraisal guidance [ID1088]. Suspended. Pembrolizumab for untreated PD-L1 positive non-small-cell lung cancer with at least 1% tumour proportion score. NICE technology appraisal guidance [ID1247]. Suspended. Veliparib with carboplatin and paclitaxel for untreated non-squamous non-small-cell lung cancer. NICE technology appraisal guidance [ID1277]. Publication date to be confirmed. Atezolizumab with carboplatin and nab-paclitaxel for untreated advanced non-squamous non-small-cell lung cancer. NICE technology appraisal guidance [ID1513]. Suspended. Durvalumab for untreated EGFR-negative, ALK-negative non-small-cell lung cancer. NICE technology appraisal guidance [ID1331]. Suspended.

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, 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 non-squamous or squamous untreated lung cancer with a PD-L1 tumour expression without EGFR- or ALK-positive mutations?

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?

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 is 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 comparator(s) still clinically relevant?

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

References

1. Lung cancer incidence by morphology. Cancer Research UK. Accessed December 2019

2. Howlader N, Noone AM, Krapcho M, Garshell J, Miller D, Altekruse SF, et al. SEER Cancer Statistics Review, 1975-2012, National Cancer Institute. 2015 [Available from: https://seer.cancer.gov/csr/1975_2012/.

3. National Lung Cancer Audit: Annual report 2017 (for the audit period 2016) (2018). Royal College of Physicians. Accessed December 2019.

4. Lung cancer mortality statistics (2016). Cancer Research UK. Accessed December 2019.

5. Lung cancer survival statistics (2010-11). Cancer Research UK. Accessed December 2019.

