NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Cemiplimab with chemotherapy for untreated advanced or metastatic non-small-cell lung cancer ID3949

Draft scope

Draft remit/evaluation objective

To appraise the clinical and cost effectiveness of cemiplimab with chemotherapy within its marketing authorisation for untreated advanced or metastatic NSCLC.

Background

Lung cancer is the third most common cancer and the most common cause of cancer death in the UK, accounting for 13% of all new cancer cases and 21% of all cancer deaths between 2017 and 2019.[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 3) or to other parts of the body (metastatic disease; stage 4). Around 30% of lung cancers are diagnosed at an early stage (stage 1 or 2).[2]

In 2021, 91% (around 31,000) of people diagnosed with lung cancer in England had NSCLC.[2] Of these people, 17% (5,333) had surgical treatment for their cancer.[2] Despite the curative intent of treatment for early-stage lung cancer, survival is poor, with only about 57% people with stage 1, 34% with stage 2 and 13% with stage 3 surviving for 5 years after diagnosis.[3] It is estimated that over half of all NSCLCs express the programmed cell death ligand-1 (PD-L1) biomarker.[4] Cancer cells expressing PD-L1 are believed to suppress certain immune responses which results in a weaker anti-tumour response.[4,5]

The treatment pathway for NSCLC can be divided into interconnected decision points based on the number staging system and line of therapy. Treatment choices are influenced by the presence of biological markers (including programmed cell death 1 ligand PD-L1 status), oncogenic driver genetic alterations, histology (squamous or non-squamous) and previous treatment.

NICE guideline 122 (NG122) 'Lung cancer: diagnosis and management' recommends surgery, radiotherapy, chemoradiotherapy or a combination of these for stage 1 to 2 NSCLC. People may be offered a neo-adjuvant (before surgical removal of cancerous tumour) treatment which could be nivolumab with chemotherapy as recommended by TA876 or may be offered platinum based chemotherapy as neo-adjuvant or adjuvant treatment.

For untreated metastatic non-squamous NSCLC people may be offered pembrolizumab with pemetrexed and platinum chemotherapy (TA683) or pemetrexed and platinum chemotherapy irrespective of PD-L1 expression (based on clinical opinion). If the non-squamous NSCLC expressed PD-L1 on less than 50% of tumour cells, people may be offered atezolizumab plus bevacizumab, carboplatin and paclitaxel (TA584) or pemetrexed with platinum doublet chemotherapy. If the non-

squamous NSCLC expressed PD-L1 on over 50% of tumour cells they may be offered pembrolizumab (TA531) or atezolizumab (TA705) monotherapy

For untreated squamous NSCLC people may be offered pembrolizumab with carboplatin and paclitaxel (TA770) if the NSCLC expresses PD-L1 on less than 50% of cells or on over 50% of cells if there is a need for urgent clinical intervention. If the squamous NSCLC expresses PD-L1 on less than 50% of its tumour cells people may be offered pembrolizumab (TA531) or atezolizumab (TA705) monotherapy. People may also be offered chemotherapy (based on clinical opinion).

The technology

Cemiplimab (Libtayo, Regeneron) with chemotherapy does not currently have a marketing authorisation as a first-line treatment for advanced or metastatic NSCLC. It is being studied in combination with chemotherapy compared to chemotherapy alone in people with advanced or metastatic untreated NSCLC.

Cemiplimab monotherapy currently has a marketing authorisation for first-line treatment of adults with locally advanced (if definitive chemoradiation is not suitable) and metastatic NSCLC which has PD-L1 expression on more than 50% of tumour cells and which has no EGFR, ALK or ROS-1 genetic alterations.

Intervention	Cemiplimab with chemotherapy
Population	People with untreated advanced or metastatic NSCLC which has no EGFR, ALK or ROS-1 genetic alterations
Subgroups	If the evidence allows, the following subgroups will be considered: • Histology • PD-L1 status • Disease stage • Prior surgery or not
Comparators	For people with squamous NSCLC whose tumours express PD-L1 on less than 50% of cells • Chemotherapy (gemcitabine or vinorelbine) in combination with a platinum drug (carboplatin or cisplatin) • Pembrolizumab with carboplatin and paclitaxel ○ With olaparib maintenance (subject to NICE appraisal) For people with squamous NSCLC whose tumours express PD-L1 on 50% or more of cells • Chemotherapy (gemcitabine or vinorelbine) in combination with a platinum drug (carboplatin or cisplatin)

	• Pembrolizumab monotherapy • Atezolizumab monotherapy For people with non-squamous NSCLC whose tumours express PD-L1 on less than 50% of cells • Pembrolizumab with pemetrexed and platinum chemotherapy • Atezolizumab with bevacizumab, carboplatin and paclitaxel • Pemetrexed with platinum doublet chemotherapy For people with non-squamous NSCLC whose tumours express PD-L1 on 50% or more of cells • Pembrolizumab with pemetrexed and platinum chemotherapy • Pembrolizumab monotherapy • Atezolizumab monotherapy • Pemetrexed with platinum doublet chemotherapy
Outcomes	The outcome measures to be considered include: • progression free survival • response rates • overall survival • 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 and cost of biosimilar and generic products should 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:** Pembrolizumab with carboplatin and paclitaxel for untreated metastatic squamous non-small-cell lung cancer (2022) NICE technology appraisals guidance 770. Review date to be confirmed. Atezolizumab in combination for treating metastatic non-squamous non-small-cell lung cancer (2019) NICE technology appraisal 584. Review date June 2022. Pembrolizumab with pemetrexed and platinum-based chemotherapy for untreated non-small-cell lung cancer (2021) NICE technology appraisals guidance 683. Review date to be confirmed. Pembrolizumab for untreated PD-L1-positive metastatic non-small-cell lung cancer (2018) NICE technology appraisal guidance 531. Review date July 2021. Atezolizumab monotherapy for untreated advanced non-small-cell lung cancer (2021) NICE technology appraisal guidance 705. Review date 2024 **Related technology appraisals in development:** Pembrolizumab with olaparib for maintenance treatment of advanced squamous non-small-cell lung cancer. NICE technology appraisal guidance [ID4006] Publication date to be confirmed **Related NICE guidelines:** Lung cancer: diagnosis and management (NG122) **Related quality standards:** Lung cancer in adults (2019) NICE quality standard 17
Related National Policy	The NHS Long Term Plan, 2019. NHS Long Term Plan NHS England (2023) Manual for prescribed specialist services (2023/2024) Chapter 105: Specialist cancer services (adults).

Questions for consultation

Where do you consider cemiplimab will fit into the existing care pathway for non-small-cell lung cancer?

Have all relevant comparators been included in the scope?

Have all relevant subgroups been included in the scope?

Would cemiplimab be a candidate for managed access?

Do you consider that the use of cemiplimab can result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation?

Would PD-L1 tumour proportion score be a factor when considering whether to offer cemiplimab?

Are the subgroups included in the draft scope appropriate?

Is having had surgery for NSCLC or not a relevant subgroup?

Please identify the nature of the data which you understand to be available to enable the committee to take account of these benefits.

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.

NICE intends to evaluate this technology through its Single Technology Appraisal process. (Information on NICE's health technology evaluation processes is available at https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/nice-technology-appraisal-guidance/changes-to-health-technology-evaluation).

References

1. Cancer Research UK (2023). Lung cancer statistics. Accessed October 2023
2. Royal College of Surgeons of England (2023). National Lung Cancer Audit: State of the Nation Report 2023. Accessed November 2023

3. 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 October 2023
4. Skov, B., Rørvig, S., Jensen, T. et al. (2020) The prevalence of programmed death ligand-1 (PD-L1) expression in non-small cell lung cancer in an unselected, consecutive population. Mod Pathol 33, 109–117
5. Han Y, Liu D, Li L. PD-1/PD-L1 pathway: current researches in cancer. Am J Cancer Res. 2020 Mar 1;10(3):727-742. PMID: 32266087; PMCID: PMC7136921.