NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Sugemalimab with chemotherapy for untreated metastatic non-small-cell lung cancer

Draft scope

Draft remit/appraisal objective

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

Background

Lung cancer falls into two main histological categories: around 88% are non-small-cell lung cancers (NSCLC) and the remainder are small-cell lung cancers.[1] NSCLC can be further classified into squamous cell carcinoma and non-squamous cell carcinoma. Approximately 85% 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 2018, 21,878 people were diagnosed with NSCLC in England, of whom around 59% had stage IV disease.[3] Around a third of people with lung cancer survive for more than 1 year after diagnosis, however this is reduced to around a fifth of people diagnosed at stage IV.[4]

Cancer cells expressing an immunologic marker called programmed cell death 1 ligand (PD-L1) are believed to suppress certain immune responses and cause increased tumour aggressiveness. The proportion of NSCLC that express PD-L1 in England is unknown.

In metastatic stage IV NSCLC, treatment aims to control the cancer for as long as possible and help with symptoms. Treatment generally includes chemotherapy, targeted drugs and symptomatic treatments. Treatment choices are influenced by histology (squamous or non-squamous), the presence of biological markers (such as mutations in epidermal growth factor receptor-tyrosine kinase [EGFR)], anaplastic-lymphoma-kinase [ALK] or programmed death-ligand 1 [PD-L1] status), and previous treatment experience.

For people with untreated non-squamous NSCLC treatment options include:

- EGFR-positive mutations: afatinib, (NICE technology appraisal guidance 310) dacomitinib (NICE technology appraisal guidance 595), erlotinib (NICE technology appraisal guidance 258), gefitinib (NICE technology appraisal guidance 192) or osimertinib (NICE technology appraisal guidance 654).
- ALK-positive mutations: alectinib (NICE technology appraisal guidance 536), brigatinib (NICE technology appraisal guidance 670), ceritinib (NICE technology appraisal guidance 500) or crizotinib (NICE technology appraisal guidance 406).

- ROS1-positive mutations: entrectinib (NICE technology appraisal guidance 643) or crizotinib (available for use within the Cancer Drugs Fund only; NICE technology appraisal guidance 529)
- No EGFR-, ALK- and ROS1-positive mutations, any PD-L1 expression level: pembrolizumab with pemetrexed and platinum chemotherapy (NICE technology appraisal guidance 683)
- PD-L1 expression under 50%: atezolizumab with bevacizumab, carboplatin and paclitaxel (NICE technology appraisal guidance 584), or pemetrexed in combination with cisplatin or other platinum doublet chemotherapy if the histology of the tumour has been confirmed as adenocarcinoma or large-cell carcinoma (NICE technology appraisal guidance 181).
- PD-L1 expression 50% or more: pembrolizumab monotherapy (NICE technology appraisal guidance 531) and atezolizumab monotherapy (NICE technology appraisal guidance 705)

For people with untreated squamous NSCLC treatment options include:

- Any PD-L1 expression level: pembrolizumab with carboplatin and paclitaxel (available for use within the Cancer Drugs Fund only; NICE technology appraisal guidance 600)
- PD-L1 expression under 50%: gemcitabine or vinorelbine and cisplatin or carboplatin (NICE technology appraisal guidance 181).
- PD-L1 expression 50% or more: pembrolizumab monotherapy (NICE technology appraisal guidance 531) and atezolizumab monotherapy (NICE technology appraisal guidance 705)

The technology

Sugemalimab (brand name unknown, EQRx) is a fully human immunoglobulin G4 (IgG4) monoclonal antibody that binds to the programmed cell death-1 (PD-1) receptor and blocks its interaction with its ligands PD-L1 and PD-L2, thereby activating the patient's immune system to attack the cancer. It is administered intravenously.

Sugemalimab with platinum-based chemotherapy does not currently have a marketing authorisation for untreated advanced NSCLC. It has been studied in a clinical trial compared with platinum-based chemotherapy alone in adults with untreated metastatic NSCLC.

Intervention(s)	Sugemalimab with platinum-based chemotherapy
Population(s)	Adults with untreated metastatic non-small-cell lung cancer

Comparators	**For adults with non-squamous histology and**
	• **EGFR-positive mutations**
	  • Afatinib
	  • Dacomitinib
	  • Erlotinib
	  • Gefitinib
	  • Osimertinib
	• **ALK-positive mutations**
	  • Alectinib
	  • Brigatinib
	  • Ceritinib
	  • Crizotinib
	• **ROS1-positive mutations**
	  • Entrectinib
	• **No EGFR-, ALK- or ROS1-positive mutations**
	  • Pembrolizumab combination (with pemetrexed and platinum chemotherapy)
	  • Atezolizumab combination (with bevacizumab, carboplatin and paclitaxel)
	  • Pemetrexed with platinum doublet chemotherapy
	  • Atezolizumab monotherapy
	  • Pembrolizumab monotherapy
	For adults with squamous histology:
	• Pembrolizumab with carboplatin and paclitaxel (subject to ongoing CDF review)
	• Platinum doublet chemotherapy (gemcitabine or vinorelbine with carboplatin or cisplatin)
	• Pembrolizumab monotherapy
	• Atezolizumab monotherapy

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. 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. The availability of any commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account. The availability of any managed access arrangement for the intervention will be taken into account.
Other considerations	If the evidence allows the following subgroups will be considered. These include: - PD-L1 expression - Histology (squamous or non-squamous) The availability and cost of biosimilar and generic products should be taken into account. 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:** Nivolumab with ipilimumab and chemotherapy for untreated advanced non-small-cell lung cancer (2021) NICE technology appraisal guidance 724. Atezolizumab monotherapy for untreated advanced non-small-cell lung cancer (2021) NICE technology appraisal guidance 705. Pembrolizumab with pemetrexed and platinum chemotherapy for untreated, metastatic, non-squamous non-small-cell lung cancer (2021) NICE technology appraisals guidance 683. Brigatinib for ALK-positive advanced non-small-cell lung cancer that has not been previously treated with an ALK inhibitor (2021) NICE technology appraisal guidance 670.

	Osimertinib for untreated EGFR mutation-positive non-small-cell lung cancer (2020) NICE technology appraisal guidance 654. Entrectinib for treating ROS1-positive advanced non-small-cell lung cancer (2020) NICE technology appraisal guidance 643. Pembrolizumab with carboplatin and paclitaxel for untreated metastatic squamous non-small-cell lung cancer (2019) NICE technology appraisals guidance 600. Subject to ongoing CDF review. Atezolizumab in combination for treating metastatic non-squamous non-small-cell lung cancer (2019) NICE technology appraisal 584. Pembrolizumab for untreated PD-L1-positive metastatic non-small-cell lung cancer (2018) NICE technology appraisal guidance 531. Crizotinib for treating ROS1-positive advanced non-small-cell lung cancer (2018) NICE technology appraisal guidance 529. Pemetrexed maintenance treatment for non-squamous non-small-cell lung cancer after pemetrexed and cisplatin (2016) NICE technology appraisal guidance 402. Afatinib for treating epidermal growth factor receptor mutation-positive locally advanced or metastatic non-small-cell lung cancer (2014, updated June 2018) NICE technology appraisal guidance 310. Pemetrexed for the maintenance treatment of non-small-cell lung cancer (2010, updated 2017) NICE technology appraisals guidance 190. Pemetrexed for the first-line treatment of non-small-cell lung cancer (2009, updated 2014) NICE technology appraisal 181. Pemetrexed for the treatment of non-small-cell lung cancer (2007, updated 2017) NICE technology appraisal guidance 124. **Appraisals in development:** Aumolertinib for untreated EGFR-positive advanced non-small-cell lung cancer. NICE technology guidance [ID4000]. Publication date to be confirmed. Cemiplimab for untreated PD-L1-postive advanced or metastatic non-small-cell lung cancer. NICE technology guidance [ID3839]. Publication expected 9 March 2022 Durvalumab for untreated advanced non-small-cell lung cancer with no EGFR or ALK mutations and high PD-L1 expression. NICE technology appraisal guidance [ID3762]. Publication date to be confirmed.

	Tepotinib for treating advanced non-small-cell lung cancer with MET gene alterations. NICE technology guidance [ID3761]. Publication expected 23 March 2022 Selpercatinib for RET fusion-positive advanced non-small-cell lung cancer NICE technology appraisal guidance [ID3743]. Publication date to be confirmed. Pembrolizumab with carboplatin and paclitaxel for untreated metastatic squamous non-small-cell lung cancer (CDF Review TA600) NICE technology appraisal guidance [ID1683]. Publication date to be confirmed. Durvalumab + Tremelimumab + standard chemotherapy for non-small cell lung cancer (NSCLC) lacking activating EGFR mutations and ALK fusions. NICE technology appraisals guidance [ID1538]. 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. Liposomal cisplatin in combination with chemotherapy for treating inoperable advanced non-small cell lung cancer. NICE technology appraisal guidance [ID657]. Publication date to be confirmed. **Related Guidelines:** Lung cancer: diagnosis and management (2019) NICE guideline 122. **Related Interventional Procedures:** Microwave ablation for treating primary lung cancer and metastases in the lung (2013). NICE interventional procedures guidance 469. Percutaneous radiofrequency ablation for primary or secondary lung cancers (2010) NICE Interventional Procedures Guidance 372. **Related quality standards:** Lung cancer in adults (2012, updated 2019) NICE quality standard 17. **Related NICE Pathway:** Lung cancer (2019) NICE pathway.
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) Department of Health and Social Care, NHS Outcomes Framework 2016-2017: Domain 1. https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017

Questions for consultation

How are treatment decisions made where multiple options exist for tumours with the same biological marker and histology?

Have all relevant comparators for sugemalimab with chemotherapy been included in the scope?

Are the outcomes listed appropriate?

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

Where do you consider sugemalimab with chemotherapy will fit into the existing NICE pathway, non-small-cell 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 sugemalimab with chemotherapy 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 sugemalimab with chemotherapy 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 sugemalimab with chemotherapy 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 (2020). Royal College of Physicians. Accessed September 2021.

[2] Non-small cell lung cancer treatment. National Cancer Institute. Accessed September 2021.

[3] National Lung Cancer Audit: 2019 information sheet (for the audit period 2018) (2020). Royal College of Physicians. Accessed September 2021.

[4] Lung cancer survival statistics (2010-11). Cancer Research UK. Accessed October 2020.