NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Pembrolizumab with olaparib for maintenance treatment of advanced squamous non-small-cell lung cancer ID4006

Draft scope

Draft remit/evaluation objective

To appraise the clinical and cost effectiveness of pembrolizumab with olaparib within its marketing authorisation as maintenance treatment of advanced squamous non-small-cell lung cancer.

Background

Lung cancer falls into two main histological categories: around 90% 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 25 to 30% of NSCLC are of squamous histology which is associated with poorer prognosis than non-squamous histology.[2]

Treatment depends on the location and stage of the cancer. 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). In 2021, 31,374 cases of NSCLC were diagnosed in England and 7%, 21% and 43% of people with lung cancer were diagnosed with stages 2, 3 and 4 disease respectively.[1] It is estimated that over half of all NSCLCs express the programmed cell death ligand-1 (PD-L1) biomarker.[3] Cancer cells expressing PD-L1 are believed to suppress certain immune responses which results in a weaker anti-tumour response.[3,4]

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), histology (squamous or non-squamous) and previous treatment. NICE's Technology Appraisal Pathway Pilot scope for treatments for non-small-cell lung cancer outlines in more detail the NSCLC treatment pathway.

Initial induction treatment for advanced squamous NSCLC depends on PD-L1 tumour proportion score. If PD-L1 tumour proportion score is between 0% to 49% platinum-based combination chemotherapy is used, or NICE technology appraisal guidance TA770 recommends pembrolizumab with carboplatin and paclitaxel. Generally, if PD-L1 tumour proportion score is 50% or more atezolizumab or pembrolizumab monotherapies are used as recommended in NICE technology appraisal guidance TA705 and TA531. Alternatively, pembrolizumab with carboplatin and paclitaxel may be offered to those in urgent need of a clinical intervention as per TA770. Maintenance therapy may be given after initial therapy to prevent cancer progression.

The technology

Pembrolizumab (Keytruda, Merck Sharp & Dohme). Olaparib (Lynparza; AstraZeneca)

Pembrolizumab in combination with olaparib does not have a marketing authorisation in the UK for maintenance treatment of advanced squamous non-small-cell lung cancer. It has been studied in a clinical trial as maintenance treatment after pembrolizumab with carboplatin and paclitaxel or nab-paclitaxel compared with a maintenance treatment of pembrolizumab with placebo, in adults with metastatic squamous NSCLC who have not had systemic treatment for metastatic disease.

Pembrolizumab in combination with olaparib does not currently have a marketing authorisation for any indication. Both pembrolizumab and olaparib have marketing authorisations in the UK as monotherapies, in combination and as maintenance therapies for several indications, including:

- Pembrolizumab in combination with carboplatin and either paclitaxel or nab-paclitaxel for the first-line treatment of metastatic squamous non-small cell lung carcinoma in adults.

- Pembrolizumab for the treatment of metastatic NSCLC for tumours that express PD-L1 with at least 50% tumour proportion score with no epidermal growth factor receptor (EGFR) or anaplastic lymphoma kinase (ALK) positive tumour mutations.

- Pembrolizumab for the treatment of locally advanced or metastatic NSCLC for tumours that express PD-L1 with at least 1% tumour proportion score after at least one prior chemotherapy regimen.

Intervention	Pembrolizumab with olaparib
Population	Adults with advanced squamous non-small-cell lung cancer (NSCLC) that has not progressed after treatment with pembrolizumab with carboplatin and paclitaxel or nab-paclitaxel
Subgroups	If the evidence allows the following subgroups will be considered • PD-L1 tumour proportion score
Comparators	Established clinical management without pembrolizumab with olaparib, including but not limited to: • Routine surveillance

Outcomes	The outcome measures to be considered include: • progression free survival • response rates • time to treatment discontinuation • 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.
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:** Atezolizumab for treating locally advanced or metastatic non-small-cell lung cancer after chemotherapy (2018) NICE technology appraisal guidance 520 Pembrolizumab for treating PD-L1-positive non-small-cell lung cancer after chemotherapy (2017) NICE technology appraisal guidance 428 Pembrolizumab with carboplatin and paclitaxel for untreated metastatic squamous non-small-cell lung cancer (2022) NICE technology appraisal guidance 770 Atezolizumab monotherapy for untreated advanced non-small-cell lung cancer (2021) NICE technology appraisal guidance 705 Pembrolizumab for untreated PD-L1-positive metastatic non-small-cell lung cancer (2018) NICE technology appraisal guidance 531

	Related NICE guidelines: 'Lung cancer: diagnosis and management' (2019). NICE guideline 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 (2018/2019) NHS manual for prescribed specialist services (2018/2019) Chapter 105: Specialist cancer services (adults).

Questions for consultation

Where do you consider pembrolizumab with olaparib to fit into the pathway depicted by NICE's Technology Appraisal non-small-cell lung cancer pathway pilot scope? Which decision node would be relevant for pembrolizumab with olaparib?

Have all relevant comparators for pembrolizumab with olaparib been included in the scope?

Are the outcomes listed appropriate?

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

Would pembrolizumab with olaparib be a candidate for managed access?

Do you consider that the use of pembrolizumab with olaparib can result in any potential 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 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 pembrolizumab with olaparib 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.

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 and https://www.nice.org.uk/about/what-we-do/proportionate-approach-to-technology-appraisals.

References

1. Royal College of Surgeons of England (2023). National Lung Cancer Audit: State of the Nation Report 2023. Accessed November 2023
2. Clinicopathologic features of advanced squamous NSCLC. (2016) Socinski. MA, Obasaju. C, Gandra. D et al. Journal of Thoracic Oncology, Volume 11, Issue 9, pp1411-1422
3. 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
4. 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.