NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Pembrolizumab with chemoradiation for untreated high-risk locally advanced cervical cancer

Draft scope

Remit/evaluation objective

To appraise the clinical and cost effectiveness of pembrolizumab with chemoradiation within its marketing authorisation for untreated high-risk locally advanced cervical cancer.

Background

Cervical cancer develops when abnormal cells in the lining of the cervix grow in an uncontrolled way and eventually form a tumour.[1] It can start from different types of cells in different parts of the cervix, which gives rise to 2 main subtypes of cancer. The most common subtype, called squamous cell carcinoma, develops from skin-like cells present on the outer surface of the cervix (ectocervix). The other subtype is called adenocarcinoma and it develops from glandular cells that produce mucus inside the cervix (endocervix).[1] The human papilloma virus (HPV) is the main cause of cervical cancer and has been detected in 99% of cases. HPV types 16 and 18 account for at least two-thirds of cases.[2]

Locally advanced cervical cancer is characterised either by a large tumour within the cervix (more than 4 centimetres) or tumour growth into the tissues around the cervix.[3]

There are around 3,300 new cervical cancer cases in the UK every year[4]. In England between 2017 and 2019, there were an average of 2,688 new cases of cervical cancer per year.[5] Between, 2017 and 2019, an average of 853 deaths were recorded in the UK because of cervical cancer per year.[6] Around half of people diagnosed with cervical cancer in England survive their disease for 10 years or more.[4]

Standard treatment for locally advanced cervical cancer is chemoradiation consisting of external beam radiotherapy, intracavity brachytherapy and chemotherapy with cisplatin.[7]

The technology

Pembrolizumab (Keytruda, Merck Sharp & Dohme) with chemoradiation does not currently have a marketing authorisation in the UK for untreated high-risk locally advanced cervical cancer. The combination has been studied in a randomised clinical trial compared with chemoradiation alone in adults with high-risk locally advanced cervical cancer.

Pembrolizumab combined with chemotherapy with or without bevacizumab has a marketing authorisation for treating persistent, recurrent, or metastatic cervical cancer in adults whose tumours express PD-L1 with a combined positive score (CPS) of 1 or more.

Intervention(s)	Pembrolizumab with chemoradiation
Population(s)	Adults with high-risk, locally advanced cervical cancer
Subgroups	If the evidence allows, the following subgroups will be considered: • histology (squamous cell carcinoma, adenocarcinoma, adenosquamous carcinoma and poorly differentiated carcinoma) • combined positive score (CPS) of PD-L1 expression (less than 10, greater than or equal to 10 and all-comers) • tumour mutational burden.
Comparators	Chemoradiotherapy (cisplatin-based, unless contraindicated)
Outcomes	The outcome measures to be considered include: • progression-free survival • overall 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. 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 plus chemotherapy with or without bevacizumab for persistent, recurrent or metastatic cervical cancer. (2023) NICE technology appraisal guidance 885 **Related NICE advice:** Cervical cancer and HPV (Last update February 2022). NICE clinical knowledge summary. **Related interventional procedures:** High dose rate brachytherapy for carcinoma of the cervix (2006) NICE interventional procedures guidance IPG160
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: Domains 1& 2. https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017

Questions for consultation

Which treatments are considered to be established clinical practice in the NHS for high risk, locally advanced cervical cancer?

Where do you consider pembrolizumab with chemoradiation will fit into the existing care pathway for untreated high-risk locally advanced cervical cancer?

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

Would pembrolizumab with chemoradiation be a candidate for managed access?

Do you consider that the use of pembrolizumab with chemoradiation 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 chemoradiation 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. What is cervical cancer? (2023). Accessed December 2024.

2. NICE clinical knowledge summary on cervical cancer and HPV. (2022). Accessed December 2024.

3. Cancer Research UK. About advanced cervical cancer (2020). Accessed December 2024.

4. Cancer Research UK. Cervical cancer statistics (2020). Accessed December 2024.

5. Cancer research UK. Cervical cancer incidence statistics (2023). Accessed December 2024.

6. Cancer research UK. Cervical cancer mortality statistics (2021) Accessed December 2024.

7. Reed N, Balega J, Barwick T et al. British Gynaecological Cancer Society (BGCS) Cervical Cancer Guidelines: Recommendations for Practice (2020). Accessed December 2024.