NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Pembrolizumab with chemotherapy for treating recurrent, persistent or metastatic cervical cancer

Draft scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of pembrolizumab with chemotherapy within its marketing authorisation for treating recurrent, persistent or metastatic 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 two 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] Infection with human papillomavirus (HPV) is associated with the development of cervical cancer.[2] It has been detected in 99.7% of cases. HPV types 16 and 18 are considered high risk for cervical cancer and cause about 75% of cases.[2]

Cervical cancer is defined as recurrent when it has returned following treatment, and as persistent when it does not respond to treatment.[3] Cervical cancer is defined as advanced or metastatic when it has spread beyond the cervix and womb to other places in the body such as the abdomen, liver, gut, or lungs (stages 2 to 4).[3]

There are around 3,200 new cervical cancer cases in the UK every year.[4] In England in 2017, there were 2,591 newly diagnosed cases of metastatic cervical cancer.[5] In the same year, 730 deaths were recorded in England and Wales due to the cervical cancer.[6] Around 6 in 10 (61.4%) of people diagnosed with cervical cancer in England survive their disease for five years or more.[4]

For people with recurrent, persistent or metastatic cervical cancer the aim of treatment is to relieve symptoms and improve quality of life. Treatment options may include chemotherapy with paclitaxel plus either cisplatin or carboplatin. NICE recommends topotecan in combination with cisplatin as an option for treating recurrent or stage 4B cervical cancer in people who have not previously received cisplatin (NICE Technology Appraisal Guidance 183). Bevacizumab in combination with paclitaxel and either cisplatin or carboplatin is also available via the Cancer Drugs Fund for untreated recurrent or metastatic cervical cancer.[7] When chemotherapy is not suitable, people may be offered best supportive care or palliative radiotherapy.[8]

The technology

Pembrolizumab (KEYTRUDA, Merck Sharp & Dohme) is a humanised monoclonal antibody which binds to the programmed cell death-1 (PD-1) receptor and blocks its

interaction with ligands PD-L1 and PD-L2, to promote an anti-tumour immune response. It is administered intravenously.

Pembrolizumab does not currently have a marketing authorisation in the UK in combination with chemotherapy for untreated recurrent, persistent or metastatic cervical cancer. The combination has been studied in a randomised clinical trial compared with placebo with chemotherapy in adults with untreated recurrent or metastatic cervical cancer. Possible chemotherapy regimens included: paclitaxel with either cisplatin or carboplatin, with or without bevacizumab.

Intervention(s)	Pembrolizumab in combination with chemotherapy
Population(s)	Adults with untreated recurrent, persistent or metastatic cervical cancer
Comparators	• Platinum chemotherapy (cisplatin or carboplatin) alone or in combination with paclitaxel or topotecan or etoposide • Paclitaxel alone (for people who cannot have platinum-based chemotherapy)
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. 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: • Squamous cell carcinoma • Adenocarcinoma Bevacizumab in combination with paclitaxel and either cisplatin or carboplatin is available in the Cancer Drugs Fund. The clinical and cost effectiveness of pembrolizumab on a background of this regimen may be presented in addition to the analysis on a background of standard chemotherapy regimens. 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:** Topotecan for the treatment of recurrent and stage IVB cervical cancer (2009). NICE Technology Appraisal 183. **Appraisals in development:** Tisotumab vedotin for treating recurrent or metastatic cervical cancer after systemic therapy. Proposed NICE technology appraisal [ID3753]. Publication date to be confirmed. **Related Interventional Procedures:** High dose rate brachytherapy for carcinoma of the cervix (2006). NICE Interventional Procedures Guidance 160. **Related Guidelines:** Cervical cancer and HPV (Last update April 2017). NICE Clinical Knowledge Summary. Cervical Cancer Guidelines: Recommendations for Practice (2020). British Gynaecological Cancer Society (BGCS). Human Papillomavirus (HPV), Cervical Screening and Cervical Cancer (2018). Royal College of Nursing. Cervical Cancer: ESMO Clinical Practice Guidelines (2017). ESMO. Comprehensive cervical cancer control (2014). WHO. **Related NICE Pathways:** Cervical cancer (Last updated 2020) NICE pathway.

Related National Policy	The NHS Long Term Plan, 2019. NHS Long Term Plan NHS England (2018) NHS England Funding and Resource 2018/19: Supporting 'Next Steps for the NHS Five Year Forward View' NHS England (2018/2019) NHS manual for prescribed specialist services (2018/2019) 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 Independent Cancer Taskforce (2015) Achieving world-class cancer outcomes: a strategy for England 2015-2020 Department of Health (2014) The national cancer strategy: 4th annual report Department of Health (2009) Cancer commissioning guidance

Questions for consultation

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

- Which treatments are considered to be established clinical practice in England for untreated recurrent, persistent or metastatic cervical cancer?
- What are the most commonly used chemotherapy regimens used in clinical practice for untreated recurrent, persistent or metastatic cervical cancer?

Are the outcomes listed appropriate?

Are the subgroups suggested in 'Other considerations' 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?

Where do you consider pembrolizumab will fit into the existing NICE pathway, Cervical Cancer (2018)?

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 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 pembrolizumab;

- 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 pembrolizumab 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 pembrolizumab 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).

References

1. Cancer Research UK. What is cervical cancer? (2020). Accessed August 2020.

2. National Institute for Health and Care Excellence. What causes cervical cancer? (2017). Accessed August 2020.

3. Cancer Research UK. Stage 4 cervical cancer (2020). Accessed August 2020.

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

5. Office for National Statistics. Cancer registration statistics, England (2019).

6. Office for National Statistics. Death registrations summary tables - England and Wales (2018). Accessed August 2020.

7. NHS England. National Cancer Drugs Fund List ver1.167 (2020). Accessed August 2020.

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