NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Pembrolizumab in combination with platinum-based chemotherapy for treating recurrent, persistent or metastatic cervical cancer

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of pembrolizumab in combination with platinum-based 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 metastatic when it has spread beyond the cervix to other places in the body such as the abdomen, liver, gut, or lungs (stage 4B).[3] Locally advanced cervical cancer (between stages 1B2 and 4A) is characterised either by a large tumour within the cervix (more than 4 centimetres) or tumour growth into the tissues around the cervix.[4]

There are around 3,200 new cervical cancer cases in the UK every year.[5] In England in 2018, there were 2,668 newly diagnosed cases of cervical cancer.[6] In 2017, 730 deaths were recorded in England and Wales due to the cervical cancer.[7] Around 6 in 10 (61.4%) of people diagnosed with cervical cancer in England survive their disease for five years or more.[5]

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.[8] When chemotherapy is not suitable, people may be offered best supportive care or palliative radiotherapy.[9]

The technology

Pembrolizumab (KEYTRUDA, MSD) 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 in combination with platinum-based chemotherapy does not currently have a marketing authorisation in the UK 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 paclitaxel and platinum-based chemotherapy (carboplatin or cisplatin) with or without bevacizumab
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 • In addition, for people who would receive bevacizumab through the Cancer Drugs Fund: paclitaxel with platinum-based chemotherapy (carboplatin or cisplatin) with bevacizumab (15 mg/kg every 3 weeks)
Outcomes	The outcome measures to be considered include: • overall survival • progression-free 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 of any managed access arrangement for the intervention will be taken into account. The economic modelling should include the costs associated with diagnostic testing for PD-L1 in people with recurrent, persistent or metastatic cervical cancer who would not otherwise have been tested. A sensitivity analysis should be provided without the cost of the diagnostic test. See section 5.9 of the Guide to the Methods of Technology Appraisals.
Other considerations	If the evidence allows the following subgroups will be considered based on: • Histology (squamous cell carcinoma, adenocarcinoma, adenosquamous carcinoma and poorly differentiated carcinoma) • Pelvic disease status (pelvic or locally recurrent cervical cancer and distant metastatic cervical cancer) • Combined positive score (CPS) of PD-L1 expression (less than 10, greater than or equal to 10 and all-comers) • Tumour Mutational Burden 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. LN-145 for treating recurrent, persistent or metastatic cervical cancer. Proposed NICE technology appraisal [ID3844]. 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 July 2021). 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 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

References

1. Cancer Research UK. What is cervical cancer? (2020). Accessed January 2022.

2. National Institute for Health and Care Excellence. What causes cervical cancer? (2017). Accessed January 2022.

3. Cancer Research UK. Stage 4 cervical cancer (2020). Accessed January 2022.

4. Cancer Research UK. About advanced cervical cancer (2020). Accessed January 2022.

5. Cancer Research UK. Cervical cancer statistics (2020). Accessed January 2022.

6. Public Health England. Case-mix adjusted percentage of cancers diagnosed at stages 1 and 2 for Clinical Commissioning Groups in England (experimental statistics), diagnosed 2013 to 2018 – Table 3 (2020). Accessed January 2022.

7. Office for National Statistics. Death registrations summary tables - England and Wales (2018). Accessed January 2022.

8. NHS England. National Cancer Drugs Fund List ver1.167 (2020). Accessed January 2022.

9. Reed N, Balega J, Barwick T et al. British Gynaecological Cancer Society (BGCS) Cervical Cancer Guidelines: Recommendations for Practice (2020). Accessed January 2022.