NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE
Health Technology Appraisal

Dostarlimab for previously treated advanced or recurrent endometrial cancer with high microsatellite instability or mismatch repair deficiency

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of dostarlimab within its marketing authorisation for previously treated advanced or recurrent endometrial cancer with high microsatellite instability or mismatch repair deficiency.

Background

Endometrial cancer is a cancer of the lining of the womb (uterus), known as the endometrium. It is the most common type of uterine cancer.[1] When diagnosed, endometrial cancer is categorised between stage 1 and 4, depending on the size of the cancer and how far it has spread. Advanced (stage 3 or 4) endometrial cancer is when the cancer has spread outside the uterus. Recurrent endometrial cancer is when the cancer returns after primary treatment. The cancer can recur anywhere; common areas include the abdominal cavity, lymph nodes, lung and vagina.[2] The symptoms of recurrence are variable but include abdominal pain, bloating, nausea, shortness of breath, vaginal bleeding and changes in bowel or bladder habits.[2]

Around 9,400 women are diagnosed with uterine cancer every year in the UK, mostly with early-stage disease.[1] Uterine cancer led to 2,400 deaths in 2018, accounting for 3% of all cancer deaths in females in the UK. Only 15% of women diagnosed with stage 4 uterine cancer survive for 5 years or longer, compared with 48% of women diagnosed at stage 3.[1]

In normal cells, the mismatch repair (MMR) system recognises and repairs genetic mismatches generated during DNA replication. Around 26% of endometrial tumours have a defect in the MMR system,[3] meaning unstable and dysfunctional DNA is not degraded. Tumours with MMR deficiency can develop microsatellite instability, which is a change in the length of repetitive sequences in tumour DNA compared with normal DNA. Tumours with high microsatellite instability may upregulate immune checkpoints, including programmed cell death protein (PD-1) and programmed cell death ligand 1 (PD-L1).[4]

The first treatment for endometrial cancer is usually removal of the uterus, fallopian tubes and ovaries.[5] In advanced endometrial cancer, debulking surgery may be carried out to remove as much of the cancer as possible, and platinum-based chemotherapy can be added on to the surgery. Radiotherapy may be used for people who cannot have surgery, or alongside surgery. Guidelines published by the British Gynaecological Cancer Society recommend that second-line carboplatin plus paclitaxel can be considered in patients for whom it is suitable, if the treatment-free interval is longer than 6 months.[6] If the treatment-free interval is less than 6 months, or if carboplatin plus paclitaxel is not suitable, single-agent chemotherapy can be considered. Some patients, including those for whom chemotherapy is not suitable, may be offered hormone therapy.

The technology

Dostarlimab (brand name unknown, GlaxoSmithKline) is a humanised monoclonal antibody, which works by attaching to the PD-1 protein on the surface of cancer cells. This helps the immune system to recognise and attack the cancer by preventing the inhibition of T-cell mediated immune responses. It is administered intravenously.

Dostarlimab does not currently have a marketing authorisation in the UK for endometrial cancer. It has been studied in a clinical trial in patients with advanced or recurrent endometrial cancer with high MSI or MMR deficiency that has progressed on or following a platinum-containing regimen.

Intervention(s)	Dostarlimab
Population(s)	People with previously treated advanced or recurrent endometrial cancer with high microsatellite instability or mismatch repair deficiency
Comparators	• Chemotherapy, including: - Carboplatin and paclitaxel - Paclitaxel monotherapy - Doxorubicin monotherapy - Carboplatin monotherapy • Hormone therapy (such as medroxyprogesterone acetate and megestrol) • Best supportive care
Outcomes	The outcome measures to be considered include: • progression-free survival • overall survival • response rates • duration of response • 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 economic modelling should include the costs associated with diagnostic testing for microsatellite instability status in people with endometrial 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	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	Proposed Technology Appraisals: Pembrolizumab for previously treated endometrial cancer. Proposed NICE technology appraisal [ID1205]. Publication date to be confirmed. Lenvatinib with pembrolizumab for previously treated advanced endometrial cancer. Proposed NICE technology appraisal [ID3811]. Publication date to be confirmed. Related NICE Pathways: Urogenital conditions (2020) NICE pathway http://pathways.nice.org.uk/pathways/urogenital-conditions
Related National Policy	The NHS Long Term Plan, 2019. NHS Long Term Plan Department of Health and Social Care, NHS Outcomes Framework 2016-2017: Domains 1-4. https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017

References

1. Cancer Research UK (2017) Uterine cancer statistics. Accessed January 2021

2. Columbia University. Uterine Cancer: Recurrence. Accessed January 2021

3. Ryan NAJ, McMahon R, Tobi S et al. (2020) The proportion of endometrial tumours associated with Lynch syndrome (PETALS): A prospective cross-sectional study. PLOS Medicine 17(9):e1003263.

4. Zhao et al. (2019) Mismatch repair deficiency/microsatellite instability-high as a predictor for anti-PD-1/PD-L1 immunotherapy efficacy. J Hematol Oncol. 12(1): 54

5. NHS (2018) Treatment: Womb (uterus) cancer. Accessed January 2021

6. British Gynaecological Cancer Society (2017) BGCS uterine cancer guidelines: recommendations for practice. Accessed January 2021