NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE
Health Technology Appraisal

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

Draft scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of dostarlimab within its marketing authorisation for treating previously treated advanced and 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 womb cancer and often diagnosed in the earlier stages. When diagnosed, endometrial cancer is categorised between stage 1 and 4. Advanced endometrial cancer is defined as stage 3 or 4, where the cancer has spread outside the womb. In stage 3 the spread of cancer is contained within the pelvis, once the cancer has spread into another area of the body it is classed as stage 4. 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. The symptoms of recurrence are variable but include abdominal pain, bloating, nausea, shortness of breath, vaginal bleeding and changes in bowel or bladder habits[1].

In normal cells, the mismatch repair (MMR) system recognises and repairs genetic mismatches generated during DNA replication. Some patients with endometrial cancer have a defect in the MMR system, meaning unstable and dysfunctional DNA is not degraded. Tumours with MMR deficiency can develop microsatellite instability (MSI), which is a change in the length of repetitive sequences in tumour DNA compared with normal DNA. Tumours with high microsatellite instability (MSI-H) may have upregulation of immune checkpoints, including programmed cell death protein (PD-1) and programmed cell death ligand 1 (PD-L1)[2].

There are approximately 9,400 new cases of uterine cancer every year in the UK. Around 2,400 deaths resulted from uterine cancer in 2018, accounting for 3% of all cancer deaths in females in the UK. An estimated figure of 71.6% of women diagnosed with uterine cancer in England survive for ten years or more[3]. Less than 5% of endometrial cancers occur in women under 45 years of age[4]. The incidence of mismatch repair deficiency and high MSI (17%) is higher in endometrial cancer than any other cancer type[5].

The first treatment for endometrial cancer is usually removal of the womb (hysterectomy) as well as both fallopian tubes and ovaries (bilateral salpingo-oophorectomy). In advanced endometrial cancer debulking surgery may be carried out to remove as much of the cancer as possible[6]. Radiotherapy may be used for people who cannot have surgery, or alongside surgical treatment. Platinum based chemotherapy can be used adjunct to surgery for people with stage 2-4 disease. Hormone therapy with progestins, or platinum-based chemotherapy may be used for cancer that has metastasised or relapsed.

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 treating previously treated advanced or recurrent endometrial cancer with high MSI or MMR deficiency that has progressed on or following prior treatment with a platinum-based chemotherapy regimen. It has been studied in trials for patients with recurrent or advanced endometrial cancer.

Intervention(s)	Dostarlimab
Population(s)	People with previously treated advanced and recurrent endometrial cancer with high microsatellite instability or mismatch repair deficiency
Comparators	• Chemotherapy (such as paclitaxel, carboplatin, cisplatin, doxorubicin and cyclophosphamide) • 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 • 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

Questions for consultation

Is the population in the scope defined appropriately?

Are microsatellite instability or mismatch repair deficiency routinely tested for in the NHS?

Have all relevant comparators for dostarlimab been included in the scope? Which treatments are considered to be established clinical practice in the NHS for previously treated advanced and recurrent endometrial cancer who have received platinum-based chemotherapy?

Are surgery and radiotherapy relevant comparators for dostarlimab?

Are the outcomes listed appropriate?

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

Where do you consider dostarlimab will fit into the current clinical pathway for endometrial cancer?

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 dostarlimab 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.

Do you consider dostarlimab 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 dostarlimab 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 Murali R, Soslow RA, Weigelt B (2014) Classification of endometrial carcinoma: more than two types. The Lancet. Oncology 15(7): 268-278.

2 Boland CR, Goel A (2010) Microsatellite instability in colorectal cancer. Gastroenterology. 138(6): 2073-2087

3 Cancer Research UK (2017) Uterine cancer statistics. Accessed September 2020.

4 British Gynaecological Cancer Society (2017) BGCS uterine cancer guidelines: recommendations for practice. Accessed September 2020.

5 Le DT, Durham JN, Smith KN et al. (2017) Mismatch repair deficiency predicts response of solid tumours to PD-1 blockade. Science. 357: 409-413.

6 NHS (2018) Treatment: Womb (uterus) cancer. Accessed September 2020.