NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Pembrolizumab with platinum-based chemotherapy then pembrolizumab maintenance for treating primary advanced or recurrent endometrial cancer ID6381

Final scope

Remit/evaluation objective

To appraise the clinical and cost effectiveness of pembrolizumab with platinum-based chemotherapy then maintenance pembrolizumab within its marketing authorisation for the treatment of primary advanced or recurrent endometrial cancer.

Background

Endometrial cancer is a cancer of the lining of the womb (uterus), known as the endometrium. Over 95% of womb cancers are endometrial cancer.[1] The most common symptom of endometrial cancer is abnormal vaginal bleeding, especially in people who have stopped having periods (post menopausal). When diagnosed, endometrial cancer is categorised between stage 1 and 4. In stages 1 and 2, the cancer is contained within the uterus and cervix. 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 or metastatic. Advanced endometrial cancer is defined as stages 3 or 4. The majority of endometrial cancer is diagnosed at stage 1.[2] Primary endometrial cancer means that the lining of the uterus is the first place in the body where the cancer began to grow.

In 2021, there were about 8,400 new cases of endometrial cancer in England.[3] It is most common in older women, with only 3% of cases occurring in women under 45 years of age.[4] Diagnosis at an early stage of the cancer's development leads to improved survival chances. About 92% of people diagnosed with stage 1 endometrial cancer survive for 5 or more years. This decreases to 15% for people diagnosed with stage 4 endometrial cancer.[4] Around 2,000 people die from uterine cancer in England each year.[5]

The first treatment for endometrial cancer is usually to remove the womb (hysterectomy) and the 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 alongside surgical treatment, or for people who cannot have surgery. In addition, chemotherapy, usually consisting of carboplatin and paclitaxel, can be used adjunct to surgery. For cancer that has metastasised or relapsed, treatment options include hormone therapy, immunotherapy, targeted therapy and chemotherapy.

NICE technology appraisal guidance 779 recommends dostarlimab for use within the Cancer Drugs Fund to treat advanced or recurrent endometrial cancer with high microsatellite instability (MSI) or mismatch repair (MMR) deficiency in people who have had platinum-based chemotherapy.

NICE technology appraisal guidance 963 recommends dostarlimab with platinum-based chemotherapy for use within the Cancer Drugs Fund to treat advanced or recurrent endometrial cancer with high MSI or MMR deficiency in adults who are candidates for systemic therapy.

The technology

Pembrolizumab (Keytruda, Merck Sharp & Dohme) in combination with platinum based chemotherapy followed by maintenance pembrolizumab does not currently have a marketing authorisation in the UK for endometrial cancer. It is being studied in a clinical trial in people with advanced or recurrent endometrial cancer. People in the trial have either pembrolizumab with chemotherapy followed by pembrolizumab maintenance therapy, or placebo with chemotherapy followed by placebo maintenance therapy.

Pembrolizumab in combination with lenvatinib has a marketing authorisation in the UK for treatment of advanced or recurrent endometrial carcinoma in adults who have disease progression on or following prior treatment with a platinum-containing therapy in any setting and who are not candidates for curative surgery or radiation. Pembrolizumab also has a marketing authorisation as monotherapy for the treatment of advanced or recurrent endometrial carcinoma with high microsatellite instability or mismatch repair deficiency, who have disease progression on or following prior treatment with a platinum-containing therapy in any setting and who are not candidates for curative surgery or radiation.

Intervention(s)	Pembrolizumab in combination with platinum-based chemotherapy followed by pembrolizumab maintenance treatment
Population(s)	People with primary advanced or recurrent endometrial cancer
Subgroups	If the evidence allows the following subgroups will be considered: • Molecular subgroups, such as mismatch repair (MMR) status • Local vs metastatic recurrence • People who have had primary debulking surgery vs those who have had not had surgery

Comparators	Following treatment options, followed by routine surveillance: • Platinum-based chemotherapy (such as paclitaxel, carboplatin, cisplatin, doxorubicin and cyclophosphamide) • Hormone therapy (such as medroxyprogesterone acetate and megestrol)
Outcomes	The outcome measures to be considered include: • progression-free survival • response rates • duration of response • overall survival • 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.
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:** Dostarlimab for previously treated advanced or recurrent endometrial cancer with high microsatellite instability or mismatch repair deficiency (2022) NICE technology appraisal guidance 779. Pembrolizumab with lenvatinib for previously treated advanced or recurrent endometrial cancer (2023). NICE technology appraisal 904.

	Pembrolizumab for previously treated endometrial, biliary, colorectal, gastric or small intestine cancer with high microsatellite instability or mismatch repair deficiency. (2023) NICE technology appraisal 914. Dostarlimab with platinum-containing chemotherapy for treating primary advanced or recurrent endometrial cancer with high microsatellite instability or mismatch repair deficiency (2024) NICE technology appraisal 963. **Related technology appraisals in development:** Durvalumab for maintenance treatment of recurrent or advanced endometrial cancer after platinum-based chemotherapy [ID6317]. Publication TBC Niraparib with dostarlimab for maintenance treatment of advanced or recurrent endometrial cancer [ID6316] Publication TBC Pembrolizumab with chemotherapy for adjuvant treatment of newly diagnosed high-risk endometrial cancer after surgery with curative intent [ID6207] Publication TBC **Related interventional procedures:** Laparoscopic hysterectomy (including laparoscopic total hysterectomy and laparoscopically assisted vaginal hysterectomy) for endometrial cancer (2010) NICE interventional procedures guidance 356. **Related diagnostics guidance:** Testing strategies for Lynch syndrome in people with endometrial cancer (2020) NICE diagnostics guidance 42.
Related National Policy	The NHS Long Term Plan (2019) NHS Long Term Plan. NHS England (2018) NHS manual for prescribed specialist services (2018/2019). Chapter 105.

1 Cancer Research UK. Uterine cancer incidence by anatomical site. Accessed Jan 2024

2 Cancer Research UK. Early Diagnosis Data Hub. Accessed Jan 2024

3 NHS Digital (2023) Cancer registration statistics, 2021. Accessed Jan 2024

4 ONS (2019) Cancer survival by stage at diagnosis for England, 2019. Accessed Jan 2024

5 Cancer Research UK. Uterine cancer mortality by UK country. Accessed Jan 2024

6 NHS (2021) Treatment: womb (uterus) cancer. Accessed Jan 2024