NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Olaparib in combination with bevacizumab for maintenance treatment of advanced ovarian, fallopian tube and peritoneal cancer after response to first-line platinum-based chemotherapy with bevacizumab

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of olaparib in combination with bevacizumab within its marketing authorisation as maintenance treatment of advanced ovarian, fallopian tube and peritoneal cancer after complete or partial response to first-line platinum-based chemotherapy with bevacizumab.

Background

Ovarian cancer is a cancerous growth that occurs in different parts of the ovary or fallopian tubes. The most common type of ovarian cancer, high-grade serous carcinoma (HGSC), is thought to arise from the fallopian tube and presents after it has spread to the ovary. Ovarian cancer is classified from stage I to stage IV. Advanced ovarian cancer falls within stages II and IV; in stage II the disease has grown outside the ovaries but is still within the pelvic area, stage III denotes disease that is locally advanced and has spread outside the pelvis into the abdominal cavity, and stage IV denotes that distant metastasis to other body organs such as the liver and the pleura (two thin layers of tissue that protect and cushion the lungs) has occurred. Most people are diagnosed with advanced stage disease. Some people have gene mutations that may increase the risk of ovarian cancer. Mutated inherited genes that increase the risk of ovarian cancer include BRCA 1 or 2.

The incidence of ovarian cancer increases with age and average age at diagnosis is 65 years[1]. In 2017, 6,236 people were diagnosed with ovarian cancer in England.[2] The 5-year survival for women diagnosed with ovarian cancer between 2013 and 2017, in England was 42.9% for all stages and 26.9% for stage III and 13.4% for stage IV cancer respectively.[3]

NICE technology appraisal guidance 55 recommends paclitaxel in combination with a platinum-based compound or platinum-based therapy alone (cisplatin or carboplatin) as alternatives for first-line chemotherapy (usually following surgery) in the treatment of ovarian cancer. Bevacizumab in combination with paclitaxel and carboplatin is not recommended for first-line treatment of advanced ovarian, fallopian tube or primary peritoneal cancer (NICE technology guideline 284). However, bevacizumab (7.5mg/kg every 3 weeks, not the licenced dose of 15mg/kg every 3 weeks) is available through the Cancer Drug Fund for a group of patients with FIGO stage III disease (debulked but residual disease more than 1 cm, or stage III at presentation and requiring neo-adjuvant chemotherapy due to low likelihood of optimal primary surgical cytoreduction), and for people with stage IV disease.

NICE technology appraisal 598 recommends olaparib for use within the Cancer Drugs Fund as an option for the maintenance treatment of BRCA mutation-positive, advanced (International Federation of Gynaecology and Obstetrics [FIGO] stages III

and IV), high-grade epithelial ovarian, fallopian tube or primary peritoneal cancer that has responded to first-line platinum-based chemotherapy in adults.[a]

The technology

Olaparib (Lynparza; AstraZeneca) is a poly-ADP-ribose polymerase (PARP) inhibitor which inhibits PARP proteins involved in DNA repair. It is administered orally.

Olaparib in combination with bevacizumab does not have a marketing authorisation in the UK for the maintenance treatment of ovarian cancer. The combination has been studied in a clinical trial compared with placebo and bevacizumab in adults with newly diagnosed advanced (FIGO stages III or IV) ovarian, fallopian tube or primary peritoneal cancer who have responded (completely or partially) to first-line platinum-based chemotherapy with bevacizumab.

Olaparib has a marketing authorisation in the UK as monotherapy for the maintenance treatment of adult patients with:

- advanced (FIGO stages III and IV) BRCA1/2-mutated (germline and/or somatic) high-grade epithelial ovarian, fallopian tube or primary peritoneal cancer who are in response (complete or partial) following completion of first-line platinum-based chemotherapy; and

- platinum-sensitive relapsed high-grade epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in response (complete or partial) to platinum-based chemotherapy.

Intervention(s)	Platinum-based chemotherapy with bevacizumab (15 mg/kg every 3 weeks) followed with olaparib and bevacizumab maintenance therapy only in responders
Population(s)	People with newly diagnosed advanced ovarian, fallopian tube, or primary peritoneal cancer
Comparators	• Platinum based chemotherapy followed with routine surveillance • In addition, for people who would receive bevacizumab through the Cancer Drugs Fund: platinum-based chemotherapy with bevacizumab (7.5 mg/kg every 3 weeks) followed with bevacizumab maintenance therapy
Outcomes	The outcome measures to be considered include: • overall survival • progression-free survival • progression-free survival 2, that is time from randomisation to a progression event after the event used for progression-free survival

[a] Products recommended for use in the Cancer Drugs Fund after 1 April 2016 should not be considered as comparators, or appropriately included in a treatment sequence, in subsequent relevant appraisals. NICE's position statement.

	• time to next line of therapy • 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 patient access schemes for the intervention or comparator technologies will be taken into account. The economic modelling should include the cost associated with diagnostic testing for BRCA and homologous recombination deficiency (HRD) status in people with ovarian 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. These include: • subgroups by BRCA mutation status, and • subgroups by HRD status. The availability and cost of biosimilar 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: Olaparib for maintenance treatment of BRCA mutation-positive advanced ovarian, fallopian tube or peritoneal cancer after response to first-line platinum-based chemotherapy (2019) NICE technology appraisal guidance TA598. Review date December 2023. Bevacizumab in combination with gemcitabine and carboplatin for treating the first recurrence of platinum-sensitive advanced ovarian cancer (2013) NICE technology

	appraisal guidance 285. Reviewed in 2016 and moved to static list. Bevacizumab in combination with paclitaxel and carboplatin for first-line treatment of advanced ovarian cancer (2013) NICE technology appraisal guidance 284. Reviewed in 2016 and moved to static list. Guidance on the use of paclitaxel in the treatment of ovarian cancer (2003) NICE technology appraisal guidance 55. Reviewed August 2015. Appraisals in development Niraparib for maintenance treatment of advanced ovarian, fallopian tube and peritoneal cancer after response to first-line platinum-based chemotherapy. NICE technology appraisal guidance [ID1680] Publication date TBC. Related Guidelines: Ovarian cancer: recognition and initial management (2011) NICE guideline CG122. Review date to be confirmed Tests in secondary care to identify people at high risk of ovarian cancer (2017) NICE diagnostics guidance 31 Related Quality Standards: Ovarian cancer (2012) NICE quality standard 18 Related NICE Pathways: Ovarian cancer (2019) NICE Pathway
Related National Policy	The NHS Long Term Plan, 2019. NHS Long Term Plan NHS England NHS manual for prescribed specialist services 2018/2019 (2018) 105. Specialist cancer services (adults) Department of Health, NHS Outcomes Framework 2016-2017 (2016) Domains 1 and 2

References

1. Patient (2016). Ovarian Cancer. Accessed September 2019.

2. Office for National Statistics (2017). Cancer registration statistics, England: 2017. Accessed September 2019.

3. Office for National Statistics (2019). Cancer survival in England - adults diagnosed. 2013 to 2017 dataset. Accessed September 2019.