NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Olaparib for maintenance treatment of BRCA mutation-positive metastatic pancreatic cancer after initial platinum-based chemotherapy

Draft scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of olaparib within its marketing authorisation for maintenance treatment of BRCA mutation-positive metastatic pancreatic cancer after initial platinum-based chemotherapy .

Background

The pancreas is a large gland located behind the stomach that is part of the digestive system. Pancreatic cancer develops when cells in the pancreas grow out of control, forming a lump (tumour). About 95% of pancreatic cancers are called exocrine tumours. Pancreatic ductal adenocarcinoma (PDAC) is the most common type of exocrine tumour (80% of cases). It starts in the cells lining the pancreatic duct.[1] BRCA1 and BRCA2 are among the most common of the known genetic mutations involved in PDAC,[2] and have been identified in 4.6% of a large cohort of people with this type of tumour.[3]

Pancreatic cancer does not usually cause any symptoms in its early stages, which can make it difficult to diagnose until the advanced stages of the disease. The first symptoms may include pain in the back or stomach area, unexpected weight loss or jaundice (yellowing of the skin and whites of the eyes). At the time of diagnosis, about 35–40% of people have locally advanced disease (meaning the cancer has grown into the tissues surrounding the pancreas) and about 45–55% have metastatic disease (meaning the cancer has spread to other parts of the body).[4]

In 2015, 8319 people were diagnosed with pancreatic cancer in England.[5] Pancreatic cancer incidence is strongly related to age, with the highest incidence rates being in older people. There were around 7816 deaths because of pancreatic cancer in 2016 in England.[6] The prognosis depends on how advanced the disease is when it is diagnosed. On average, about 21% of people with pancreatic cancer survive 12 months.[7]

Surgery is usually the only way pancreatic cancer can be cured, but it is only suitable for the 15-20% of people who have early stage disease. The NICE clinical guideline on pancreatic cancer in adults (NG85) recommends that people with metastatic pancreatic cancer should be offered a combination of folic acid, fluorouracil, irinotecan and oxaliplatin (FOLFIRINOX) as a first-line treatment if they have a good performance status. For people who are unable to tolerate FOLFIRINOX, the clinical guideline recommends gemcitabine combination therapy, or gemcitabine monotherapy or in combination with

albumin bound paclitaxel nanoparticles (TA476) if they are not well enough to tolerate combination therapy. In people whose disease relapses following initial therapy, the clinical guideline recommends considering oxaliplatin-based chemotherapy for people who have not had first-line oxaliplatin, or gemcitabine-based chemotherapy for people whose cancer has progressed after first-line. There are currently no treatments licensed for the maintenance treatment of BRCA mutation-positive metastatic pancreatic cancer.

The technology

Olaparib (Lynparza, AstraZeneca) is a poly-ADP-ribose polymerase (PARP) enzyme inhibitor which selectively kills tumour cells with an impaired homologous recombination DNA repair pathway whilst sparing normal cells. Olaparib is administered orally.

Olaparib does not currently have a marketing authorisation in the UK for maintenance treatment of BRCA mutation-positive metastatic pancreatic cancer after initial platinum-based chemotherapy. It has been studied as a monotherapy in a randomised, placebo-controlled clinical trial as maintenance treatment of metastatic BRCA1 or BRCA2 positive pancreatic cancer in adults whose disease has not progressed on first line platinum-based chemotherapy.

Olaparib has a marketing authorisation in the UK as a monotherapy for the maintenance treatment of adult patients with platinum-sensitive relapsed BRCA-mutated (germline and/or somatic) high-grade serous epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in response (complete response or partial response) to platinum-based chemotherapy.

Intervention(s)	Olaparib
Population(s)	People with BRCA mutation-positive metastatic pancreatic cancer whose disease has responded to initial platinum-based chemotherapy.
Comparators	Established clinical practice without olaparib.
Outcomes	The outcome measures to be considered include: • progression free survival • overall 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.
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	Related Technology Appraisals: Olaparib for maintenance treatment of relapsed, platinum-sensitive, BRCA mutation-positive ovarian, fallopian tube and peritoneal cancer after response to second-line or subsequent platinum-based chemotherapy (2016). NICE technology appraisal guidance 381. Paclitaxel as albumin-bound nanoparticles with gemcitabine for untreated metastatic pancreatic cancer (2017) NICE technology appraisal guidance 476. Technology appraisals in development: Olaparib for maintenance treatment of recurrent, platinum-sensitive ovarian, fallopian tube and peritoneal cancer that has responded to platinum-based chemotherapy (including a review of technology appraisal no. 381). NICE technology appraisal guidance. Publication expected: TBC Olaparib for maintenance treatment of ovarian, fallopian tube or peritoneal cancer that has a BRCA germline mutation after response to first-line platinum-based chemotherapy. NICE technology appraisal guidance. Publication expected: July 2019 Olaparib for treating BRCA 1 or 2 mutated metastatic breast cancer after prior chemotherapy. NICE technology appraisal guidance. NICE technology

	appraisal guidance. Publication expected: July 2020 Related Guidelines: Pancreatic cancer in adults: diagnosis and management (2018) NICE guideline 85 Suspected cancer: recognition and referral (2015) NICE guideline 12 Related Quality Standards: Pancreatic cancer (2018) NICE quality standard 177 Suspected cancer (2018) NICE quality standard 124 End of life care for adults (2011) NICE quality standard 13 Related NICE Pathways: Pancreatic cancer (2018) NICE pathway Suspected cancer recognition and referral (2018) NICE pathway
Related National Policy	**National Service Frameworks:** Cancer **Department of Health:** Department of Health, NHS Outcomes Framework 2016-2017 Department of Health (2014) The national cancer strategy: 4th annual report Department of Health (2011) Improving outcomes: a strategy for cancer Department of Health (2009) Cancer commissioning guidance Department of Health (2007) Cancer reform strategy 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), Chapter 131: Specialist services for complex liver, biliary and pancreatic diseases in adults Department of Health and Social Care, NHS Outcomes Framework 2016-2017: Domains 1, 4 & 5.

	https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017 NHS England (2013) 2013/14 NHS standard contract for cancer: pancreatic (adult). Service specification no. A02/S/b **Other policies** Independent Cancer Taskforce (2015) Achieving world-class cancer outcomes: a strategy for England 2015-2020

Questions for consultation

Is the population defined appropriately?

Which treatments are considered to be established clinical practice in the NHS in England for the maintenance treatment of BRCA mutation-positive metastatic pancreatic cancer in people whose disease has responded to initial platinum-based chemotherapy?

Are the outcomes listed appropriate?

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

Where do you consider olaparib will fit into the existing NICE pathway, Pancreatic 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 olaparib 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 olaparib 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 olaparib 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. Pancreatic Cancer UK (2019) What is pancreatic cancer? Accessed April 2019.

2. Kowalewski A, Szylberg Ł, Saganek M et al. (2018) Emerging strategies in BRCA-positive pancreatic cancer. Journal of cancer research and clinical oncology 144(8), 1503-7.

3. Holter S, Borgida A, Dodd A et al. (2015) Germline BRCA mutations in a large clinic-based cohort of patients with pancreatic adenocarcinoma. Journal of Clinical Oncology 33(28), 3124-9.

4. Pancreatic cancer UK (2019) Facts about pancreatic cancer. Accessed April 2019.

5. Cancer Research UK (2019) Pancreatic cancer incidence statistics. Accessed April 2019.

6. Cancer Research UK (2019) Pancreatic cancer mortality statistics. Accessed April 2019.

7. Cancer Research UK (2019) Pancreatic cancer survival statistics. Accessed April 2019.