NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Olaparib with abiraterone for untreated hormone-relapsed metastatic prostate cancer

Draft scope

Draft remit/evaluation objective

To appraise the clinical and cost effectiveness of olaparib with abiraterone within its marketing authorisation for treating hormone-relapsed metastatic prostate cancer in people who have not received prior chemotherapy or new hormonal agents (NHAs).

Background

Prostate cancer is a condition in which tumours develop in the prostate, a gland in the male reproductive system. The exact cause is unknown but environmental and genetic factors are associated with an increased risk of developing prostate cancer.[1,2]

Prostate cancer is the most common cancer in men[3], and the incidence increases with age. It is more common in those who have a family history of prostate cancer, in black African men compared to white men, and is least common in Asian men.[1]

In England and Wales, around 52,580 people were newly diagnosed with prostate cancer between 2018 and 2019.[4] Of this, 13% had metastatic disease, that is, disease that has spread to other parts of the body (such as the bones).[4] In 2018, around 11,900 people died from prostate cancer.[5]

NICE clinical guideline 131 recommends radical treatment (surgery and radiotherapy) and androgen deprivation therapy (ADT) for the treatment of local and locally advanced prostate cancer. The aim of ADT is to suppress androgen levels and cause prostate cancer cell death. This can be achieved by orchidectomy (surgical removal of the testes) or by hormonal treatments such as luteinising hormone-releasing hormone agonist (e.g., goserelin) and antagonist (e.g., degarelix), and androgen receptor inhibitor (e.g., bicalutamide). For newly diagnosed metastatic prostate cancer cases, docetaxel (chemotherapy) can be offered within 12 weeks of starting ADT. In other metastatic cases, ADT is recommended initially.

Prostate cancer may initially be responsive to hormone therapy but eventually become resistant to it. This is known as hormone-relapsed prostate cancer (also known as hormone-resistant, hormone-refractory, and castration-resistant) and refers to prostate cancer which has progressed following ADT. Hormone-relapsed prostate cancer is characterised by a rise in prostate-specific antigen (PSA) despite ADT.

New hormonal agents (NHAs) refer to recently developed medicines which decrease androgen levels. These include apalutamide, enzalutamide, darolutamide and abiraterone. Two treatments are currently recommended for hormone-relapsed metastatic prostate cancer before chemotherapy. Enzalutamide is recommended for treating hormone-relapsed metastatic prostate cancer after ADT has failed, and before chemotherapy is indicated (TA377). Similarly, abiraterone in combination with prednisone or prednisolone is recommended for treating hormone-relapsed

metastatic prostate cancer in people who have no or mild symptoms after ADT has failed, and before chemotherapy is indicated (TA387).

Chemotherapy docetaxel is recommended for people with hormone-relapsed metastatic prostate cancer with a Karnofsky Performance Status Score of 60% or more (NICE clinical guideline 131 and TA101).

Abiraterone in combination with prednisone or prednisolone is recommended for the treatment of hormone-relapsed metastatic prostate cancer if the disease has progressed on or after one course of docetaxel-containing regimen (TA259). Enzalutamide is also recommended for treating hormone-relapsed metastatic prostate cancer in adults whose disease has progressed during or after docetaxel-containing chemotherapy (TA316).

Cabazitaxel in combination with prednisone or prednisolone is recommended for treating hormone-relapsed metastatic prostate cancer in people whose disease has progressed during or after docetaxel chemotherapy (TA391). Radium-223 dichloride is recommended as an option for treating hormone-relapsed prostate cancer in people with symptomatic bone metastases and no known visceral metastases if they have already had docetaxel or if docetaxel is contraindicated or unsuitable (TA412).

The technology

Olaparib with abiraterone does not currently have a marketing authorisation in the UK for the treatment of hormone-relapsed metastatic prostate cancer. It is being studied in a phase III clinical trial (NCT03732820) compared with placebo and abiraterone in adults with hormone-relapsed metastatic prostate cancer who have not received prior chemotherapy or NHAs.

Olaparib has a marketing authorisation in the UK for the treatment of:

- BRCA1/2-mutated hormone-relapsed metastatic prostate cancer.

Abiraterone has a marketing authorisation in the UK for the treatment of:

- newly diagnosed high risk hormone-sensitive metastatic prostate cancer in adults, in combination with ADT
- hormone-relapsed metastatic prostate cancer in adults who are asymptomatic or mildly symptomatic after failure of ADT in whom chemotherapy is not yet clinically indicated
- hormone-relapsed metastatic prostate cancer in adults whose disease has progressed on or after a docetaxel-based chemotherapy regimen.

Intervention(s)	Olaparib with abiraterone (and prednisone or prednisolone).
Population(s)	Adults with hormone-relapsed metastatic prostate cancer who have not received prior chemotherapy or new hormonal agents (NHAs).

Subgroup	If the evidence allows, the following subgroup will be considered:
	• homologous recombination repair (HRR) status including:
	  ○ breast cancer gene (BRCA1 and BRCA2)
	  ○ ataxia-telangiectasia mutated (ATM) gene.
	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.

Comparators	• Enzalutamide • Abiraterone with prednisone or prednisolone • Docetaxel
Outcomes	The outcome measures to be considered include: • overall survival • progression-free 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. 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 cost associated with diagnostic testing for people with hormone-relapsed metastatic prostate cancer who would not otherwise have been tested. A sensitivity analysis should be provided without the cost of the diagnostic test. See section 4.8 of the guidance development manual (available here: https://www.nice.org.uk/process/pmg36/chapter/introduction-to-health-technology-evaluation).
Related NICE recommendations	**Related Technology Appraisals:** Radium-223 dichloride for treating hormone-relapsed prostate cancer with bone metastases (2016) NICE technology appraisal guidance 412 Cabazitaxel for hormone-relapsed metastatic prostate cancer treated with docetaxel (2016) NICE technology appraisal guidance 391 Abiraterone for treating metastatic hormone-relapsed prostate cancer before chemotherapy is indicated (Last updated 2016) NICE technology appraisal guidance 387 Enzalutamide for treating metastatic hormone-relapsed prostate cancer before chemotherapy is indicated (2016) NICE technology appraisal guidance 377 Abiraterone for castration-resistant metastatic prostate cancer previously treated with a docetaxel-containing regimen (Last updated 2016) NICE technology appraisal guidance 259 Enzalutamide for metastatic hormone-relapsed prostate cancer previously treated with a docetaxel-containing regimen (2014) NICE technology appraisal guidance 316 Docetaxel for the treatment of hormone-refractory metastatic prostate cancer (2006) NICE technology appraisal guidance 101 **Related appraisals in development (including suspended appraisals):**

	Olaparib for previously treated, hormone-relapsed metastatic prostate cancer with homologous recombination repair gene mutations NICE technology appraisal guidance [ID1640]. Expected publication date TBC Ipatasertib with abiraterone and prednisone for hormone-relapsed metastatic prostate cancer NICE technology appraisal guidance [ID3889]. Expected publication date TBC Talazoparib with enzalutamide for untreated hormone-relapsed metastatic prostate cancer NICE technology appraisal guidance [ID4004]. Expected publication date TBC Nivolumab with docetaxel for treating hormone-relapsed advanced prostate cancer after 1 or 2 hormonal therapies NICE technology appraisal guidance [ID4048]. Expected publication date TBC Pembrolizumab with docetaxel for treating hormone-relapsed metastatic prostate cancer untreated with chemotherapy NICE technology appraisal guidance [ID3801]. Expected publication date TBC 177Lu-PSMA-617 for treating PSMA-positive hormone-relapsed metastatic prostate cancer after 2 or more therapies NICE technology appraisal guidance [ID3840]. Expected publication date TBC Pembrolizumab with olaparib for treating hormone-relapsed metastatic prostate cancer after abiraterone or enzalutamide and chemotherapy NICE technology appraisal guidance [ID3814]. Expected publication date TBC **Related Guidelines:** Prostate cancer: diagnosis and management (Last updated 2021) NICE guideline 131 Hormone-sensitive metastatic prostate cancer: docetaxel (2016) NICE evidence summary 50 **Related Quality Standards:** 'Prostate cancer' (Last updated 2021) NICE quality standard 91.
Related National Policy	The NHS Long Term Plan, 2019. NHS Long Term Plan. NHS England (2018/2019) NHS manual for prescribed specialist services (2018/2019). Department of Health (2016) Department of Health and Social Care, NHS Outcomes Framework 2016-2017 Domains 1-5. NHS England (2013) NHS England B14/S/a 2013/14 NHS standard contract for cancer: specialised kidney, bladder and prostate cancer services (adult). NHS England (2016) Clinical Commissioning Policy Statement: Docetaxel in combination with androgen

	deprivation therapy for the treatment of hormone naïve metastatic prostate cancer.

Questions for consultation

Where do you consider olaparib with abiraterone, will fit into the existing care pathway for hormone-relapsed metastatic prostate cancer?

Have all the relevant comparators for olaparib with abiraterone been included in the scope?

Have all the new hormonal agents (NHAs) used in clinical practice in the NHS been captured?

Is it appropriate to exclude treatments recommended after chemotherapy as comparators?

As commissioned by NHS England, enzalutamide and abiraterone can only be used once in the treatment pathway. Does this affect comparator considerations, including in relation to cost-effectiveness?

Are interim treatment option recommendations by NHS England for prostate cancer during the COVD-19 pandemic likely to influence the treatment pathway?

Have all the appropriate outcomes been captured?

Do you consider radiological progression free survival (rPFS) to be an appropriate outcome measure for hormone-relapsed metastatic prostate cancer?

Are there any subgroups for which olaparib with abiraterone would be expected to be more clinically effective and cost-effective?

Would it be appropriate to consider olaparib with abiraterone as first-line treatment irrespective of HRR status?

Would olaparib with abiraterone be a candidate for managed access?

Do you consider olaparib with abiraterone 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 with abiraterone can result in any potential 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 committee to take account of these benefits.

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 with abiraterone 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.

NICE intends to evaluate this technology through its Single Technology Appraisal process. We welcome comments on the appropriateness of appraising this topic through this process. (Information on NICE's health technology evaluation processes is available at https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/nice-technology-appraisal-guidance/changes-to-health-technology-evaluation).

NICE's health technology evaluations: the manual states the methods to be used where a cost comparison case is made.

- Would it be appropriate to use the cost-comparison methodology for this topic?

- Is the new technology likely to be similar in its clinical efficacy and resource use to any of the comparators?

- Is the primary outcome that was measured in the trial or used to drive the model for the comparator(s) still clinically relevant?

- Is there any substantial new evidence for the comparator technology/ies that has not been considered? Are there any important ongoing trials reporting in the next year?

References

1. Cancer Research UK (2020) Prostate cancer risks and causes. Accessed January 2022.

2. Macmillan Cancer Support (2018) Potential causes of prostate cancer. Accessed January 2022.

3. Cancer Research UK (2018) Prostate cancer incidence statistics. Accessed March 2022.

4. National Prostate Cancer Audit (2021) Annual Report 2020. Accessed January 2022.

5. Cancer Research UK (2018) Prostate cancer mortality statistics. Accessed March 2022.