NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Talazoparib with enzalutamide for untreated hormone-relapsed metastatic prostate cancer

Draft scope

Draft remit/evaluation objective

To appraise the clinical and cost effectiveness of talazoparib with enzalutamide within its marketing authorisation for treating hormone-relapsed metastatic prostate cancer in adults for whom chemotherapy is not clinically indicated.

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 45,885 people were newly diagnosed with prostate cancer between 2019 and 2020.[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 2019, around 12,000 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).

Olaparib is recommended for treating hormone-relapsed metastatic prostate cancer with BRCA1 or BRCA2 mutations that has progressed after a newer hormonal treatment such as abiraterone or enzalutamide (TA887). Olaparib with abiraterone and prednisone or prednisolone is recommended as an option for untreated hormone-relapsed metastatic prostate cancer in adults who cannot have or do not want chemotherapy (TA951).

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

Talazoparib (Talzenna, Pfizer) with enzalutamide (Xtandi, Astellas Pharma) has a marketing authorisation in the UK for 'the treatment of adult patients with metastatic castration-resistant prostate cancer (mCRPC) in whom chemotherapy is not clinically indicated'.

Enzalutamide has a marketing authorisation in the UK for treating adult men with:

- Hormone-sensitive metastatic prostate cancer in combination with ADT
- High-risk hormone-relapsed non-metastatic prostate cancer
- Hormone-relapsed metastatic prostate cancer, whose disease is asymptomatic or mildly symptomatic after failure of ADT and for whom chemotherapy is not yet clinically indicated
- Hormone-relapsed metastatic prostate cancer, whose disease has progressed on or after docetaxel therapy.

Interventions	Talazoparib in combination with enzalutamide
Population	Adults with hormone-relapsed metastatic prostate cancer for whom chemotherapy is not clinically indicated

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 • Olaparib with abiraterone (and prednisone or prednisolone)
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. If the technology is likely to provide similar or greater health benefits at similar or lower cost than technologies recommended in published NICE technology appraisal guidance for the same indication, a cost comparison may be carried out. 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:** Olaparib with abiraterone for untreated hormone-relapsed metastatic prostate cancer (2024). NICE technology appraisal guidance 951. No current plans to review this guidance. Lu vipivotide tetraxetan for treating PSMA-positive hormone-relapsed metastatic prostate cancer after 2 or more therapies (2023). NICE technology appraisal guidance 930. No current plans to review this guidance. Olaparib for previously treated BRCA mutation-positive hormone-relapsed metastatic prostate cancer (2023). NICE technology appraisal guidance 887. No current plans to review this guidance. Enzalutamide for treating hormone-sensitive metastatic prostate cancer (2021). NICE technology appraisal guidance 712. Review date 2024. Enzalutamide for hormone-relapsed non-metastatic prostate cancer (2019). NICE technology appraisal guidance 580. Review date 2022. Radium-223 dichloride for treating hormone-relapsed prostate cancer with bone metastases (2016). NICE technology appraisal guidance 412. Review date to be confirmed.

	Cabazitaxel for hormone-relapsed metastatic prostate cancer treated with docetaxel (2016). NICE technology appraisal guidance 391. No current plans to review this guidance. Abiraterone for treating metastatic hormone-relapsed prostate cancer before chemotherapy is indicated (2016). NICE technology appraisal guidance 387. No current plans to review this guidance. Enzalutamide for treating metastatic hormone-relapsed prostate cancer before chemotherapy is indicated (2016). NICE technology appraisal guidance 377. No current plans to review this guidance. Enzalutamide for metastatic hormone-relapsed prostate cancer previously treated with a docetaxel-containing regimen (2014). NICE technology appraisal guidance 316. No current plans to review this guidance. Abiraterone for castration-resistant metastatic prostate cancer previously treated with a docetaxel-containing regimen (2016). NICE technology appraisal guidance 259. No current plans to review this guidance. Docetaxel for the treatment of hormone-refractory metastatic prostate cancer (2006). NICE technology appraisal guidance 101. No current plans to review this guidance. **Related Guidelines:** Prostate cancer: diagnosis and management (2021). NICE guideline 131. No current plans to review this. **Related Quality Standards:** 'Prostate cancer' (2021). NICE quality standard 91. No current plans to review this.
Related National Policy	The NHS Long Term Plan (2019) NHS Long Term Plan NHS England (2023) Manual for prescribed specialist services (2023/2024) Chapter 105: Specialist cancer services (adults) 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 talazoparib with enzalutamide will fit into the existing care pathway for adults with untreated hormone-relapsed metastatic prostate cancer?

Please select from the following, will talazoparib with enzalutamide be:
A. Prescribed in primary care with routine follow-up in primary care
B. Prescribed in secondary care with routine follow-up in primary care
C. Prescribed in secondary care with routine follow-up in secondary care
D. Other (please give details):
For comparators and subsequent treatments, please detail if the setting for prescribing and routine follow-up differs from the intervention.

Have all the relevant comparators for talazoparib with enzalutamide been included in the scope?

Are there any testing costs related to this treatment or disease that should be included in the economic modelling?

Would talazoparib with enzalutamide be a candidate for managed access?

Do you consider that the use of talazoparib 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 talazoparib is 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 is considering evaluating this technology through its cost comparison evaluation process.
Please provide 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).

Technologies can be evaluated through the cost-comparison process if they are expected to provide similar or greater health benefits, at a similar or lower cost,

compared with technologies that have been previously recommended (as an option) in published NICE guidance for the same indication. Companies can propose cost-comparison topics to NICE at any stage during topic selection and scoping. NICE will route technologies for evaluation through the cost-comparison process if it is agreed during scoping that the process is an appropriate route to establish the clinical and cost effectiveness of the technology.

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

- Is the technology likely to be similar in its clinical effectiveness and resource use to any of the comparators? Or in what way is it different to the comparators?
- Will the intervention be used in the same place in the treatment pathway as the comparator(s)? Have there been any major changes to the treatment pathway recently? If so, please describe.
- Will the intervention be used to treat the same population as the comparator(s)?
- Overall is the technology likely to offer similar or improved health benefits compared with the comparators?
- Do the comparators have substantial use in the NHS in England for treating adults with hormone-relapsed metastatic prostate cancer for whom chemotherapy is not clinically indicated?
- Would it be appropriate to use the cost-comparison methodology for this topic?

References

1. Cancer Research UK (2022) Prostate cancer risks and causes. Accessed May 2024.
2. Macmillan Cancer Support (2021) Potential causes of prostate cancer. Accessed May 2024.
3. Cancer Research UK (2018) Prostate cancer incidence statistics. Accessed May 2024.
4. National Prostate Cancer Audit (2022) Annual Report 2021. Accessed May 2024.
5. Cancer Research UK (2019) Prostate cancer mortality statistics. Accessed May 2024.