NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Pembrolizumab with olaparib for treating hormone-relapsed metastatic prostate cancer after abiraterone or enzalutamide and chemotherapy

Draft scope

Draft remit/ appraisal objective

To appraise the clinical and cost effectiveness of pembrolizumab with olaparib within its marketing authorisation for treating metastatic hormone-resistant prostate cancer that has progressed on one next-generation hormonal agent (abiraterone or enzalutamide) and has been treated with taxane-based chemotherapy.

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]

The incidence of prostate cancer 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 between April 2018 and April 2019, around 52,580 people were diagnosed with prostate cancer and in 2018 11,900 died from the condition.[3,4] Around 13% had metastatic disease, that is a disease that has spread to other parts of the body (for example, the bones).[4]

NICE clinical guideline 131 recommends androgen deprivation therapy (luteinising hormone-releasing hormone agonist therapy, bicalutamide or bilateral orchidectomy) for people whose prostate cancer is sensitive to such hormonal therapy. Docetaxel can be added to luteinising hormone-releasing hormone agonist therapy if the prostate cancer is metastatic.

Hormone-relapsed prostate cancer (also known as hormone-resistant, hormone-refractory, and castration-resistant) refers to prostate cancer which has progressed on androgen deprivation therapy. Darolutamide with androgen deprivation therapy is recommended for treating hormone-relapsed non-metastatic prostate cancer (TA660). Apalutamide with androgen deprivation therapy is recommended for treating high-risk hormone-relapsed non-metastatic prostate cancer (TA740). Similarly, enzalutamide is recommended for treating high-risk hormone-relapsed non-metastatic prostate cancer (TA580). Abiraterone in combination with prednisone or prednisolone is recommended for treating metastatic hormone-relapsed prostate cancer in people who have no or mild symptoms after androgen deprivation therapy has failed, and before chemotherapy is indicated (TA387). Similarly, enzalutamide is recommended for treating metastatic hormone-relapsed prostate cancer in people who have no or mild symptoms after androgen deprivation therapy has failed, and before chemotherapy is indicated (TA377).

NICE guideline 131 and TA101 recommends chemotherapy (docetaxel) as a treatment option for people with hormone-relapsed prostate cancer if their Karnofsky performance-status score is 60% or more.

Abiraterone in combination with prednisone or prednisolone and enzalutamide are also recommended for metastatic hormone-relapsed prostate cancer if it has progressed on a docetaxel-containing chemotherapy regimen (TA259 and TA316 respectively).

Radium-223 dichloride is recommended for treating hormone-relapsed prostate cancer with bone metastases in people who already had docetaxel, or for whom docetaxel is contraindicated or unsuitable (TA412).

Cabazitaxel in combination with prednisone or prednisolone is recommended as an option for treating people whose disease has progressed during or after docetaxel therapy (TA391).

The technology

Pembrolizumab (Keytruda, MSD) is a humanised, antiprogrammed cell death 1 (PD-1) antibody involved in the blockade of immune suppression and the subsequent reactivation of anergic T-cells. It is administered intravenously.

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

Pembrolizumab with olaparib does not currently have a marketing authorisation in the UK for the treatment of metastatic hormone relapsed prostate cancer. It is being studied in a phase III clinical trial compared with abiraterone acetate or enzalutamide, in adult male patients with metastatic hormone-resistant prostate cancer who have failed to respond to either abiraterone acetate or enzalutamide (but not both) and taxane-based chemotherapy.

Intervention(s)	Pembrolizumab with olaparib
Population(s)	Adults with hormone-relapsed metastatic prostate cancer previously treated with either abiraterone acetate or enzalutamide and taxane based chemotherapy
Comparators	• Cabazitaxel • Lutetium-177 prostate-specific membrane antigen-617 (subject to ongoing NICE appraisal) • Radium-223 dichloride (for people with bone metastases) • Best supportive care

Outcomes	The outcome measures to be considered include: • progression free survival • overall survival • response rate • time to first symptomatic skeletal event • 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 and NICE Pathways	**Related Technology Appraisals:** Apalutamide with androgen deprivation therapy for treating hormone-sensitive metastatic prostate cancer (2021) NICE technology appraisal guidance 741 Apalutamide for treating non-metastatic hormone-sensitive prostate cancer (2021) NICE technology appraisal guidance 740 Abiraterone for treating newly diagnosed high-risk metastatic hormone-naive prostate cancer (2021) NICE technology appraisal guidance 721 Enzalutamide with androgen deprivation therapy for untreated metastatic hormone-sensitive prostate cancer (2021) NICE technology appraisal guidance 712 Darolutamide with androgen deprivation therapy for treating hormone-relapsed non-metastatic prostate cancer (2020)

	NICE technology appraisals guidance 660 Enzalutamide for hormone-relapsed non-metastatic prostate cancer (2019) NICE technology appraisal guidance 580 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):** Niraparib for previously treated hormone-relapsed metastatic prostate cancer with DNA-repair anomalies [ID3782]. NICE medical technologies guidance. Suspended Apalutamide with abiraterone acetate and prednisone for treating metastatic hormone-relapsed prostate cancer. NICE technology appraisal guidance ID 1480. Publication date: TBC Nivolumab in combination for treating hormone-relapsed metastatic prostate cancer after chemotherapy NICE technology appraisal guidance ID 1621. Publication date: TBC Olaparib for previously treated, hormone-relapsed metastatic prostate cancer with homologous recombination repair gene

	mutations NICE technology appraisal guidance ID 1640. Publication date: TBC **Related Guidelines:** Prostate cancer: diagnosis and management (2019) NICE guideline 131 Hormone-sensitive metastatic prostate cancer: docetaxel. (2016) NICE evidence summary 50 Prostate cancer (2019) NICE pathway
Related National Policy	Department of Health (2009) Cancer commissioning guidance The NHS Long Term Plan, 2019. NHS Long Term Plan NHS England (2018/2019) NHS manual for prescribed specialist services (2018/2019) 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

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

Which treatments are considered to be established clinical practice in the NHS for metastatic hormone-resistant prostate cancer which is previously treated abiraterone or enzalutamide and taxane-based chemotherapy?

What treatments used in UK clinical practice are classed as next-generation hormonal agents?

Is it appropriate to exclude abiraterone and enzalutamide as potential comparators because patients can only receive them once in UK clinical practice and it is expected that pembrolizumab with olaparib will be used after a next-generation hormonal agent (e.g. abiraterone or enzalutamide)?

Where do you consider pembrolizumab with olaparib will fit into the existing NICE pathway, Prostate cancer?

Are the outcomes listed appropriate?

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

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 pembrolizumab with 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 pembrolizumab with 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 pembrolizumab with 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).

NICE has published an addendum to its guide to the methods of technology appraisal (available at https://www.nice.org.uk/Media/Default/About/what-we-do/NICE-guidance/NICE-technology-appraisals/methods-guide-addendum-cost-comparison.pdf), which 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 mortality statistics. Accessed January 2022.
4. National Prostate Cancer Audit (2021) Annual Report 2020. Accessed January 2022