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Newcastle University

Health Technology Briefing
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Niraparib with abiraterone acetate and prednisone for metastatic castration resistant prostate cancer

Company/Developer	Janssen-Cilag Ltd

☐ New Active Substance ☒ Significant Licence Extension (SLE)

NIHRIO ID: 27006	NICE TSID: 10523	UKPS ID: 655364

Licensing and Market Availability Plans

Currently in phase III clinical development.

Summary

Niraparib with abiraterone acetate and prednisone (AAP) is in clinical development for patients with prostate cancer which has spread from its original site (metastatic) and is untreatable via testosterone suppression therapy (castration resistant). Prostate cancer is a cancer of the prostate gland (a small organ in a man's pelvis) and is the most common cancer in men in the UK. The symptoms may vary depending on the stage of cancer but can include pain, tiredness, and problems emptying the bladder and the bowels. The castration-resistant form of metastatic prostate cancer is particularly dangerous and leads to a very poor prognosis, hence additional treatment options are needed.

Niraparib is a medicinal product taken orally. It works by blocking a protein called poly (adenosine diphosphate-ribose) polymerase (PARP). It blocks the action of PARP-1 and PARP-2 enzymes that help in repairing damaged DNA in cells when they divide to make new cells. By blocking PARP enzymes, the damaged DNA in cancer cells cannot be repaired, and the cells die. Niraparib, administered orally, in combination with AAP will offer an additional treatment option for men with mCRPC.

Proposed Indication

For the treatment of adults with metastatic castration resistant prostate cancer (mCRPC).[1]

Technology

Description

Niraparib (MK-4827[2], Zejula) is an inhibitor of poly(ADP-ribose) polymerase (PARP) enzymes, PARP-1 and PARP-2, which play a role in DNA repair. *In vitro* studies have shown that niraparib-induced cytotoxicity may involve inhibition of PARP enzymatic activity and increased formation of PARP-DNA complexes resulting in DNA damage, apoptosis and cell death.[3]

Niraparib is currently in development with abiraterone acetate and prednisone for the treatment of mCRPC, in those patients who are not yet recommended chemotherapy. In the phase III trial (NCT03748641, MAGNITUDE), participants receive a 200 mg capsule of niraparib, a 1000 mg tablet of abiraterone acetate once daily and a 10 mg tablet of prednisone daily until disease progression.[1]

Key Innovation

Treatment options for patients with mCRPC are noncurative, and life expectancy is only about 3 years.[4] Approximately 20% of mCRPC has alterations in genes associated with HRR and is responsive to PARP inhibitors (PARPi) such as niraparib. Combined PARPi with androgen receptor pathway targeting may also benefit unselected mCRPC.[5]

Niraparib in combination with abiraterone acetate and prednisone (AAP) has shown the ability to improve progression free survival (PFS) and other clinically relevant outcomes in patients with mCRPC and alterations in HRR associated genes.[5] If licensed, niraparib in combination with AAP will offer an additional treatment option for patients with mCRPC and alterations in HRR associated genes.

Regulatory & Development Status

Niraparib in combination with AAP does not currently have Marketing Authorisation in the EU/UK for any indication.

Niraparib currently has Marketing Authorisation in the EU/UK for the following indications:[3,6]

- Fallopian tube neoplasms
- Peritoneal neoplasms
- Ovarian neoplasms

Patient Group

Disease Area and Clinical Need

Prostate cancer is the most common cancer in older men in the UK.[7] It affects the prostate, a small gland in the pelvis found only in men which is located between the penis and the bladder and surrounds the urethra. The main function of the prostate is to help in the production of semen.[8] In advanced prostate

cancer, the cancer has spread from the prostate to other parts of the body (metastatic). It most commonly spreads to lymph nodes in other parts of the body or to the bones.[9] Prostate cancer cells usually need testosterone to grow.[10] Prostate cancer that has spread to other parts of the body and which keeps growing even when the amount of testosterone in the body is reduced to very low levels (via androgen deprivation therapy) is identified as mCRPC.[11] Prostate cancer is more common in black Caribbean and black African men than in white men and is less common in Asian men.[7] Prostate cancer does not usually cause any symptoms until the cancer has grown large enough to put pressure on the tube that carries urine from the bladder out of the penis (urethra).[8] Prostate cancer is a significant cause of morbidity and mortality in men, especially in those over the age of 75 years and impacts on their daily lives, particularly physical and emotional health, relationships and social life.[12]

Prostate cancer accounts for 27% of all new cancer cases in males in the UK (2017 data).[13] Around 55–65% of people with prostate cancer develop metastatic disease. Over 90% of people with metastatic prostate cancer initially respond to hormonal therapy but eventually become resistant to it.[14] In England, in 2017 there were 41,201 registrations of newly diagnosed cases of malignant neoplasm of prostate (ICD10 code C61). Of these, 8,490 cases were diagnosed at stage 4 (metastatic).[15] According to Hospital Episode Statistics (HES) data, in 2020-21 there were 55,799 admissions with a primary diagnosis of neoplasm of the prostate (ICD-10 code C61), resulting in 60,023 finished consultant episodes (FCE), 58,293 bed days and 39,040 day cases.[16] In England and Wales in 2020, there were 10,971 deaths where malignant neoplasm of prostate (ICD-10 code C61) was recorded as the underlying cause.[17] Latest published survival statistics (patients diagnosed in 2013-2017) report a 1-year net survival rate of 88.3% and a 5-year net survival rate of 49% for men diagnosed with stage 4 prostate cancer.[18]

Recommended Treatment Options

As an option for treating metastatic hormone-relapsed prostate cancer after androgen deprivation therapy has failed, and before chemotherapy is indicated, NICE recommends:[19]

- docetaxel, within its licensed indications, as a treatment option for people with hormone-refractory prostate cancer only if their Karnofsky Performance-Status score is 60% or more.[20]
- androgen deprivation therapy (ADT)
- docetaxel plus ADT
- enzalutamide plus ADT

Clinical Trial Information

Trial	**MAGNITUDE;** NCT03748641; EudraCT2017-003364-12; A Phase 3 Randomized, Placebo-controlled, Double-blind Study of Niraparib in Combination With Abiraterone Acetate and Prednisone Versus Abiraterone Acetate and Prednisone in Subjects With Metastatic Prostate Cancer **Phase III –** Active, not recruiting **Location(s):** 12 EU countries, UK, USA, Canada, and other countries **Primary completion date:** October 2021
Trial Design	Randomised, quadruple masking, parallel assignment
Population	n=765 (actual); subjects aged 18 years and over with mCRPC in the setting of castrate levels of testosterone less than or equal to (<=) 50 nanogram per deciliter

	(ng/dL) on a gonadotropin releasing hormone analog (GnRHa) or bilateral orchiectomy
Intervention(s)	Niraparib 200 mg is administered orally in combination with abiraterone acetate 1000 mg plus prednisone 10 mg
Comparator(s)	Matching placebo and abiraterone acetate 1000 mg plus prednisone 10 mg
Outcome(s)	Radiographic Progression Free Survival (rPFS) [Time frame: up to 28 months] See trial records for full list of other outcomes
Results (efficacy)	Niraparib + abiterone acetate + prednisone improves rPFS and other clinically relevant outcomes in patients with mCRPC and alterations in homologous recombinant repair associated genes.[5]
Results (safety)	No safety signals were seen.[5]

Estimated Cost

The NHS indicative price for 56 capsules of niraparib (100mg) is £4,500.00 (Hospital only). The NHS indicative price for 84 capsules of niraparib (100mg) is £6,750.00 (Hospital only).[21]

Relevant Guidance

NICE Guidance

- NICE technology appraisal guidance in development. Nivolumab in combination for treating hormone relapsed metastatic prostate cancer before chemotherapy (GID-TA10490). Expected date of issue to be confirmed.
- NICE technology appraisal guidance in development. Pembrolizumab with docetaxel for treating hormone-relapsed metastatic prostate cancer untreated with chemotherapy (GID-TA10668). Expected date of issue to be confirmed.
- NICE technology appraisal guidance. Radium–223 dichloride for treating hormone-relapsed prostate cancer with bone metastases (TA412). September 2016.
- NICE technology appraisal guidance. Abiraterone for treating metastatic hormone-relapsed prostate cancer before chemotherapy is indicated (TA387). July 2016.
- NICE technology appraisal guidance. Enzalutamide for treating metastatic hormone-relapsed prostate cancer before chemotherapy is indicated (TA377). January 2016.
- NICE clinical guideline. Prostate cancer: diagnosis and management (NG131). May 2019.
- NICE quality standard. Prostate cancer (QS91). December 2021.

NHS England (Policy/Commissioning) Guidance

- NHS England. 2013/14 NHS Standard Contract for Cancer: Specialised Kidney, Bladder and Prostate Cancer Services (Adult). B14/S/a.
- NHS England. Clinical Commissioning Policy: The use of Stereotactic Ablative Radiotherapy (SABR) in the treatment of Prostate Cancer. 16031/P. July 2016.
- NHS England. Clinical Commissioning Policy: Proton Beam Therapy for Cancer of the Prostate. 16020/P. July 2016.

Other Guidance

- Cassinello J, Arranz JÁ, Piulats JM, Sánchez A, Pérez-Valderrama B, Mellado B, et al. SEOM clinical guidelines for the treatment of metastatic prostate cancer. 2017.[22]
- Public Health England. Prostate Cancer Risk Management Programme. March 2016.[23]
- ESMO Guidelines Committee. Cancer of the prostate: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. 2015.[24]

Additional Information

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