Health Technology Briefing
November 2023

Apalutamide for treating high-risk, localised or locally advanced prostate cancer

Company/Developer	Janssen-Cilag Ltd

☐ New Active Substance ☒ Significant Licence Extension (SLE)

NIHRIO ID: 27147	NICE TSID: Not available	UKPS ID: 666017

Licensing and Market Availability Plans

Currently in phase III clinical trials.

Summary

Apalutamide in combination with androgen deprivation therapy (ADT) is in clinical development for patients with high-risk, localised or locally advanced prostate cancer who are candidates for radical prostatectomy. Prostate cancer is a cancer of the prostate gland (a small organ in a man's pelvis) and is the most common cancer in older men. Locally advanced prostate cancer is cancer that has started to break out of the prostate or has spread to the area just outside the prostate. ADT uses medicines to reduce testosterone levels and treat prostate cancer. Despite significant advances in treatment options for prostate cancer management, the outcome in some patients is still poor. There is therefore need for more therapy options with significant survival benefits.

Apalutamide is a cancer medicine that works by blocking the action of testosterone and other male hormones known as androgens. Because prostate cancer cells need testosterone and other male hormones to survive and grow, by blocking the effects of these hormones, apalutamide slows down the growth of the cancer. Apalutamide is administered orally. If licensed, apalutamide in combination with ADT would offer an additional treatment option for patients with high-risk, localised or locally advanced prostate cancer who are candidates for radical prostatectomy.

Proposed Indication

Patients with high-risk, localised or locally advanced prostate cancer who are candidates for radical prostatectomy.[1]

Technology

Description

Apalutamide (Erleada, ARN-509) is a selective androgen receptor (AR) inhibitor that binds directly to the ligand-binding domain of the AR. Apalutamide prevents AR nuclear translocation, inhibits DNA binding, impedes AR-mediated transcription, and lacks androgen receptor agonist activity. Apalutamide treatment decreases tumour cell proliferation and increases apoptosis leading to potent antitumor activity.[2]

Apalutamide in combination with androgen deprivation therapy (ADT) is in clinical development for the treatment of patients with high-risk, localised or locally advanced prostate cancer who are candidates for radical prostatectomy. In the phase III trial (NCT03767244, PROTEUS), participants receive 240mg of apalutamide orally once daily, in addition to ADT daily in each cycle (each cycle of 28 days). Participants will receive six cycles of treatment, followed by radical prostatectomy with pelvic lymph node dissection (pLND), followed by an additional six cycles of treatment.[1]

Key Innovation

Radical prostatectomy (RP) and radiotherapy with 18–36 months of ADT are standard therapeutic options for men with high-risk prostate cancer (HRPC). While HRPC only accounts for 20% of all localised prostate cancers, outcomes after definitive therapy are guarded with about 50% of men experiencing biochemical recurrence (BCR) after undergoing radical prostatectomy for HRPC.[3] Neoadjuvant studies have shown that 6 months of androgen blockade may improve local disease control at the time of RP.[4]

Analysis from previous studies showed apalutamide significantly improved overall survival (OS), radiographic progression-free survival, delayed castration resistance, maintained health-related quality of life, and had a consistent safety profile in a broad population of patients with metastatic castration-sensitive prostate cancer (mCSPC) receiving ongoing ADT.[5] The addition of apalutamide to the treatment pathway provides eligible prostate cancer patients with a therapy option with significant survival benefit. Apalutamide provides a vital step towards improving outcomes in prostate cancer and enabling patients to have a better prognosis.[6]

Regulatory & Development Status

Apalutamide currently has Marketing Authorisation in the EU/UK for the following indications:[2,7]

- metastatic hormone-sensitive prostate cancer (mHSPC) in combination with ADT in adult men
- non-metastatic castration-resistant prostate cancer (nmCRPC) in combination with ADT in adult men who are at high risk of developing metastatic disease

Apalutamide is currently in phase II clinical development for small cell neuroendocrine carcinoma and salivary gland neoplasms.[8]

Patient Group

Disease Area and Clinical Need

Prostate cancer is cancer of the prostate gland.[9] The prostate, which is a small gland in the pelvis and part of the male reproductive system, 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.[10] Prostate cancer cells usually need testosterone to grow.[11] Locally advanced prostate cancer is cancer that has started to break out of the prostate, or has spread to the area just outside the prostate.[12] Prostate cancer is most common in older men, and also more common in black Caribbean and black African men than in white men and less common in Asian men.[9] Prostate cancer does not usually cause symptoms until the prostate has grown large enough to put pressure on the urethra.[13] Prostate cancer is a significant cause of morbidity and mortality in men and impacts on their daily lives, particularly physical and emotional health, relationships and social life.[14]

Prostate cancer accounts for 27% of all new cancer cases in males in the UK (2016-2018). Incidence rates for prostate cancer in the UK are highest in males aged 75 to 79 (2016-2018).[15] In England, in 2017, there were 41,201 registrations of newly diagnosed cases of malignant neoplasm of prostate (ICD-10 code C61).[16] In England, in 2021-22, there were 73,256 admissions with a primary diagnosis of neoplasm of the prostate resulting in 77,547 finished consultant episodes (FCE), 71,095 bed days and 54,896 day cases.[17] In England and Wales in 2020, there were 10,971 deaths where malignant neoplasm of prostate was recorded as the underlying cause.[18]

Recommended Treatment Options

The treatment options for locally advanced prostate cancer include:[12,19]

- active surveillance
- external beam radiotherapy with hormone therapy (and sometimes with high dose-rate brachytherapy or permanent seed brachytherapy)
- hormone therapy alone, sometimes with docetaxel chemotherapy
- surgery (radical prostatectomy), usually with radiotherapy or hormone therapy and sometimes with both

Clinical Trial Information

Trial	NCT03767244; EudraCT2018-001746-34; **PROTEUS;** A Randomized, Double-blind, Placebo-controlled, Phase 3 Study of Apalutamide in Subjects With High-risk, Localized or Locally Advanced Prostate Cancer Who Are Candidates for Radical Prostatectomy **Phase III:** Recruiting **Location(s):** 7 EU countries, UK, USA, Canada and other countries **Primary completion date:** April 2024
Trial Design	Randomised, quadruple blind, parallel assignment, placebo controlled
Population	N= 2500 (estimated); Male; Subjects aged 18 years and older with histologically confirmed adenocarcinoma of the prostate
Intervention(s)	Apalutamide 240 mg (oral) once daily + ADT daily in each cycle (each cycle of 28 days). Participants will receive six cycles of treatment, followed by RP with pLND, followed by an additional six cycles of treatment

Comparator(s)	Matched placebo
Outcome(s)	• Percentage of participants with pathologic complete response (pCR) [Time frame: approximately 4 years] • Metastasis-free survival (MFS) [Time Frame: up to 7 years and 5 months] See trial records for full list of other outcomes
Results (efficacy)	-
Results (safety)	-

Estimated Cost

Apalutamide is already marketed in the UK; a pack of 112 x 60mg tablet costs £2,735.[20]

Relevant Guidance

NICE Guidance

- NICE technology appraisal guidance. Padeliporfin for untreated localised prostate cancer (TA546). November 2018.
- NICE clinical guideline. Prostate cancer: diagnosis and management (NG131). May 2019. Updated December 2021.
- NICE quality standard. Prostate cancer (QS91). December 2021.
- NICE interventional procedure guidance. Irreversible electroporation for treating prostate cancer (IPG572). December 2016.
- NICE interventional procedure guidance. Focal therapy using cryoablation for localised prostate cancer (IPG423). April 2012.
- NICE interventional procedure guidance. Laparoscopic radical prostatectomy (IPG193). November 2006.
- NICE interventional procedure guidance. High dose rate brachytherapy in combination with external-beam radiotherapy for localised prostate cancer (IPG174). May 2006.
- NICE interventional procedure guidance. Low dose rate brachytherapy for localised prostate cancer (IPG132). July 2005.
- NICE interventional procedure guidance. High-intensity focused ultrasound for prostate cancer (IPG118). March 2005.

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

- Public Health England. Prostate Cancer Risk Management Programme. March 2016.[21]
- ESMO Guidelines Committee. Cancer of the prostate: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. 2020.[22]

Additional Information

References

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4 Taplin M-E, Gleave M, Evans CP, Efstathiou E, Kantoff PW, Ross A, et al. PROTEUS: A randomized, double-blind, placebo (PBO)-controlled, phase III trial of apalutamide (APA) plus androgen deprivation therapy (ADT) versus PBO plus ADT prior to radical prostatectomy (RP) in patients with localized high-risk or locally advanced prostate cancer (PC). 2020. https://ascopubs.org/doi/10.1200/JCO.2020.38.6_suppl.TPS383.

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