

Health Technology Briefing October 2022

Apalutamide with primary radiation therapy for treating high-risk, localised or locally advanced prostate cancer

Company/Developer

Janssen-Cilag Ltd

New Active Substance

Significant Licence Extension (SLE)

NIHRIO ID: 14915

NICE TSID: 10323

UKPS ID: 645185

Licensing and Market Availability Plans

Currently in phase III clinical trials

Summary

Apalutamide with androgen deprivation therapy (ADT), is in clinical development for patients with high-risk localised or locally advanced prostate cancer who are receiving primary radiation therapy. 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. Prostate cancer growth and spread depends on the hormone testosterone. 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.

Apalutamide is an oral tablet in development in combination with ADT for the treatment of patients with localised or locally advanced prostate cancer who are receiving primary radiation. Apalutamide acts by blocking the androgen receptor (target binding site of various steroid hormones including testosterone) to prevent the effects of testosterone in the prostate and the body. If licensed, apalutamide in addition to ADT will offer an additional treatment option for patients with localised or locally advanced prostate cancer who are receiving primary radiation therapy.

Proposed Indication

This briefing reflects the evidence available at the time of writing and a limited literature search. It is not intended to be a definitive statement on the safety, efficacy or effectiveness of the health technology covered and should not be used for commercial purposes or commissioning without additional information. A version of the briefing was sent to the company for a factual accuracy check. The company was available to comment.

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For the treatment of adult patients with high-risk, localised or locally advanced prostate cancer receiving treatment with primary radiation therapy.¹

Technology

Description

Apalutamide (Erleada, ARN-509), is an orally administered, 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. A major metabolite, N-desmethyl apalutamide, exhibited one-third the in vitro activity of apalutamide.²

Apalutamide is in clinical development, in addition to androgen deprivation therapy (ADT), for the treatment of patients with high-risk, localised or locally advanced prostate cancer receiving treatment with primary radiation therapy. In the phase III trial (NCT02531516, ATLAS) participants receive 240mg of apalutamide orally once daily for 30 months, plus bicalutamide placebo orally for four months from randomisation. All participants are treated with gonadotropin releasing hormone (GnRH) agonist for 30 months from randomisation and radiation therapy to the prostate, which started approximately 8 weeks after randomisation.¹

Key Innovation

At present, patients with high-risk localised and locally advanced prostate cancer receiving primary radiation therapy and long-term ADT have a high risk of metastases and death. The addition of apalutamide, a selective androgen receptor agonist to the current regimen of radiation therapy, may improve metastasis-free survival in patients with high-risk localised and locally advanced prostate cancer.³

Regulatory & Development Status

Apalutamide currently has Marketing Authorisation in the EU/UK for the following types of prostate cancer:^{2,4}

- Metastatic Hormone-sensitive Prostate Cancer (mHSPC)
- Non-Metastatic Castration Resistant Prostate Cancer (nmCRPC)

Apalutamide is currently in phase II clinical development for small cell neuroendocrine carcinoma and salivary gland neoplasms.⁵

Patient Group

Disease Area and Clinical Need

Prostate cancer is the most common cancer in older men in the UK.⁶ 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.⁷ 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.⁸ Prostate cancer cells usually need testosterone to grow.⁹ 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.¹⁰ Prostate cancer is more common in black Caribbean and black African men than in white men and is less common in Asian men.⁶ 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).⁷ 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.¹¹

Prostate cancer accounts for 27% of all new cancer cases in males in the UK (2017 data).¹² Around 55–65% of people with prostate cancer develop metastatic disease. In England, in 2017 there were 41,201 registrations of newly diagnosed cases of malignant neoplasm of prostate (ICD10 code C61).¹³ 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.¹⁴ 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.¹⁵

Recommended Treatment Options

According to NICE guidance, current treatment options for locally advanced prostate cancer include:¹⁶

- active surveillance
- radical prostatectomy
- radical radiotherapy

Clinical Trial Information

Trial	ATLAS, NCT02531516, EudraCT2015-003007-38; A Randomized, Double-blind, Placebo-controlled Phase 3 Study of JNJ-56021927 in Subjects With High-risk, Localized or Locally Advanced Prostate Cancer Receiving Treatment With Primary Radiation Therapy Phase III – Active, not recruiting Location(s): 9 EU countries, UK, US, Canada and other countries Primary Completion date: December 2022
Trial Design	Randomised, double blind, parallel assignment
Population	N= 1503 (actual); subjects aged 18 and older with a histologically confirmed adenocarcinoma of an intact prostate; have indicated and planned to receive primary radiation therapy for prostate cancer
Intervention(s)	Participants receive 240mg apalutamide orally once daily for 30 months, plus oral bicalutamide placebo daily for 4 months. All participants receive gonadotropin releasing hormone (GnRH) agonist for 30 months from randomisation, and radiation therapy to the prostate which started at about 8 weeks after randomisation.
Comparator(s)	Matched placebo
Outcome(s)	Metastasis-free survival [Time frame: 108 months] See trial record for full list of other outcomes

Results (efficacy)	-
Results (safety)	-

Estimated Cost

A 112 pack of 60mg apalutamide tablet costs £2,735.¹⁷

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.
- 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

- Public Health England. Prostate Cancer Risk Management Programme. March 2016.¹⁸
- ESMO Guidelines Committee. Cancer of the prostate: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. 2020.¹⁹

Additional Information

References

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