Apalutamide: a better option for the treatment of non-metastatic castration resistant prostatic carcinoma

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ABSTRACT
Prostate cancer is cancer of the prostate, a gland in the male reproductive system. Most prostate cancers are slow growing; however, some grow relatively quickly. The cancer cells may spread from the prostate to other area of the body, particularly the bones and lymph nodes. Factors that increase the risk of prostate cancer include older age, a family history of the disease, and race. About 99% of cases occur in males over the age of 50. Clinical features include hematuria, dysuria (painful urination), nocturia (urination at night). Lower blood levels of vitamin D may increase the risk of developing prostate cancer. Infection with the sexually transmitted diseases, chlamydia, gonorrhea, syphilis and prostatitis seem to increase risk of prostate cancer. Diagnosis can be confirmed by digital rectal examination (DRE) with prostate-specific antigen (PSA) blood test, cystoscopy, transrectal ultrasonography and biopsy (The removal of small pieces of the prostate for microscopic examination). Medicines like 5-alpha-reductase inhibitors (finasteride and dutasteride) reduce the overall risk of prostate cancer. Apalutamide, sold under the brand name Erleada, is a nonsteroidal antiandrogen (NSAA) medication which is used in the treatment of prostate cancer. It is specifically indicated for use in conjunction with castration in the treatment of non-metastatic castration-resistant prostate cancer (NM-CRPC). It is taken by mouth. Apalutamide was first described in 2007 and was approved for the treatment of prostate cancer in February 2018. Apalutamide is used in conjunction with castration, either via bilateral orchiectomy or gonadotropin-releasing hormone analogue (GnRH analogue) therapy, as a method of androgen deprivation therapy in the treatment of non-metastatic castration-resistant prostate cancer (NM-CRPC).

Keywords: Prostatitis, Nonsteroidal antiandrogen, Non-metastatic castration-resistant prostate cancer

INTRODUCTION
Most prostate cancers are slow growing; however, some grow relatively quickly. The cancer cells may spread from the prostate to other area of the body, particularly the bones and lymph nodes. It may initially cause no symptoms. In later stages, it can lead to difficulty urinating, blood in the urine or pain in the pelvis, back, or when urinating. Factors that increase the risk of prostate cancer include older age, a family history of the disease, and race. About 99% of cases occur in males over the age of 50. Having a first-degree relative with the disease increases the risk two to threefold. In the United States, it is more common in the African American population than the White American population. Other factors that may be involved include a diet high in processed meat, red meat or milk products or low in certain vegetables. Treatments may include a combination of surgery, radiation therapy, hormone therapy or chemotherapy. When it only occurs inside the prostate, it may be curable. In those in whom the disease has spread to the bones, pain medications, bisphosphonates and targeted therapy, among others, may be useful. Most people with prostate cancer do not end up
APLATUMIDE

Apalutamide is a nonsteroidal antiandrogen (NSAA) medication which is used in the treatment of prostate cancer. It is specifically indicated for use in conjunction with castration in the treatment of non-metastatic castration-resistant prostate cancer (NM-CRPC). It is taken by mouth. Side effects of apalutamide when added to castration include fatigue, nausea, abdominal pain, diarrhea, high blood pressure, rash. Rarely, it can cause seizures. Apalutamide is an antiandrogen, and acts as an antagonist of the androgen receptor, the biological target of androgens like testosterone and dihydrotestosterone. In doing so, it prevents the effects of these hormones in the prostate gland and elsewhere in the body. Apalutamide was first described in 2007 and was approved for the treatment of prostate cancer in February 2018. It was the first medication to be approved specifically for the treatment of NM-CRPC. Apalutamide is used in conjunction with castration, either via bilateral orchiectomy or gonadotropin-releasing hormone analogue (GnRH analogue) therapy, as a method of androgen deprivation therapy in the treatment of NM-CRPC. It is also a promising potential treatment for metastatic castration-resistant prostate cancer (mCRPC), which the NSAA enzalutamide and the androgen synthesis inhibitor abiraterone acetate are used to treat. Apalutamide is provided in the form of 60mg oral tablets. It is taken at a dosage of 240mg once per day (four tablets) when used in the treatment of NM-CRPC. Apalutamide is contraindicated in pregnancy and persons who susceptible to seizures.

PHARMACOLOGY

Pharmacodynamics

Apalutamide acts as a selective competitive silent antagonist of the androgen receptor (AR) of the androgen receptor, via the ligand-binding domain, and hence is an antiandrogen. It is similar both structurally and pharmacologically to the second-generation NSAA[Nonsteroidal antiandrogen] enzalutamide, but shows some advantages, including higher antiandrogenic activity as well as several-fold reduced central nervous system distribution. The latter difference may reduce its comparative risk of seizures and other central side effects. Apalutamide has 5- to 10-fold greater affinity for the AR than bicalutamide, a first-generation NSAA. The acquired F876L mutation of the AR identified in advanced prostate cancer cells has been found to confer resistance to both enzalutamide and apalutamide. A newer NSAA, darolutamide, is not affected by this mutation, nor has it been found to be affected by any other tested/well-known AR mutations.

Other activities

Apalutamide shows potent induction potential of cytochrome P450 enzymes similarly to enzalutamide. It is a strong inducer of CYP3A4 and CYP2C19 and a weak inducer of CYP2C9, as well as an inducer of UDP-glucuronosyltransferase. In addition, apalutamide is an inducer of P-glycoprotein, ABCG2, and OATP1B1. Apalutamide binds weakly to and inhibits the
Apalutamide is a better option for the treatment of castration resistant non-metastatic prostate carcinoma in adult. It is better option than other Anti-androgen or 5-alpha reductase inhibitors. Apalutamide possess less side effects as comparison to other anti-androgens or 5-alpha reductase inhibitors.

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