Use of abirateronе in castration resistant prostate cancer nursing essay

Prostate cancer is the most common type of cancer diagnosis of men in Canada. In 2012, approximately 26, 500 men in Canada were diagnosed with prostate cancer and approximately 4, 000 died from the disease <1>. Prostate cancer is strongly influenced by androgenic steroids <2>. In advanced stage prostate cancer patients are typically treated using androgen deprivation therapy. <2>. Androgen therapy is not curative and may only improve patient's symptoms and may even reduce metastatic lesions <2>. The benefit seen in androgen deprivation is often reduced over years of androgen therapy as the tumour will continue to grow despite low androgen levels. When this occurs the tumour is known to be " castration resistant" and is known to lead to prostate cancer- related mortality <2>. Castration-resistant prostate cancer (CRPC) may present as either a continuous rise in serum prostate- specific antigen levels (PSA), progression of pre-existing disease, or appearance of new metastases <3>.

Many endocrine based therapies have been evaluated for CRPC with minimal success in prolonging patient survival <4>. Systemic nonhormonal therapies using docetaxel, carbaztaxel, and active cellular immunotherapy with sipuleucel-T have been shown to prolong survival <4>. A new drug abiraterone (Zytiga) has shown to improve survival and lower PSA levels in patients with CRPC. This article is to be used by health professionals to gain a thorough understanding of abiraterone's indication, mechanism of action, side effects, dosage, clinical evidence, monitoring parameters, and contraindications.

Indication

According to the product monograph for abiraterone the drug is “ indicated with prednisone for the treatment of CRPC in patients who have received prior chemotherapy containing docetaxel”<5>.

Mechanism of Action

Abiraterone is formulated as a prodrug, abiraterone acetate, which is converted to abiraterone by the body and acts as a selective inhibitor of 17Î±-hydroxylase/C17, 20-lyase (CYP17) <4>. CYP17 is responsible for androgen biosynthesis in testicular, adrenal and prostatic tumor tissues <5>. As illustrated in Figure 1, CYP17 catalyzes the conversion of pregnolone and progesterone into testosterone precursors, DHEA and androstenedione <5>. The reduction in androgen production is beneficial for androgen-sensitive prostatic carcinoma.

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Figure 1. Abiraterone’s mechanism of action in androgen synthesis <6>

Side Effects

The most common side effects of abiraterone are caused by the mechanism of the drug on CYP17. As seen in Figure 2, inhibition of CYP17 causes on increase in the production of mineralocorticoids, which lead to hypokalemia, fluid retention, and hypertension <4>. Other common side effects of abiraterone include myopathy, joint pain, abnormal liver function, hot flashes, diarrhea, urinary tract infections, bone fractures and cough <5>.

http://jco. ascopubs. org/content/28/9/1481/F4. large. jpg

Figure 2. Effects of abiraterone on mineralocorticoid production <7>.

Dosage and Administration

The recommended dosage of abiraterone is 1000 milligrams daily as a single dose <4>. The tablets need to be swallowed whole and the dose should be taken on an empty stomach <5>. To reduce the mineralocorticoid effects of abiraterone the patient should also use a low dose prednisone. The recommended dose or prednisone is 10 mg daily <5>.

Clinical Trials Evaluating Abiraterone

The effectiveness of abiraterone in CRPC has been demonstrated in several randomized trials. In 2009, a study Attard et al., using forty-two chemotherapy-naÃ¨ve patients with CRPC received 1000 mg abiraterone <8>. At follow up (median 505 days) a decline in PSA of â‰¥ 50% of was observed in 67% of patients, with declines of â‰¥ 90% in 19% of patients <8>.

A 2010 study by Danila et al., of fifty-eight men with CRPC previously on docetaxel received abiraterone 1000 mg daily with 5 mg of prednisone <9>. Results of study illustrated that 36 % of patients had a PSA decline of â‰¥ 50% <9>.

In 2011, De Bono et al. conducted a study including 1195 patients who had previously received docetaxel <4>. Groups were assigned in a 2: 1 ratio to receive 5 mg of prednisone twice daily with either 1000 mg of abiraterone or placebo <4>. The primary end point of the study was overall survival <4>. The secondary endpoints of the study were time to prostate-specific antigen

progression, progression-free survival according to radiological findings based on specified criteria, and PSA response rate <4>. At a median 12. 8 month follow-up overall survival was significantly longer in the abiraterone group compared to the placebo (14. 8 months vs. 10. 9 months, p <0. 001) <4>. The secondary end points all favoured the treatment group; time to PSA progression (10. 2 vs. 6. 6 months; p <0. 001), progression-free survival (5. 6 months vs. 3. 6 months; p <0. 001), and PSA response rate (29% vs. 6%, p <0. 001) <4>.

The studies using abiraterone in CRPC illustrate that the drug provides a moderate improvement in cancer progression and improves survival in patients.

Monitoring Parameters

Health professionals should place on emphasis of monitoring patients using abiraterone. Before treatment hypokalemia and hypertension must be normalized in patients who are scheduled to use the drug <5>.

It is important to routinely monitoring a patient’s blood pressure while they are on this product. Potassium levels should be checked at baseline and regularly to prevent hypokalemia in patients. Patients should also be checked for signs of fluid retention, such as peripheral edema. Liver function tests (ALT, AST, and bilirubin) should be measured prior to initiating abiraterone treatment and continued every two weeks for the first three months of treatment and monthly afterwards <5>. Patients should routinely be assessed for other common side effects, including joint pain and urinary tract infections.

Conclusion

CRPC is a very advanced stage of prostate cancer that is fatal. Abiraterone (Zytiga) has been shown to prolong survival and lower PSA in men with CRPC. The drug works by selectively inhibiting CYP17 and lowering the production of testosterone via upstream inhibition of precursors in prostate, adrenal, testicular tissues. The selective inhibition of CYP17 leads to a large increase in mineralocorticoid activity in the body leading to hypertension, edema, and hypokalemia. The excess mineralocorticoid activity is typically diminished by administering 10 mg of prednisone daily with abiraterone. It is important to note that abiraterone is indicated as a second line therapy for patients who have failed treatment with docetaxel. While on abiraterone patients need to be monitored for hepatic function, hypertension, hypokalemia, and edema.

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