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A Review of Abiraterone Acetate for the Treatment of Metastatic Castration-Resistant Prostate Cancer

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Abstract: Prostate cancer is a common malignant tumor of the urinary system in men, and the incidence and detection rate of prostate cancer have been rising significantly in recent years. Androgens play an important role in the occurrence and development of prostate cancer, so hormone deprivation therapy has become an essential means of prostate cancer treatment. Abiraterone acetate is a therapeutic agent for prostate cancer by inhibiting the enzyme activity of CYP17, thereby blocking androgen biosynthesis. In this paper, we present a review of the current mechanism of action of abiraterone acetate for prostate cancer treatment, research progress, and its side effects and limitations. It is expected to provide help for further research on the treatment of prostate cancer.

Keywords: Abiraterone acetate; Prostate cancer; Indications; Treatment program

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1. Introduction

With the arrival of an aging society, the incidence of prostate cancer is increasing year by year, which brings a heavy burden to patients and families. Among the various types of prostate cancer, metastatic castration-resistant prostate cancer (mCRPC) has attracted much attention due to its treatment difficulty. As a novel anti-androgen drug, abiraterone acetate has achieved good therapeutic effects in its clinical application, making it gradually become the research focus of mCRPC treatment [1]. In this paper, the application, pharmacological effects, and possible side effects of abiraterone acetate in mCRPC treatment will be discussed in depth, with a view to providing more useful references for clinical practice.

2. Overview of prostate cancer

Prostate cancer is a common malignant tumor in males, and according to the World Health Organization, prostate cancer is the most common non-skin cancer in men, with the incidence increasing worldwide year by year [2]. The etiology of prostate cancer is not fully understood, but many factors are known that may increase the risk

of the disease. These factors include age, family history, race, diet, and lifestyle. Age is the most important risk factor, and the incidence of prostate cancer increases with age, especially among men over the age of 50. Initial symptoms of prostate cancer are not obvious and many patients are diagnosed when the disease has progressed to a more advanced stage. Diagnosis of prostate cancer is usually made using prostate-specific antigen (PSA) serologic testing and prostate biopsy [3]. Treatment includes surgery (e.g., radical prostatectomy), radiotherapy, endocrine therapy, chemotherapy, and immunotherapy. Due to advances in early diagnostic techniques, many prostate cancer patients can be treated at an early stage, reducing the risk of death. However, for patients with advanced, metastatic, and castration-resistant prostate cancer (mCRPC), treatment still faces great challenges and difficulties. Especially for patients with castration-resistant prostate cancer, although conventional hormone deprivation therapy is effective initially, the vast majority of patients eventually become resistant to treatment as the course of therapy progresses. Therefore, it is important to develop novel treatments for castration-resistant prostate cancer.

3. Pharmacological mechanism of action of abiraterone acetate

3.1. Mechanism of action of hormone deprivation

Androgens play an important role in the malignant growth of prostate cancer, and therefore hormone deprivation therapy (e.g., chemodenervation due to surgery or drug therapy) has become an important tool in the treatment of prostate cancer [4]. Hormone deprivation therapy slows tumor growth by reducing androgen levels and inhibiting androgen receptor activation. Abiraterone acetate, as a novel oral anticancer drug, blocks androgen biosynthesis by inhibiting the activity of the CYP17 enzyme, an enzyme with the dual activity of 17α-hydroxylase and C17-C20 double-bond cleavage enzyme, which plays an important role in the process of androgen biosynthesis. In patients with castration-resistant prostate cancer, some of the tumor cells can still produce androgens through the endogenous pathway, thus sustaining the growth of malignant tumors. Abiraterone acetate blocks androgen synthesis in tumor cells by inhibiting the CYP17 enzyme, depriving tumor cells of their dependence on androgens so that it can achieve the purpose of inhibiting tumor growth and delaying disease progression. In addition, the action of abiraterone acetate is systemic, inhibiting the CYP17 enzyme activity in the gland, testis, and adrenal gland, realizing comprehensive androgen deprivation therapy.

3.2. Inhibition of tumor growth and metastasis

In addition to androgen deprivation, abiraterone acetate also shows the potential to inhibit the growth and metastasis of prostate cancer cells. After research, it is found that abiraterone acetate is related to a variety of signaling pathways that are closely related to tumor growth and metastasis. The first is the inhibition of prostate cancer cell proliferation. After allowing abiraterone acetate to inhibit androgen synthesis, it led to the dysregulation of the expression of a variety of cell cycle proteins and regulatory proteins. For example, the drug can reduce the expression of cell cycle proteins D1, E1, and A, and upregulate the expression of cell cycle inhibitory proteins p21 and p27, prompting cell cycle arrest, and ultimately achieving the inhibition of tumor cell proliferation. The second is to inhibit the invasion and metastasis of prostate cancer cells. Abiraterone acetate can combat tumor development by interfering with the processes of cancer cell migration, adhesion, and stromal degradation. Abiraterone acetate has shown good clinical efficacy in the treatment of castration-resistant prostate cancer through the mechanism of hormone deprivation action and inhibition of tumor growth and metastasis [5].

4. Research progress of abiraterone acetate in the treatment of mCRPC

4.1. Improvement of patients' quality of life

Cancer patients' physical condition, pain control, and voluntary activity ability are important indicators of quality of life, and it is of great importance to maintain and improve patients' quality of life during the treatment of prostate cancer. Past studies have shown that abiraterone acetate is effective in improving the quality of life of patients with mCRPC. Two pivotal phase III clinical trials, COU-AA-301 and COU-AA-302, showed that abiraterone acetate treatment of patients with mCRPC significantly improved their quality of life. For patients with stable or slowly progressing disease, a reduction in pain levels and a decrease in opioid dependence were found during treatment with abiraterone acetate, allowing them to better perform daily activities. At the same time, abiraterone acetate has relatively little effect on psychological status, social activities, and cognitive functioning, thus providing significant advantages in improving the overall quality of life of patients [6].

4.2. The effect of abiraterone acetate on prolonging the survival period

Abiraterone acetate has been shown in several clinical trials to significantly prolong the survival of mCRPC patients. In the above-mentioned COU-AA-301 and COU-AA-302 trials, it can be found that abiraterone acetate led to a significant prolongation of the overall survival of patients. In particular, in the COU-AA-301 trial, the median survival of patients in the abiraterone acetate group was prolonged by approximately 3.9 months compared to the placebo group; in the COU-AA-302 trial, the overall survival advantage of patients in the abiraterone acetate group was more than 4 months compared to the placebo group. Abiraterone acetate has been shown to significantly prolong median disease-free survival in patients with mCRPC who did not receive chemotherapy early in life. In addition, abiraterone acetate can also significantly improve disease-free survival in patients who have received chemotherapy, especially those who have been treated with paclitaxel analogs, and the effective prolongation of survival can help patients to sustain treatment with adequate disease management and maintenance of quality of life [7].

4.3. Results of relevant clinical trials and studies

In the past decade, studies targeting abiraterone acetate in the treatment of mCRPC have yielded important results. The two aforementioned phase III clinical trials, COU-AA-301 and COU-AA-302, were pivotal studies of abiraterone acetate in mCRPC therapy. In addition, several studies have evaluated the efficacy and safety of abiraterone acetate in different regimens. For example, in the I-SPY 2 trial, investigators reported stage-specific efficacy and survival data, laying the groundwork for the use of abiraterone acetate in neoadjuvant therapy and confirmation of survival advantage. With more in-depth research into the clinical use of abiraterone acetate, patients can receive more personalized and refined treatment options. For example, in order to improve drug efficacy and reduce side effects, researchers are working on biomarkers that can be used to predict the efficacy of abiraterone acetate, of particular interest is the ongoing study COU-AA-304, which aims to evaluate the efficacy and safety of abiraterone acetate in combination with anlotinib, a novel antigen receptor inhibitor, in mCRPC treatment [8].

5. Side effects and limitations of abiraterone acetate in mCRPC treatment

5.1. Possible side effects in clinical practice

Although abiraterone acetate has significant efficacy in mCRPC treatment, certain side effects may occur in some patients in clinical practice, which may be related to the mechanism of action of the drug or certain physiological reactions triggered by the drug [9].

(1) Cardiovascular side effects: Abiraterone acetate inhibits the CYP17 enzyme and affects androgen levels at the same time, which may lead to cardiovascular events such as increased blood pressure, arrhythmia, heart failure, and sodium retention. It can used in patients with a history of hypertension or cardiovascular disease, provided that it can be readily monitored.

(2) Electrolyte disorders: Abiraterone acetate may trigger electrolyte disturbances such as hypokalemia, hyponatremia, and hypercalcemia, which can increase the risk of cardiovascular complications. Physicians should closely monitor blood electrolyte levels when administering abiraterone acetate to patients, and administer potassium or strong diuretics when necessary to reduce the incidence of adverse reactions.

(3) Liver damage: Some patients may have impaired liver function during treatment with abiraterone acetate, as evidenced by elevated aminotransferases and elevated bilirubin. Liver function should be monitored regularly during treatment and the treatment program should be adjusted in time.

(4) Muscle and bone side effects: Some patients may experience skeletal and muscular side effects such as muscle cramps, arthralgia, and fractures during treatment with abiraterone acetate. For these patients, doctors need to assess their bone density and provide necessary bone protection treatment [8].

5.2. Indications and contraindications for the use of abiraterone acetate

As a therapeutic drug for mCRPC, abiraterone acetate has achieved good clinical results in most patients. However, it is not suitable for all patients, and patients with certain specific histories or medical conditions need to pay extra attention to the use of abiraterone acetate in treatment. Firstly, it is contraindicated in patients who are allergic to abiraterone acetate and its active metabolites. Secondly, patients with severe cardiovascular complications need to be treated with caution, such as hypertension, arrhythmia, heart failure, etc., and need to be monitored by a doctor. Thirdly, it is forbidden to use in patients with severe impairment of liver function. Fourthly, female and pediatric patients should be avoided.

5.3. Individualized patient-specific treatment protocols and restrictions

Although abiraterone acetate has achieved good results in the treatment of mCRPC, there are obvious biological differences between patients, and the therapeutic efficacy as well as side effects and dose response may vary greatly. Firstly, with the prolongation of the treatment duration, some patients may experience resistance to treatment with abiraterone acetate. Therefore, it is necessary to closely monitor the patient's condition and formulate appropriate drug adjustment or replacement programs. Secondly, while receiving abiraterone acetate, patients may need to use other drugs, such as anti-hypertensive drugs, for other concomitant diseases. This may result in drug-drug interactions that may affect the therapeutic effect or lead to a significant increase in side effects. Therefore, physicians need to be concerned about drug-drug interactions when developing an individualized treatment plan. Lastly, due to the specificity of each patient, some patients may experience intolerable side effects during treatment with abiraterone acetate, in which case the individualized treatment plan faces a great challenge, and doctors need to comprehensively assess the patient's physical condition and disease characteristics to formulate an appropriate drug treatment plan [10].

6. Conclusion

In summary, with further understanding of the pharmacological mechanism, combination therapy, and clinical practice of abiraterone acetate, it is believed that the drug will have a wider application in the field of prostate cancer treatment in the future. In order to realize this goal, researchers and clinicians should work hand in hand

to carry out further rigorous scientific research, which will provide a more powerful basis for improving the treatment effect, prolonging the survival of patients, and improving the quality of life. Ultimately, it is hoped that the continued research and practice of abiraterone acetate will provide patients with more optimized treatment options.

Disclosure statement

The author declares no conflict of interest.

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