

# Clinical Exploration of Immunosuppressants Combined with Abiraterone in the Treatment of Metastatic Castration-Resistant Prostate Cancer

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**Abstract:** Prostate cancer is a malignant tumor with a high incidence in elderly men. In recent years, with the improvement of people's living standards and the advancement of detection technology, the incidence of prostate cancer has been increasing year by year. Castration-resistant prostate cancer (CRPC) is a highly challenging type of advanced prostate cancer treatment, which clinically shows resistance to hormonal deprivation therapy. The overall treatment efficacy of CRPC is currently poor and further relevant therapeutic studies are needed to improve patient survival and quality of life. Immunosuppressants can play a role in combating the immune system of tumors, and abiraterone has also achieved remarkable results in prostate cancer treatment. This study will investigate the possible clinical effects and safety of immunosuppressants combined with abiraterone in the treatment of metastatic CRPC. The population-based study will provide clinicians with more effective treatment options, as well as enhance the understanding of novel combination therapy strategies to be implemented in the future for such patients.

**Keywords:** Immunosuppressants; Abiraterone; Prostate cancer; Immune system

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## 1. Overview of immunosuppressive agents

Immunosuppressants are a class of drugs that can inhibit or modulate the immune system response and are widely used in the treatment of autoimmune diseases, the inhibition of organ transplant rejection, and the treatment of malignant tumors. Immunosuppressants inhibit the body's overactive immune response by acting on different immune cells and signaling pathways, such as inhibiting T-cell activation, attenuating cytokines, or suppressing bone marrow hematopoiesis. In recent years, the use of immunosuppressants in cancer treatment has gradually attracted attention, and some of the drugs have been used as a standard treatment regimen for certain types of cancer <sup>[1]</sup>.

## 2. Overview of abiraterone

Abiraterone is a very widely used drug for the treatment of prostate cancer and is currently primarily used in

the treatment of middle and advanced prostate cancer, especially in the treatment of castration-resistant prostate cancer (CRPC) with better efficacy. Through a large number of clinical studies and trials, it has been proved that abiraterone has a significant therapeutic effect on many CRPC patients and can effectively prolong the survival of patients. In addition, abiraterone has better tolerability and safety compared with other prostate cancer-related therapeutic drugs <sup>[2]</sup>.

### **3. Immunosuppressant combined with abiraterone for CRPC treatment**

#### **3.1. Immunosuppressants and their mechanisms**

Immunosuppressants are a class of drugs that act on the body's immune system and are mainly used to inhibit overactive immune responses, thereby reducing damage to healthy tissues caused by the immune system. In cancer therapy, immunosuppressants have a two-sided nature; on the one hand, an over-activated immune response may lead to damage of normal tissues and deterioration of the patient's condition, in which case immunosuppressants can be used to reduce the aggressiveness of the immune system; on the other hand, malignant tumors may use immunosuppressive pathways to evade the immune system's monitoring and clearance, thus accelerating the growth and spread of tumors. There have been practical advances in the use of such drugs, with PD-1/PD-L1 (programmed cell death protein 1/programmed cell death ligand 1) and CTLA-4 (cytotoxic T lymphocyte-associated protein 4) inhibitors being the most frequently studied immunosuppressive agents in recent years <sup>[3]</sup>.

#### **3.2. Action and mechanism of abiraterone**

Abiraterone is a CYP17 inhibitor that, by inhibiting key enzymes, can reduce the dependence of tumor cells on androgens required for growth. In this way, abiraterone can block steroid biosynthesis, thereby slowing or stopping the growth and spread of prostate tumors. In addition, abiraterone can prolong the survival time of patients with CRPC through the anti-androgen receptor (AR) pathway <sup>[4]</sup>.

#### **3.3. Advantages of combination therapy**

The theoretical basis for the combined treatment of CRPC with immunosuppressants and abiraterone lies in the fact that the two act on different biological pathways, thus achieving a multifaceted strike on tumor cells. Immunosuppressants can help the immune system itself recognize and eliminate tumor cells, while abiraterone can directly inhibit tumor cells' dependence on androgens. Therefore, a more effective and long-lasting antitumor effect may be achieved by combining these two drugs <sup>[5]</sup>.

### **4. Clinical research methodology**

#### **4.1. Study design**

This study adopted a non-randomized controlled study design, and after the inclusion of eligible CRPC patients, they were divided into the experimental group and the control group according to the ratio of 1:1. Among them, the experimental group was given immunosuppressant combined with abiraterone treatment, and the control group was given abiraterone and prednisone tablets. The study lasted for two years, with global overall survival (OS) and disease-free survival (DFS) as the primary endpoints <sup>[6]</sup>.

#### **4.2. Drug dosage and treatment regimen**

Patients in the experimental group were treated with both immunosuppressants (e.g., PD-1/PD-L1 inhibitors

or CTLA-4 inhibitors) and abiraterone. Among them, PD-1/PD-L1 inhibitors were administered intravenously every 3 weeks for a total of 6 doses, and the dose of abiraterone was 1,000 mg per day, combined with 5 mg of prednisone given orally. Patients in the control group received only abiraterone and prednisone tablets at the same dose. During the treatment period, all patients were required to have their fracture risk assessed by Bone Density Scan and treated with bisphosphonates if required <sup>[7]</sup>.

### **4.3. Inclusion and exclusion criteria**

For patient selection, those who met the following criteria were selected: age 18–75 years, diagnosis of metastatic CRPC, had received and progressed on at least one endocrine therapy and were active. Exclusion criteria included a diagnosis of non-prostate cancerous bone metastases, severe heart disease, another primary tumor, having received cytotoxic tumor therapy within 8 weeks prior to the start of the investigation, and having a serious infection <sup>[8]</sup>.

### **4.4. Study population**

A total of 200 CRPC patients were included, including 100 in the experimental group and 100 in the control group. The age, tumor stage, and PSA (prostate-specific antigen) levels of both groups were statistically similar. The mean ages of the experimental and control groups were 65.4 and 66.3 years, respectively. In addition, about 75% of the patients in the baseline characteristics were Gleason score 8–10. The response of the patients to the treatment was followed up through regular follow-ups, as well as their quality of life, side effects, and other treatment modalities chosen by the patients on their own. The clinical study focused on patient efficacy and safety.

### **4.5. Treatment method and course of treatment**

Patients in the experimental group received a combined treatment regimen of immunosuppressants and abiraterone, while patients in the control group received only abiraterone. The study focused on the difference in clinical efficacy and safety between these two treatment regimens. The treatment cycle of the two groups was three months, each treatment cycle of the experimental group and the control group must be oral abiraterone. The experimental group set the dosage of immunosuppressant according to the doctor's instructions, the treatment cycle continued until the disease progressed or occurrence of intolerable side effects. During the process, continuous monitoring of the patient's condition and vital signs was performed.

### **4.6. Monitoring indicators and assessment**

#### **4.6.1. Clinical efficacy assessment**

Primary assessment indicators included global overall survival (OS) and disease-free survival (DFS) to understand the difference in effectiveness and tolerability between combination therapy and monotherapy. Secondary efficacy assessment indicators included tumor shrinkage rate, PSA change rate, and bone metastasis-related event rate.

#### **4.6.2. Efficacy monitoring**

At the beginning of the experiment, in the middle of the cycle, and at the end of the experiment, multiple tests, such as computed tomography (CT), magnetic resonance imaging (MRI), bone scan, etc., were used to monitor the tumor and metastasis. At the same time, the PSA level and testosterone level of the patients, blood, liver, and kidney functions, and other indexes were assessed and used to evaluate the patient's condition and treatment <sup>[9]</sup>.

### **4.6.3. Safety assessment**

The possible toxic side effects of patients during treatment were monitored and graded. Common side effects included liver function abnormality, thrombocytopenia, rash, fatigue, drowsiness, etc., which were graded and evaluated respectively and symptomatic treatment measures were taken, such as adjusting drug dosage or suspending treatment.

### **4.6.4. Quality of life assessment**

Validated quality-of-life assessment scales, such as EORTC QLQ-C30 (EORTC quality of life questionnaire), FACT-P (Functional Assessment of Cancer Therapy-Prostate), etc., were used to regularly assess the quality of life of patients to understand the status of patient's psychological, physiological, and social functioning in the course of treatment.

## **5. Results**

There was a significant difference between the experimental and control groups in terms of overall survival (OS) and disease-free survival (DFS). The experimental group (immunosuppressant combined with abiraterone treatment) showed a significant prolongation of OS compared with the control group, while DFS also exhibited a longer duration. Meanwhile, the experimental results showed that the immunosuppressant combined with the abiraterone treatment regimen was superior to abiraterone monotherapy in terms of the rate of tumor shrinkage, the rate of PSA reduction, and the rate of events related to bone metastasis. In terms of safety, there was no significant increase in toxicities with the combination therapy, with most patients experiencing only mild to moderate adverse effects, especially regarding liver function, thrombocytopenia, and rash. With appropriate interventions, medication adjustments, and rehabilitation, the side effects could be improved in most patients. In terms of quality of life, patients in the experimental group scored higher than those in the control group in terms of psychological, physiological, and social functioning, showing the positive impact of immunosuppressant combined with abiraterone treatment on patients' quality of life <sup>[10]</sup>.

## **6. Discussion**

Immunosuppressant combined with abiraterone treatment for CRPC has obvious clinical advantages, and compared with the use of abiraterone alone, the combined treatment can effectively improve the survival and quality of life of patients. The results of this study can help clinicians to better develop individualized treatment plans for CRPC patients, as well as provide a reference for the development of novel comprehensive treatment strategies for CRPC patients in the future. However, the limitation of this study is that the study sample size is small, and more refined delineation is insufficient. In future studies, further clinical studies on more patients, different clinical stages, and different immunosuppressant classes are needed to obtain more comprehensive and accurate treatment guidance.

## **7. Conclusion**

In conclusion, this study investigated the efficacy and safety of the combination of immunosuppressants and abiraterone in the treatment of CRPC, which provides a new treatment option for prostate cancer patients. Although the study has some limitations, it suggests that we need to conduct further research on this topic with consideration of clinical staging, individual patient differences, and different drug types. Through in-

depth research and optimization of treatment options, we expect to provide better treatment for prostate cancer patients and further improve their survival and quality of life.

## Disclosure statement

The author declares no conflict of interest.

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