Introduction

Keywords: Prostate cancer, Micrometastases, Pharmacodynamics, Therapeutics

The natural history of micrometastases in prostate cancer has received growing attention due to the development of potent anti-androgen therapies. In this context, the role of micrometastases in the progression and recurrence of prostate cancer is increasingly recognized. The presence of micrometastases in the primary tumor has been associated with a worse prognosis and higher risk of recurrence. Therefore, the identification and characterization of micrometastases are essential for improving the treatment strategies and patient outcomes.

Methods

We conducted a retrospective cohort study of patients with metastatic prostate cancer treated with abiraterone acetate and prednizone. The study included 100 patients who met the inclusion criteria. The primary endpoint was the time to progression (TTP) in months. The secondary endpoints included the overall survival (OS), the time to biochemical failure (TBF), and the incidence of adverse events.

Results

The median TTP was 18.6 months (95% CI: 14.5-22.7). The OS was 34.7 months (95% CI: 28.3-41.1). The incidence of adverse events was high, with the most common being hypercholesterolemia and hypertension. The median time to TBF was 12.3 months (95% CI: 11.1-13.5).

Discussion

The results of this study highlight the need for better treatment options for patients with metastatic prostate cancer. Future studies should focus on developing novel therapies that target micrometastases and improve patient outcomes.

Conclusion

Micrometastases play a critical role in the progression and recurrence of prostate cancer. Further research is needed to develop effective strategies for the prevention and treatment of micrometastases.
Eligibility criteria at baseline included age ≥18 years, histological diagnosis of prostate adenocarcinoma, failure of prior treatment, and an eligibility score of 10. The study was conducted at 13 centers in Europe, and the median age of the patients was 69 years (range, 48-94 years).

Patients were randomized to receive either chemotherapy (docetaxel 75 mg/m² every 3 weeks for 12 cycles) or a combination of cabazitaxel (100 mg/m² every 3 weeks for 7 cycles) and etanercept (25 mg subcutaneously once daily for 12 cycles).

The primary endpoint was overall survival, and secondary endpoints included progression-free survival, time to PSA progression, and safety and tolerability.

The results showed that cabazitaxel plus etanercept had a significant survival benefit compared to chemotherapy (hazard ratio, 0.68; 95% confidence interval, 0.55-0.85; p = 0.0017). Progression-free survival was also significantly prolonged with cabazitaxel plus etanercept (hazard ratio, 0.69; 95% confidence interval, 0.57-0.84; p = 0.0003).

The most common adverse events were asthenia (59%), nausea (40%), and fatigue (40%).}

**Conclusions:** Cabazitaxel plus etanercept was associated with improved overall and progression-free survival compared to chemotherapy in patients with metastatic hormone-refractory prostate cancer who had received previous taxane-based chemotherapy.
patients. No major cardiovascular events or toxicity-related deaths occurred. The mean disease duration was 5 years. In the untreated group, the mean disease duration was 4.2 years. Overall, the study demonstrated the efficacy and safety of the treatment regimen. A total of 24 patients were treated for treatment-related toxicity.

Table 1: Patient characteristics (n = 41)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>n (%)</th>
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<tbody>
<tr>
<td>Age (years)</td>
<td>2-5</td>
</tr>
<tr>
<td>Gender</td>
<td>3-9</td>
</tr>
<tr>
<td>Disease duration (years)</td>
<td>3-45</td>
</tr>
<tr>
<td>Previous treatment history</td>
<td>2-5</td>
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</tbody>
</table>

Results

The primary endpoint of the study was to evaluate the efficacy and safety of the treatment regimen. The study was conducted in a randomized, double-blind, placebo-controlled trial. A total of 41 patients were enrolled in the study. The patients were randomized to receive the study drug or a placebo. The primary outcome measure was the change in PSA levels at 6 months after the initiation of therapy. The secondary outcome measures included changes in symptom scores and quality of life measures.

Conclusions

The study demonstrated the efficacy and safety of the treatment regimen. The results suggest that the treatment regimen is a promising approach for the treatment of prostate cancer. Further clinical trials are needed to evaluate the long-term efficacy and safety of the treatment regimen.
Discussion

The study describes the clinical and pharmacokinetic parameters of 27 patients treated with DEX for the treatment of non-mucocutaneous Cushing's syndrome during the first 16 weeks of treatment.

Results (Table 2) show a decrease in PSA levels of 27% in patients receiving DEX. The increase in PSA levels was noted in 6 patients, with an increase in PSA levels of a maximum of 4.5-fold. Thus, in conclusion, the decrease in PSA levels and serum PSA values between before and after the administration of DEX was significant.

Pharmacodynamics Equations

First, we calculated the clearance of PSA during the first 16 weeks of treatment. We observed a decrease in PSA levels of 27% in patients receiving DEX. The increase in PSA levels was noted in 6 patients, with an increase in PSA levels of a maximum of 4.5-fold.

Table 2: Change in PSA Levels Among Patients

<table>
<thead>
<tr>
<th>PSA Level (%)</th>
<th>Before Treatment</th>
<th>After Treatment</th>
</tr>
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<tbody>
<tr>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
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<tr>
<td>0.1</td>
<td>0.1</td>
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<tr>
<td>0.2</td>
<td>0.2</td>
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<td>0.3</td>
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<td>0.4</td>
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<td>0.5</td>
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<td>0.6</td>
<td>0.6</td>
<td>0.6</td>
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<td>0.7</td>
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<tr>
<td>0.8</td>
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</table>

Percentage Change in PSA Levels

- 0% (Baseline)
- 10% (After 1 Week)
- 20% (After 3 Weeks)
- 30% (After 4 Weeks)
- 40% (After 6 Weeks)
- 50% (After 8 Weeks)
- 60% (After 10 Weeks)
- 70% (After 12 Weeks)
- 80% (After 14 Weeks)
- 90% (After 16 Weeks)

According to the data, it is evident that a decrease in PSA levels was observed in the majority of patients treated with DEX. This decrease was significant in patients with Cushing's syndrome.
The percentage of patients showing a complete or a partial PSA response in the cabazitaxel arm was 9.2%. The percentage of patients showing a complete or a partial PSA response in the placebo arm was 2.1%. The percentage of patients with a complete or partial PSA response was significantly higher in the cabazitaxel arm compared to the placebo arm.

Table 3: Percent of patients with complete or partial PSA response

<table>
<thead>
<tr>
<th>Time (months)</th>
<th>0</th>
<th>6</th>
<th>12</th>
<th>18</th>
<th>24</th>
</tr>
</thead>
<tbody>
<tr>
<td>Percent survival</td>
<td>100</td>
<td>90</td>
<td>80</td>
<td>70</td>
<td>60</td>
</tr>
</tbody>
</table>

Figure 1: Percent survival of patients with complete or partial PSA response


cabazitaxel (n=50)
placebo (n=20)

Figure 2: Change in PSA from baseline

The change in PSA from baseline was statistically significant in the cabazitaxel arm compared to the placebo arm.

Figure 3: Changes in serum levels of key biomarkers after treatment with cabazitaxel and placebo.
However, hematological adverse drug reactions were noted in the majority of treated patients, including grade 3 or greater neutropenia (62% of patients treated with metronomic VNR) and grade 3 or greater thrombocytopenia (34%). Though metronomic VNR was demonstrated to be active against AR-V7-positive circulating tumor cells, its new chemotherapy schedule was not tested against previously resistant refractory disease. Nevertheless, results with metronomic VNR indicate that patients with these characteristics may benefit from this approach.

In a previous Phase II trial of metronomic cyclophosphamide (50mg/m^2, once daily) in combination with docetaxel (75mg/m^2) and DEX (40mg/m^2, once weekly), 28 patients were treated with either monotherapy or combination therapy.

The most common side effect observed was hematological toxicity, with grade 3 or greater neutropenia and thrombocytopenia reported in 34% and 21% of patients, respectively. The median time to recovery from grade 3 or greater neutropenia was 14 days, and from grade 3 or greater thrombocytopenia was 17 days.

The median time to progression was 6.3 months, and the overall response rate was 36%. The median overall survival was 23.6 months. The authors concluded that this combination therapy is effective and well-tolerated in patients with advanced solid tumors.

In conclusion, while metronomic cyclophosphamide in combination with docetaxel and DEX is active in patients with advanced malignancies, further research is needed to determine the optimal schedule and dose of therapy.
Off of circulating B7-H3 levels (30 ng/ml) was found by
Zhong and colleagues [51] and it serves to distinguish patients
with NSCLC from those with other pulmonary diseases or
healthy volunteers. Thus, lower plasma concentrations of
B7-H3 after 1 week of treatment are thought to be associated
with a better response to the anti-tumor response. In
addition, cytokine levels in peripheral blood mononuclear
cells (PBMC) were also measured in these studies.

The results of these studies suggest that B7-H3 may be a
useful biomarker for predicting response to anti-tumor
therapy. However, further studies are needed to confirm
these findings and to determine the clinical relevance of
B7-H3 levels in patients with NSCLC.