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Abstract
Study Type - Therapy (case series)Level of Evidence 4

OBJECTIVES: To assess the efficacy of ketoconazole in patients with castration-resistant prostate cancer (CRPC).

PATIENTS AND METHODS: From April 2008 to November 2009, 37 patients with CRPC have been treated with ketoconazole. The primary endpoint was the prostate-specific antigen (PSA) response; the secondary endpoints were progression-free survival and safety profile. Ketoconazole was administered by oral route at a dose of 200 mg every 8 h continuous dosing until the onset of serious adverse events or disease progression. The study was based on a two-step design with an interim efficacy analysis carried out on the first 12 patients accrued.

RESULTS: Main characteristics of population were: median age 75 years (range 60-88); baseline mean PSA 28.8 ng/mL (4.3-1000); 30 patients previously challenged with at least two lines of hormone therapy; 15 patients previously treated with chemotherapy. Biochemical responses accounted for: two complete responses (5%), six partial responses (16%), 13 patients with stable disease (35%), and 14 with progressive disease (38%). Of 15 patients resistant to chemotherapy, overall disease control (complete plus partial responses plus stable disease) was recorded in seven of them. Treatment was feasible without inducing grade 3-4 adverse events. The most common grade 1-2 adverse events were asthenia (27%), vomiting (8%) and abdominal pain (8%).

CONCLUSIONS: Treatment with low-dose ketoconazole is feasible and well tolerated. The efficacy was satisfactory in patients previously treated with chemotherapy.


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Abstract
OBJECTIVE: To assess the efficacy of the androgen-synthesis inhibitor ketoconazole as a secondary hormonal therapy in patients with castration-resistant prostate cancer (CRPC) previously treated with chemotherapy, as persistent androgens appear to play a role in the development and maintenance of CRPC.

PATIENTS AND METHODS: We retrospectively identified 34 patients with CRPC who were treated with ketoconazole as a secondary hormonal therapy after paclitaxel- or docetaxel-based chemotherapy for CRPC. They were treated with ketoconazole 200-400 mg three times daily with or without hydrocortisone. Patients with previous use of ketoconazole were excluded. Half the patients had received estramustine as part of their chemotherapy regimen. The primary endpoint was the proportion of patients with a decline of > or =50% in their prostate-specific antigen (PSA) level. PSA progression was defined by the PSA Working Group 1 Criteria.

RESULTS: Eight of the 32 evaluable patients (25%) had a PSA decline of > or =50%. The median time to progression (TTP) was 3 months (95% confidence interval, 1.2-5.4). A history of previous response to taxane-based chemotherapy was not associated with the response to ketoconazole. However, previous use of oestrogens for CRPC was significantly associated with a shorter TTP on ketoconazole (1.5 vs 10.2 months; P = 0.03).

CONCLUSIONS: Ketoconazole has moderate activity as secondary hormonal therapy in patients with CRPC previously treated with taxane-based chemotherapy, although the TTP was short. Previous treatment with oestrogenic therapy is associated with a shorter TTP.

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