Eficácia do ketoconazol em baixa dose no câncer de próstata resistente à castração – 2 estudos

[Efficacy of low dose ketoconazole therapy for Chinese patients with castration resistant prostate cancer].

[Article in Chinese]

Source
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Abstract

OBJECTIVE:
To assess the efficacy of low dose ketoconazole therapy for Chinese patients with castration resistant prostate cancer (CRPC) and explore possible prognosis factors.

METHODS:
From August 2006 to August 2011, 71 patients with CRPC were analyzed retrospectively, who received oral ketoconazole 200 mg, three times a day with prednisone 5 mg, twice a day. Prostate specific antigen (PSA) response rate was defined as the percentage of patients with PSA decline ≥ 50% compared to baseline PSA level during low dose ketoconazole therapy. Multivariate Logistic regression analysis and receiver operating characteristic curve were used to assess the prognostic factors and their accuracy.

RESULTS:
The mean initial serum PSA level was (205 ± 38) ng/ml for these patients with mean age (69 ± 1) years old. After first androgen deprivation therapy failure, the prostate cancer progressed into castration resistant stage. The baseline PSA was (93 ± 24) ng/ml and the baseline serum testosterone was (0.13 ± 0.02) ng/ml. During the low dose ketoconazole therapy, 31 patients (43.7%) had PSA decrease and 22 cases (31.0%) were effective with PSA decline more than 50%. PSA doubling time and baseline serum testosterone were positive correlation with PSA response rate by multivariate Logistic regression analysis. Patients with PSA doubling time of ≥ 3.0 months had a PSA response rate of 64.3% and the PSA response rate in those with < 3.0 months decreased to 22.8%, hazard rate (HR) = 0.149 (95% confidence interval [CI] 0.029 - 0.766), P = 0.023, area under the curve (AUC) = 0.707. The PSA response rate for patients with baseline serum testosterone ≥ 0.1 and < 0.1 µg/L were 55.6% and 5.7%, respectively, HR = 0.068 (95%CI 0.012 - 0.380), P = 0.002, AUC = 0.749. The common adverse reactions included liver dysfunction (17.9%), renal dysfunction (16.4%), fatigue (11.9%), nausea (6.0%) and anorexia (4.5%) and so on.

CONCLUSIONS:
Low dose ketoconazole therapy was a moderate, low toxicity hormonal therapy option for patients with CRPC. PSA doubling time ≥ 3 months and baseline serum testosterone ≥ 0.1 µg/L were predictors of desired effect for low dose ketoconazole therapy.

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Low dose of ketoconazole in patients with prostate adenocarcinoma resistant to pharmacological castration.

Procopio G, Guadalupi V, Giganti MO, Mariani L, Salvioni R, Nicolai N, Capone F, Valdagni R, Bajetta E.

Source

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Abstract

OBJECTIVE:

• 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%).

CONCLUSION:

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

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