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CASUISTRY

Initial experience with abiraterone acetate in patients with castration-resistant prostate cancer☆

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17α-Hydroxylase

Abstract

Objective: To describe the results obtained in 25 men with metastatic castration-resistant prostate cancer (MCRPC) treated with abiraterone (AA). A comparative analysis of abiraterone effectiveness and safety between our results and data published in the literature was conducted.

Materials and method: Bi-institutional prospective analysis of 25 consecutive patients with MCRPC undergoing treatment with abiraterone, with a mean follow-up 7.9 (3–15) months was carried out. Treatment effectiveness and safety analyses regarding baseline characteristics of patients (age, prior treatments, basal PSA, performance status, pain, and metastasis) were conducted.

Results: At 13.6 months of follow-up, the overall survival is 80% (CI 95%: 11.8–15.4). Clinical and radiological-free progression survival is 9.5 ± 1 months (CI 95%: 7.7–11.3) and biochemical response is 6.8 ± 1 months (CI 95%: 5–8.7). Only the treatment with chemotherapy impaired significantly the response time to AA [6.4 months for radiological-free progression survival (CI 95%: 4.2–8.6) and 4.3 months for biochemical-free progression survival (CI 95%: 2.6–6)]. The incidence of adverse drug events was 36%; all of them were of grade 1–2/4 and, in no case, suspension or reduction of the dose of AA was needed.

Conclusions: The treatment with AA has been effective in our series, with a tolerability considerably higher than what other studies published.

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PALABRAS CLAVE
Abiraterona acetato;
Cáncer de próstata resistente a la castración;
Terapia hormonal secundaria;
Nuevas terapias hormonales;
CYP17;
17α-hidroxilasa

Experiencia inicial con acetato de abiraterona en pacientes con cáncer de próstata resistente a la castración

Resumen

Objetivo: Describir los resultados obtenidos de la experiencia en el tratamiento con acetato de abiraterona (AA) en 25 hombres con cáncer de próstata metastásico resistente a la castración (CPMRC). Realizamos el análisis comparativo de la eficacia y seguridad de este fármaco en relación con la literatura existente.

Material y método: Estudio biinstitucional prospectivo de una cohorte de 25 pacientes consecutivos que reciben tratamiento con AA por CPMRC, con un seguimiento medio 7,9 (3-15) meses. Análisis de la seguridad y eficacia del tratamiento en relación con las características basales de los pacientes (edad, tratamientos previos, PSA basal, *performance status*, dolor, metástasis).

Resultados: La supervivencia global es del 80% a los 13,6 meses de seguimiento (IC 95%: 11,8-15,4). La supervivencia libre de progresión clínico-radiológica de la serie es de 9,5 ± 1 meses (IC 95%: 7,7-11,3) y el de respuesta bioquímica de 6,8 ± 1 meses (IC 95%: 5-8,7). Solo el tratamiento previo con quimioterapia empeora significativamente el tiempo de respuesta a AA (supervivencia libre de progresión radiológica 6,4 meses [IC 95%: 4,2-8,6] y bioquímica de 4,3 meses [IC 95%: 2,6-6]). La incidencia de efectos adversos fue del 36%, todos grado 1-2/4, y en ningún caso requiere suspender o disminuir la dosis de AA.

Conclusiones: El tratamiento con AA ha sido eficaz en nuestra serie, con una tolerabilidad considerablemente mayor a lo publicado en otros estudios.

Introduction

Prostate cancer is the second most frequent neoplasm among men and the fifth cause of cancer death.[1] Although less than 5% of patients show metastatic disease at diagnosis, approximately 40% of patients are going to develop metastasis after curative local treatment.[2] The disease is incurable once metastasis has occurred. Surgical or medical castration is highly effective in shrinking tumor burden, decreasing prostate-specific antigen (PSA) levels, enhancing quality of life, and improving survival.[2] However, most patients will eventually experience disease progression despite castration, with a median duration of response of 12–24 months, being the average survival for patients with castration-resistant prostate cancer (CRPC) 2–3 years lower than 20%.[3] Three systemic hormonal treatments are able to improve in 1 year the survival rates in patients with advanced CRPC: docetaxel[4] as first-line therapy, cabazitaxel[5] in second-line therapy and active cellular immunotherapy with sipuleucel-T.[6]

However, recent research suggests that CRPC remains dependent on a signaling pathway androgen receptor, which is active for cell survival and tumor growth.[7] As consequence, news treatments have been developed, like abiraterone acetate (AA) which has changed metastatic CRPC treatment paradigm. AA is a selective oral inhibitor of androgen biosynthesis that potently blocks cytochrome P450 CYP17 (17α-hydroxylase and C17,20 lyase), in the adrenal glands and testes and within the prostate tumor.[8] In phase III clinical trials have demonstrated an increase in overall survival in patients with metastatic castration-resistant prostate cancer after chemotherapy,[9] and delay the chemotherapy if it is used before docetaxel.[10]

Materials and method

Bi-institutional prospective study of 25 consecutive patients with MCRPC treated with AA from February 2012 until April 2013; mean follow-up 7.9 ± 0.7 (3–15) months.

Patients' characteristics

Mean age 70 years (59–87) when starting treatment with AA. 60% of them showed metastasis at the diagnosis of prostate adenocarcinoma. All patients had received at least 2 hormonal treatment lines before AA treatment; 16% of them (4 patients) received third-line hormonal treatment with ketoconazole. 36% of patients received chemotherapy before AA treatment (12% of whom received 2 treatment lines with docetaxel and cabazitaxel).

48% of patients were defined as asymptomatic: visual analog scale score (VAS)[11] ≥ 3 requiring additional treatment with strong opiates or ^{89}SrCl and/or palliative radiotherapy.

Series characteristics are resumed in Table 1.

Treatment

All patients received 1.000 mg of AA, 10 mg of oral prednisone every 24 h and a GnRH analog. AA treatment was interrupted when radiological and clinical or biochemical progression was confirmed.

At the diagnosis of metastatic bone disease, all patients were supplemented with calcium-vitamin D and zoledronic acid (68%) or denosumab (32%).