Original Article

Feasibility of abiraterone acetate treatment in patients with metastatic castration-resistant prostate cancer and atrial fibrillation

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A B S T R A C T

Background: Abiraterone acetate (AA), a selective inhibitor of the CYP17 enzyme, demonstrated a significant improvement in the treatment of patients with metastatic castration-resistant prostate cancer. The risk of endocrine side effects, mainly an increased adrenal mineralocorticoid production, could limit its use in patients with atrial fibrillation.

Methods: We retrospectively reviewed the clinical records of 85 metastatic castration-resistant prostate cancer patients treated with AA at our institutions and identified six patients suffering from concomitant atrial fibrillation.

Results: In these six patients, the median duration of AA treatment was 11.5 months (range 4–22 months) with a biochemical response in three patients. No significant cardiac events were observed during the treatment.

Conclusion: Our data suggest that AA may be safely administered in patients with atrial fibrillation.

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1. Introduction

As most cases of prostate cancer are diagnosed in patients aged >70 years,1 the development of metastatic castration-resistant prostate cancer (mCRPC) is generally observed in senior adults whose burden of comorbidities, mainly cardiovascular, leads to more frequent physical frailty and a higher risk of treatment-related side effects.2

Abiraterone acetate (AA) is a selective and irreversible inhibitor of CYP17, a microsomal enzyme involved in testosterone synthesis in the testis, adrenal glands, and the tumor itself.3 AA demonstrated an overall survival improvement in mCRPC patients, both in a first and second line setting.4,5

Consistently to its mechanism of action, the AA toxicity profile is related to mineralocorticoid excess potentially leading to hypertension, hypokalemia, and fluid retention. Inhibition of CYP17 reduces cortisol levels and, consequently, produces a compensatory flare of adrenocorticotropic hormone associated with secondary hyperaldosteronism. These side effects can be readily managed by adding low-dose steroids. Nevertheless, clinically significant heart disease, atrial fibrillation (AF), or other cardiac arrhythmias represented exclusion criteria in AA pivotal trials.3,5 At the same time, these conditions are frequently encountered in clinical practice due to the increasing age profile of mCRPC patients. The prevalence and incidence of AF increase with age and are higher in men than in women, with 6.9% of men aged 70–74 years suffering from this arrhythmia.6 As the mean age of mCRPC patients is 71 years,7 AF can be common in these patients.

Procopio et al8 evaluated the safety profile of AA in 51 patients with mCRPC and concomitant cardiovascular risk factors. Three of them suffered from cardiac arrhythmia not further specified. The authors concluded that AA appears to be safe and well tolerated even in patients with cardiovascular comorbidities or with an increased risk for cardiovascular disease. To date, the literature did not provide further data about the AA safety profile in patients with cardiovascular comorbidities, especially AF. The aim of the present
study was to evaluate the safety of AA in patients with mCRPC and concomitant paroxysmal or permanent AF.

2. Materials and methods

Patients with mCRPC treated with AA after docetaxel failure were prospectively followed at our institutions. All these patients received once-daily oral treatment with AA 1,000 mg (four 250 mg tablets) plus prednisone at a dose of 5 mg twice daily until progression. Furthermore, if clinically indicated, patients underwent a baseline cardiologic examination with electrocardiography and echocardiographic assessment.

3. Results

In our institutions between May 2013 and September 2015, a total of 85 mCRPC patients received AA after docetaxel failure. Six (7.1%) patients with a median age of 75.5 years (range 59–85 years) had a history of permanent (n = 4) or paroxysmal (n = 2) AF at the initiation of AA treatment. All patients showed a normal cardiac ejection fraction before treatment without significant valvular heart disease. The mean CHADS-VASc score was 3.2 (range 2–5). Concomitant cardiovascular medications consisted of beta-blockers (bisoprolol, n = 1; atenolol, n = 1; sotalol, n = 1), anticoagulants (phenprocoumon, n = 5; low-molecular-weight heparin, n = 1), diuretics (loop diuretics n = 2, Indapamid n = 1), and antihypertensives (ramipril, n = 2; enalapril, n = 1; losartan, n = 2; telmisartan, n = 1; amlopidin, n = 2; diltiazem, n = 1; manidipin, n = 1). In addition, four of these six patients had concomitant Type 2 diabetes mellitus. The median duration of AA treatment in patients with AF was 11.5 months (range 4–22 months), with a biochemical response in three patients. Three patients repeated echocardiography after 6 treatment months (Table 1). The only change was observed in the left atrial volume, which increased from a mean of 32 mL/m² to 48 mL/m², corresponding to an increase of 50%. Left atrial enlargement is associated with an increased risk for stroke and cardiovascular death.1–3 Although the increase in left atrial volume observed in our study could reflect fluid retention and thus be related to AA treatment, it is also known that the natural history of atrial fibrillation itself is characterized by left atrial structural changes.4–12 However, the increase in left atrial volume observed in our patients had no clinical impact during the follow-up period. In addition, no grade 1–4 adverse cardiac events were observed and no significant adjustment in the antihypertensive or diuretic medication was necessary.

4. Discussion

In our report, no adverse cardiac event was observed in patients with mCRPC and concomitant atrial fibrillation being treated with AA. However, due to the small case number the present data do not allow definitive conclusions regarding the safety of AA in patients with atrial fibrillation. Further studies with larger patient cohorts and long-term follow up are warranted. A close monitoring of baseline echocardiography in combination with cardiac biomarkers (e.g., BNP) should be performed prior and during the treatment with AA in this unique patient population.

Conflicts of interest

All contributing authors declare no conflicts of interest.

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