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Safety and clinical outcomes of patients treated with abiraterone acetate after docetaxel: results of the Italian Named Patient Programme

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Objective

To assess the safety and efficacy of abiraterone acetate (AA) in patients with metastatic castration-resistant prostate cancer (mCRPC) treated in a compassionate named patient programme (NPP).

Patients and Methods

We retrospectively reviewed the clinical records of patients with mCRPC treated with AA at the standard daily oral dose of 1000 mg plus prednisone 10 mg/day in 19 Italian hospitals.

Results

We assessed 265 patients with mCRPC treated with AA. The most frequent (>1%) grade 3–4 toxicities were anaemia (4.2%), fatigue (4.2%), and bone pain (1.5%). The median progression-free survival was 7 months; median overall survival was 17 months after starting AA, and 35 months after the first docetaxel administration. Our study reproduced the clinical outcomes reported in the AA pivotal trial, including those relating to special populations such as the elderly, patients with a poor performance status, symptomatic patients, and patients with visceral metastases.

Conclusions

Our data show the safety and activity of AA when administered outside clinical trials, and confirm the findings of the post-docetaxel pivotal trial in the patients as a whole population and in special populations of specific interest.

Keywords

abiraterone acetate, castration-resistant prostate cancer, pre-treated patients, compassionate programme, safety

Introduction

The treatment of metastatic castration-resistant prostate cancer (mCRPC) has undergone revolutionary changes over the last decade. After 2004, when it was discovered that docetaxel significantly improved symptom control and survival [1,2], post-docetaxel disease management remained an unmet medical need for several years but, since 2010, it has been found that several other drugs with different mechanisms of action can improve survival [3–7].

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One of these drugs is abiraterone acetate (AA), a potent, irreversible and selective small-molecule inhibitor of cytochrome P (CYP) 17 [8]. After phase II trials had shown that AA was active in patients with mCRPC [9–11], its efficacy was demonstrated by the results of the phase III, placebo-controlled COU-AA-301 trial, which showed that AA plus prednisone offered a survival benefit over placebo plus prednisone at the time of the initial interim analysis [5] and the end of the study [12]. Moreover, additional papers describing the COU-AA-301 trial have provided further data concerning the advantages of AA in terms of pain relief and skeletal-related events [13], reduced fatigue [14], an improved quality of life [15], and outcomes in special populations such as patients with visceral metastases [16] or aged >75 years [17]. However, beyond these reports, there are few data concerning the safety and activity of AA in everyday clinical practice [18–23].

We describe the safety and clinical outcomes of AA in 265 patients with mCRPC previously treated with docetaxel, who were administered the drug in 19 Italian centres within the context of a named patient programme (NPP) developed before it became commercially available.

Patients and Methods

The European Medicines Agency approved AA for the treatment of mCRPC in patients failing on docetaxel in September 2011, and the drug was approved for reimbursement by the Italian National Health Service in April 2013. During the intervening period, an NPP that allowed access to AA for patients with mCRPC was active in Italy from April 2011 to September 2012.

To be included in the AA NPP, the patients needed to have a diagnosis of histologically confirmed mCRPC that had to have been treated by at least one, but no more than two cytotoxic chemotherapy regimens of which at least one had to have included docetaxel; be in a phase of disease progression, defined as PSA progression as assessed using the Prostate Cancer Working Group 2 (PCWG2) criteria [24] and/or radiographic progression as assessed using the Response Evaluation Criteria in Solid Tumors (RECIST) [25]; be undergoing androgen deprivation; and have castration levels of testosterone (<50 ng/dL), an Eastern Cooperative Oncology Group (ECOG) performance status of ≤2, haemoglobin levels of ≥9.0 g/dL, a platelet count of ≥100 000/μL, serum albumin levels of ≥3.0 g/dL, serum creatinine levels <1.5-times the upper limit of normal (ULN) or a calculated creatinine clearance of ≥60 mL/min, and serum potassium levels of ≥3.5 mmol/L.

Patients were excluded if they had abnormal liver function [serum bilirubin ≥1.5-times the ULN, aspartate aminotransferase or alanine aminotransferase ≥2.5-times the ULN], a serious concomitant non-malignant disease, active or symptomatic viral hepatitis or chronic liver disease, uncontrolled hypertension, a history of pituitary or adrenal dysfunction, or clinically significant heart disease, or if they had been previously treated with ketoconazole.

After Ethics Committee approval of their participation in the NPP, all of the patients were orally treated with AA 1000 mg (four 250 mg tablets) once daily at least 1 h before or 2 h after a meal, plus prednisone at a dose of 5 mg twice daily. The treatment was continued until the occurrence of disease progression, unacceptable toxicity or death, or until the patient or his physician decided on its discontinuation. All of the patients who were still treated at the time AA became commercially available were to continue treatment, with the drug being provided at the cost of National Health Service.

It was recommended to evaluate safety and dosing compliance every 2 weeks for the first 3 treatment months, and then monthly until treatment discontinuation. It was also recommended to assess renal, liver and bone marrow function monthly, whereas imaging studies to assess the objective response of metastatic disease were left to the discretion of the treating physician. Dosing compliance and safety were evaluated regularly as stated above in all of the participating hospitals unless the patients' worsening clinical status did not allow it; PSA levels were assessed monthly; and a radiographic evaluation was usually made every 3 or 4 months, or in the presence of PSA progression.

For the purposes of this study, we reviewed the patients' clinical records and collected their pre-AA history of prostate cancer, their baseline characteristics, their AA treatment history and outcomes, and their post-AA history. The safety data recorded in the patients' clinical records were analysed using the National Cancer Institute's Common Terminology Criteria for Adverse Events (CTCAE) v.4.0.

Statistical Analysis

The continuous variables were expressed as median values, and the discrete variables as relative frequencies. Overall survival (OS) and progression-free survival (PFS) were calculated using the Kaplan–Meier method. PFS was calculated from the start of AA therapy until progression (according to the PCWG2 criteria [24]) or the time of the last follow-up visit (whichever occurred first). Cox regression analysis was used to calculate the differences in PFS and OS between groups stratified on the basis of the patients' Gleason scores at the time of diagnosis, the time between the diagnoses of prostate cancer and the development of mCRPC, the duration of hormonal manipulation before starting docetaxel, the number of docetaxel-based lines, the biochemical response to docetaxel, baseline ECOG performance status, baseline PSA levels, baseline haemoglobin levels, baseline alkaline phosphatase levels, baseline lactate dehydrogenase levels, the

baseline presence of pain, and the presence of visceral metastases. We categorised continuous variables by their median values.

The data were statistically analysed using SPSS 12 software (SPSS Inc., Chicago, IL, USA).

Results

Between February 2011 and September 2012, 19 Italian hospitals enrolled 265 patients in the Italian NPP. Table 1 [5,12,26] shows their main characteristics in comparison with those of the patients enrolled in the COU-AA-301 pivotal trial: there was no statistically significant difference between the two populations except in the percentage of patients aged ≥75 years (39.6% vs 27.6%; $P < 0.001$, Fisher's exact test). Table 2 shows the patients' comorbidities. At the time of the diagnosis of prostate cancer, 96 patients (36.2%) had metastatic disease, 49 (18.5%) underwent radical prostatectomy, 56 (21.1%) underwent radical prostatectomy plus external beam radiotherapy, and 44 (16.6%) received external beam radiotherapy alone. The median (range) time from the initial diagnosis of prostate cancer to the development of mCRPC was 53 (1–230) months, and the median (range) time from the start of the first hormonal manipulation before docetaxel to the development of mCRPC was 39 (3–179) months. Before docetaxel, the patients underwent a median (range) of 2 (1–6) hormonal manipulations. Baseline laboratory and clinical data were available for most of the patients: in particular, data for ECOG performance status, PSA level, and the presence of pain were always available, but there were some missing data for baseline haemoglobin (10.5%), baseline alkaline phosphatase (23.1%), and baseline lactate dehydrogenase levels (20.9%).

Table 1 The patients' characteristics in the present study and the AA arm of the COU-AA-trial [5,12,26].

Characteristic	Present study	COU-AA-301 AA arm
No. of patients	265	797
Median (range) age, years	73 (45–91)	69 (42–95)
No. of patients aged ≥75 years, n (%)	105 (39.6)	220 (27.6)
Disease location, n (%)		
Bone	223 (84.1)	220 (88.9)
Nodes	150 (56.6)	361 (45.3)
Liver	21 (7.9)	90 (11.3)
Lung	31 (11.7)	105 (13.2)
Presence of pain, n (%)	126 (47.5)*	353 (44.2)**
No. of previous cytotoxic chemotherapy regimens, n (%)		
1	204 (77)	558 (70)
2	61 (23)	239 (30)
ECOG performance status:		
0–1	224 (84.5)	715 (89.7)
2	33 (12.5)	82 (10.3)
Unknown	8 (3.0)	–
Median (range) PSA level, ng/mL	86 (0.33–>100000)	128.8 (0.4–9253)
Gleason score at time of initial diagnosis, n (%)		
≤ 7	97 (36.6)	341 (42.8)
≥ 8	137 (51.7)	356 (44.7)
Unknown	31 (11.7)	100 (12.5)
Median (range) baseline haemoglobin level, g/dL	12.0 (6.9–16.4)	11.8 (7.3–16.1)
Radiographic progression before AA, n (%)	196 (73.9)	559 (70.1)

**As assessed by investigators; **Brief Pain Inventory score ≥4.*

Drug Administration and Safety Profile

All of the patients received the full daily AA dose (1000 mg): the treatment was temporarily suspended due to reduced compliance or side-effects in 41 patients (15.5%). By the end of a median (range) follow-up of 12 (1–33) months, 234 patients had discontinued AA, and 31 were still being treated. The median (range) duration of AA exposure was 7 (1–33) months; 72 patients (27.1%) had early progression within the first 3 months of treatment. The main reasons for the discontinuations were disease progression (89%), the occurrence of comorbidities contraindicating continuation (5%), toxicity (2%), and death in the absence of progression (1%); the remaining 3% stopped the drug for various other reasons. Table 3 shows the toxicities recorded in the patients' clinical records during AA administration.

Clinical Outcomes

There was a reduction in PSA level of ≥50% compared with baseline in 50% of the patients, and confirmed at least 3–4 weeks later (Fig. 1). The median (95% CI) PFS was 7 (6–8) months: data for clinical and biochemical progression were available for all of the patients, whereas data for radiological progression were available for 190 (71.7%). The type of progression is detailed in Table 4. At the time of analysis, after the deaths of 152 patients (57.3%), the median (95% CI) OS from the start of AA was 17 (14–20) months and 35 (31–39) months from the first docetaxel administration. Table 5 [12,27] compares the survival outcomes with those observed in the AA pivotal trial, and Figures 2 and 3 respectively show PFS and OS on the basis of the stratification variables.

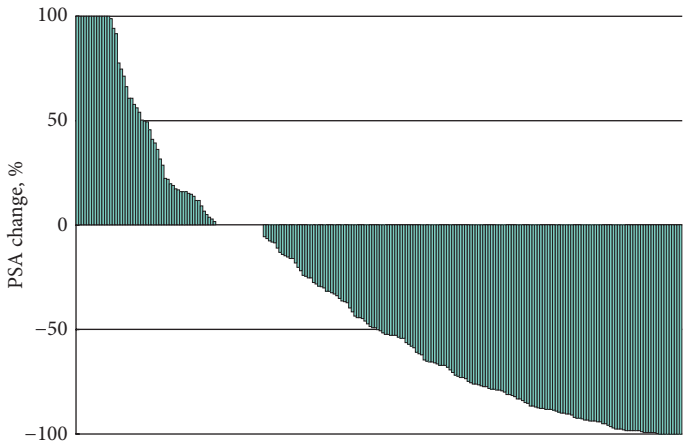
Table 2 Comorbidities.

Comorbidity	No. of patients (%)
Hypertension	147 (55)
No comorbidities	52 (20)
Diabetes	46 (17)
Cardiac ischaemia	33 (11)
Arrhythmia	29 (10)
Chronic obstructive pulmonary disease	15 (5)
Peripheral vascular disease	13 (4)
Arthropathies	13 (4)
Cerebrovascular disease	9 (2)
Gastroduodenal ulcer	7 (2)
Chronic renal failure	5 (1)

Table 3 Recorded toxicities as assessed using NCIC, version 4.0.

	All grades, n (%)	Grade 1, n (%)	Grade 2, n (%)	Grade 3, n (%)	Grade 4, n (%)
Fatigue	76 (28.7)	31 (11.7)	34 (12.8)	11 (4.2)	0
Anaemia	33 (12.5)	10 (3.8)	12 (4.5)	11 (4.2)	0
Bone pain	32 (12.1)	9 (3.4)	19 (7.2)	4 (1.5)	0
Limb pain	23 (8.7)	10 (3.8)	13 (4.9)	0	0
Oedema	21 (7.9)	13 (4.9)	7 (2.6)	1 (0.4)	0
Constipation	17 (6.4)	14 (5.3)	1 (0.4)	2 (0.8)	0
Non-neutropenic fever	16 (6.0)	12 (4.5)	4 (1.5)	0	0
Muscle pain	15 (5.7)	5 (1.9)	10 (3.8)	0	0
Nausea	13 (4.9)	11 (4.2)	1 (0.4)	1 (0.4)	0
Thrombocytopenia	11 (4.2)	5 (1.9)	4 (1.5)	1 (0.4)	1 (0.4)
Vomiting	10 (3.8)	10 (3.8)	0	0	0
Cardiac problems	10 (3.8)	8 (3.0)	2 (0.8)	0	0
Liver toxicity	7 (2.6)	3 (1.1)	4 (1.5)	0	0
Hypertension	7 (2.6)	5 (1.9)	1 (0.4)	1 (0.4)	0
Diarrhoea	6 (2.3)	2 (0.8)	3 (1.1)	1 (0.4)	0
Urinary infections	5 (1.9)	4 (1.5)	1 (0.4)	0	0
Hypokalaemia	5 (1.9)	3 (1.1)	1 (0.4)	1 (0.4)	0
Abdominal pain	4 (1.5)	3 (1.1)	1 (0.4)	0	0
Dyspnoea	4 (1.5)	3 (1.1)	1 (0.4)	0	0
Hyperglycaemia	3 (1.1)	1 (0.4)	2 (0.8)	0	0
Deep vein thrombosis	2 (0.8)	0	2 (0.8)	0	0
Neutropenia	1 (0.4)	1 (0.4)	0	0	0
Hyperbilirubinaemia	1 (0.4)	0	0	0	1 (0.4)
Hyponatraemia	1 (0.4)	1 (0.4)	0	0	0
Hypomagnesaemia	1 (0.4)	1 (0.4)	0	0	0

Fig. 1 Best PSA response to AA treatment.



Finally, 29% of the 123 patients with pain at baseline reported an improvement during treatment, 32% no change, and 28% a worsening; no data on changes in pain were available for 11% of the symptomatic patients.

Discussion

To the best of our knowledge, the present study is the largest study of AA safety and activity in a non-clinical trial population since the COU-AA-301 trial and, although with the limitations due to the retrospective nature of the study, our findings confirm the drug's safety and efficacy as the clinical outcomes and toxicities were similar to those reported in the pivotal study. However, the fact that our present patients were treated in the context of an NPP may have made them more similar to patients treated in a clinical trial than those seen and treated in everyday clinical practice.

Table 4 Type of progression and corresponding median (95% CI) PFS.

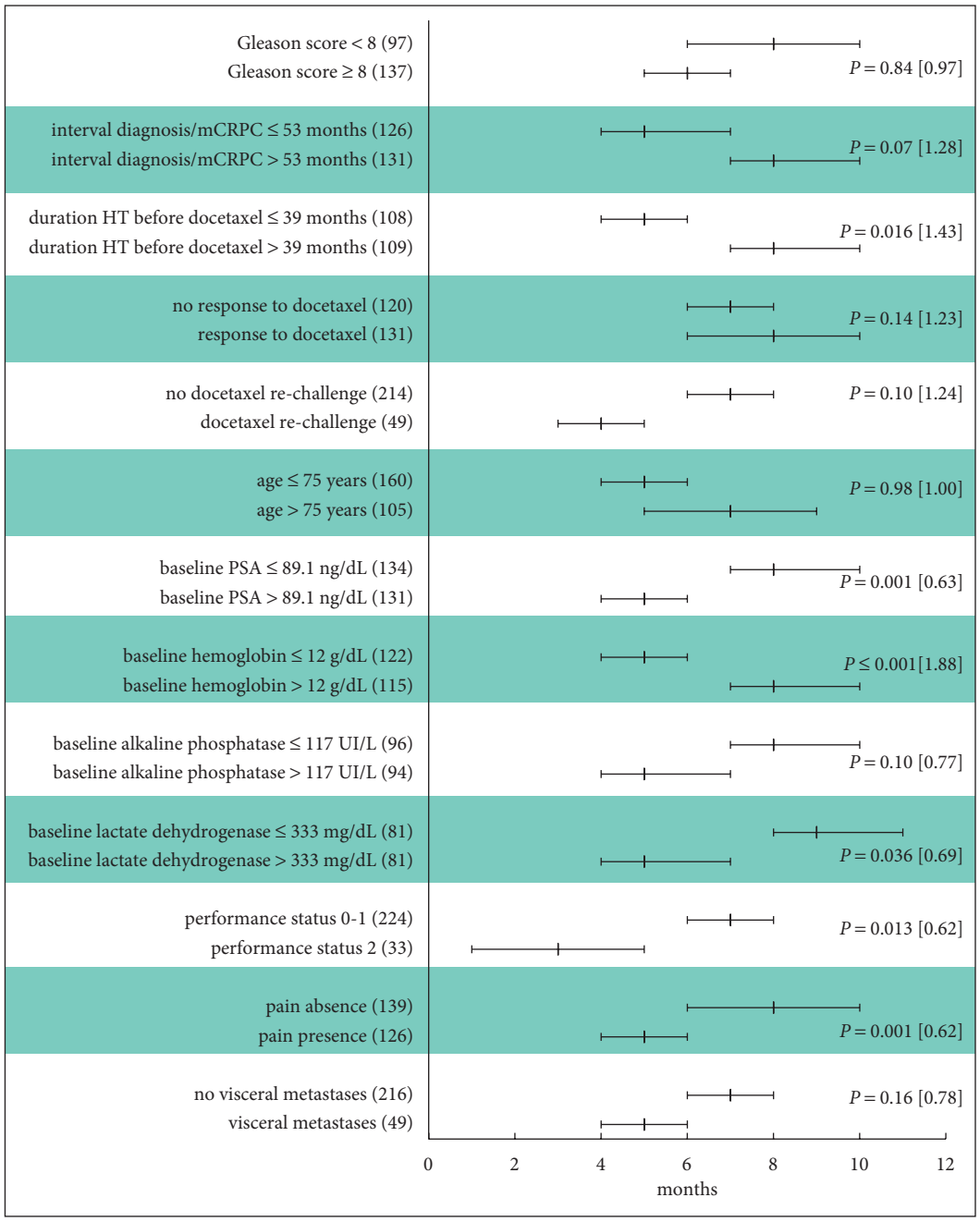
Type of progression	No. of patients (%)	Median (95% CI) PFS, months
Radiographic	5 (1.9)	8.1 (1.5–14.4)
Biochemical	45 (17.0)	5.3 (3.9–6.0)
Clinical	21 (7.9)	1.1 (0.1–2.2)
Radiographic/biochemical	57 (21.5)	8.5 (6.6–9.3)
Radiographic/clinical	6 (2.3)	9.6 (5.9–12.0)
Biochemical/clinical	32 (12.1)	3.4 (1.4–4.5)
Radiographic/biochemical/clinical	55 (20.8)	5.6 (3.6–6.3)
No progression	31 (11.7)	NA
Unknown	13 (4.9)	NA

Table 5 Survival outcomes in the present study and the AA pivotal trial [12,27]. Survival expressed in months (95% CIs).

Survival outcome	Present study	AA pivotal trial
Median (95% CI):		
PFS, months	7 (6–8)*	8.5 (8.3–11.1)** 5.6 (5.6–6.5)***
OS from start of AA, months	17 (14–20)	15.8 (14.8–17.0)
OS from start of docetaxel, months	35 (31–39)	32.6 (30.7–35.0)

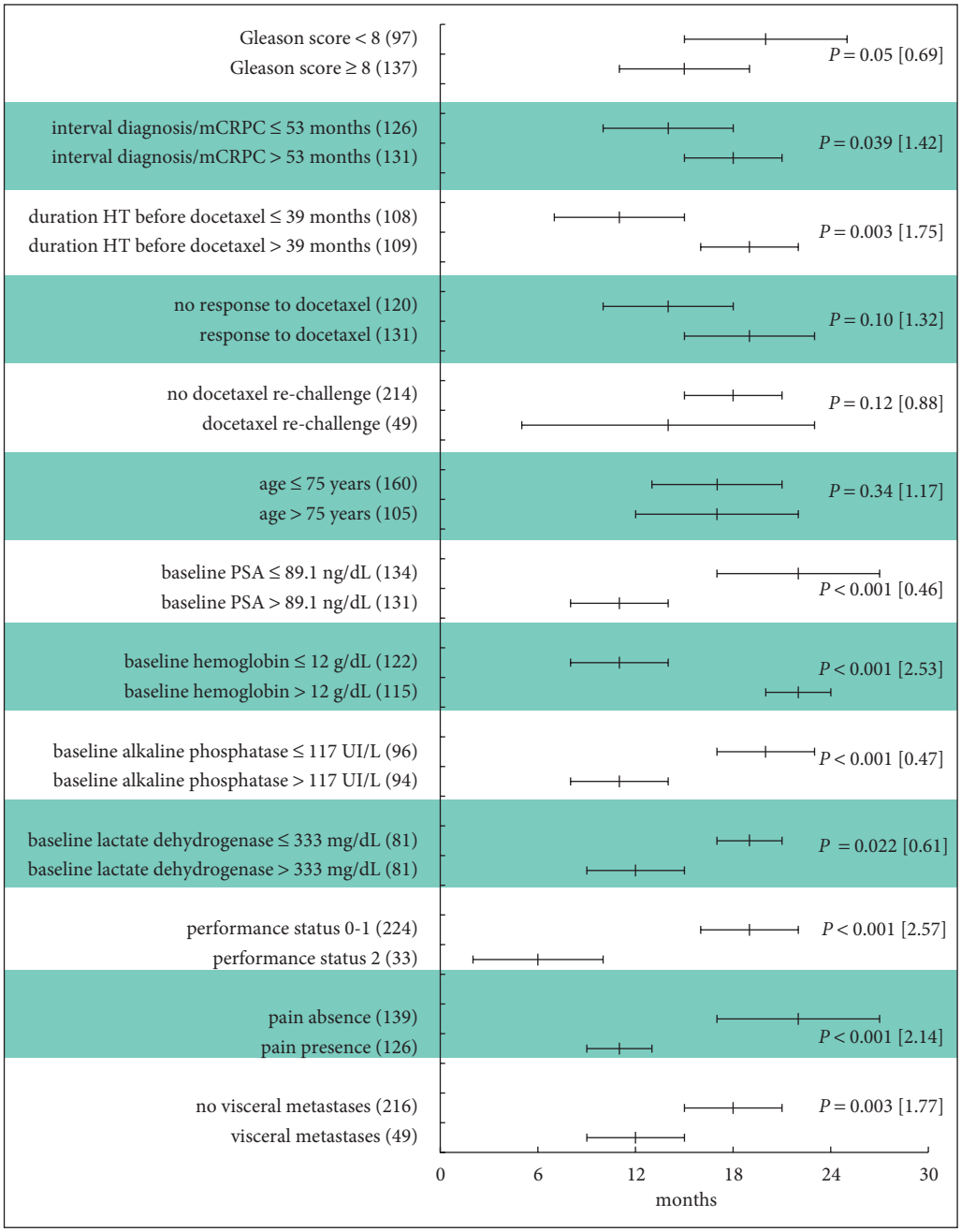
**Prostate Cancer Working Group 2 criteria; **Biochemical; ***Radiographic.*

Fig. 2 PFS by selected factors (the number of patients in each group is shown in brackets): the central dot indicates the median value and the lines the 95% CI. The *P*-values were calculated using the Cox regression analysis, with hazard ratios indicated in square brackets.



Since the publication of the final results of the COU-AA 301 trial [12], no information has been published concerning the safety and efficacy of AA in a large an population of patients pre-treated with docetaxel outside a clinical trial. One study by Canadian cancer centres collected data from 519 pre-treated and chemotherapy-naïve patients who received AA, but only to differentiate AA activity on the basis of performance status [20]. Two small studies have described safety and outcomes in 25 patients treated in Spain [23], and 39 in Germany [19]. One study of 116 patients concentrated on the variables associated with a biochemical response to AA, but only 62 patients were pre-treated with docetaxel and the rest were chemotherapy naïve [21]. Finally, two small studies respectively described the outcomes of 36 patients who had previously received more than three lines of chemotherapy [22], and drug safety in 51 patients with cardiovascular morbidities [18].

Fig. 3 OS by selected factors (the number of patients in each group is shown in brackets): the central dot indicates the median value and the lines the 95% CI. The *P*-values were calculated using the Cox regression analysis, with hazard ratios indicated in square brackets.



Our present study is based on a series of 265 patients treated in 19 Italian hospitals within the context of an NPP. Their baseline characteristics were similar to those of the patients enrolled in the COU-AA-301 pivotal trial, but there are some interesting differences. First of all, they showed more signs of aggressive disease at the time of diagnosis (51.7% had a Gleason score of ≥8 vs 44.7% in the COU-AA-301 trial), although the difference was not statistically significant. Moreover, a greater proportion had nodal metastases (56.6% vs 45.3%), whereas liver and lung metastases were relatively less frequent (7.9% vs 11.3% and 11.7% vs 13.2%). Another interesting difference is that 39.6% of our patients were aged ≥75 years, as against 27.6% of those in the COU-AA-301 trial ($P < 0.001$, Fisher's exact test) but, despite this higher rate of patients who may have had a greater burden of comorbidities, the safety profile of AA was favourable and there was a very low incidence of grade 3–4 toxicities (Table 3). The most frequent side-effects were anaemia and

fatigue, which were high grade in 4% of our present patients, but in respectively 7% and 8% of the patients in the COU-AA-301 trial [5].

Our present study reproduced the results of the COU-AA-301 trial not only for AA toxicity, but also for disease control. Although we assessed PFS using the PCWG2 criteria and the COU-AA-301 trial considered biochemical and radiographic PFS separately, the results were similar. PFS was shorter not only in the patients with more advanced disease, but also in those who had undergone a shorter period of hormonal treatment before docetaxel. This suggests that the duration of hormone sensitivity may have predictive value, and confirms the findings of a preliminary study showing that the PFS of patients receiving new- or old-generation hormonal treatments after docetaxel is significantly longer in those undergoing androgen deprivation for longer [28].

Although coming from a non-trial population, our present OS results were surprisingly similar to those reported in the COU-AA-301 trial. The median OS of 17 months from the start of AA was similar to the 15.8 months reported in the final analysis of the pivotal trial [12], and the same was true of the median OS calculated from the first docetaxel administration (35 vs 32.6 months) [27]. It is interesting to assess the clinical outcomes of special populations such as the elderly, patients with a poor performance status, symptomatic patients, and patients with visceral metastases. Although our present study involved a significantly higher proportion of patients aged ≥75 years than the AA pivotal trial, the median duration of their PFS and OS (7 and 17 months, respectively) was not significantly different from that of their younger counterparts. The elderly patients in the COU-AA-301 trial had a time to biochemical progression of 11 months, a median radiological PFS of 6.6 months, and an OS of 15.6 months [17]. No full paper has been published concerning the COU-AA-301 patients with a poor performance status (ECOG ≥2), but the full trial report indicates that they had a median OS of 7.3 months [12]; our present findings are similar, with a median OS of 6 months and a median PFS of 3 months, and are also strikingly similar to the post-docetaxel findings of Azad et al. [20], who reported that their patients with a poor performance status had a median OS of 8.7 months and a median biochemical PFS of 3.5 months.

The clinical records of our present symptomatic patients indicated an improvement in pain in 29%. However, as these findings are on the physicians' notes, they do not allow a direct assessment of the impact of AA on the patients' own perception of pain or a comparison with the findings of the COU-AA-301 trial, which made a formal assessment using the Brief Pain Inventory-Short Form. This may explain the better results of the pivotal trial, in which 45% of the symptomatic patients treated with AA reported a reduction in pain intensity as against 28.8% in the placebo plus prednisone group ($P < 0.001$) [13].

Finally, the median radiological PFS of the patients with visceral metastases enrolled in the COU-AA-301 trial was 5.6 months and their median OS was 12.9 months [26]; our present findings of respectively 5 and 12 months are surprisingly similar.

Our present study has some of the limitations typical of retrospective studies, such as the incompleteness of some data, the possible error in relating treatment withdrawal to reasons different from therapy-related effects, the possible under-reporting of acute effects and over-estimation of treatment response, which mean that the results need to be cautiously interpreted. However, we think that these limitations did not affect its ability to capture the effect of AA on survival outcomes. Our present data confirm the results of the pivotal trial in the population as a whole and in special populations of specific interest, and support the safety and efficacy of AA in everyday clinical practice.

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Conflict of Interest

U.B. received honoraria from Sanofi Aventis.

O.C. received honoraria from Sanofi Aventis, and Janssen.

U.D.G. received honoraria from Janssen.

G.P. received honoraria from Bayer, Bristol, GSK, Novartis, Astellas, Janssen, and Pfizer.

All remaining authors have declared no conflicts of interest.

References

1 **Tannock IF, de Wit R, Berry WR et al.** Docetaxel plus prednisone or mitoxantrone plus prednisone for advanced prostate cancer. *N Engl J Med* 2004; 351: 1502–12

2 **Petrylak DP, Tangen CM, Hussain MH et al.** Docetaxel and estramustine compared with mitoxantrone and prednisone for advanced refractory prostate cancer. *N Engl J Med* 2004; 351: 1513–20

3 **de Bono JS, Oudard S, Ozguroglu M et al.** Prednisone plus cabazitaxel or mitoxantrone for metastatic castration-resistant prostate cancer progressing after docetaxel treatment: a randomised open-label trial. *Lancet* 2010; 376: 1147–54

4 **Kantoff PW, Higano CS, Shore ND et al.** Sipuleucel-T immunotherapy for castration-resistant prostate cancer. *N Engl J Med* 2010; 363: 411–22

5 **de Bono JS, Logothetis CJ, Molina A et al.** Abiraterone and increased survival in metastatic prostate cancer. *N Engl J Med* 2011; 364: 1995–2005

6 **Scher HI, Fizazi K, Saad F et al.** Increased survival with enzalutamide in prostate cancer after chemotherapy. *N Engl J Med* 2012; 367: 1187–97

7 **Parker C, Nilsson S, Heinrich D et al.** Alpha emitter radium-223 and survival in metastatic prostate cancer. *N Engl J Med* 2013; 369: 213–23

8 **Jarman M, Barrie SE, Llera JM.** The 16,17-double bond is needed for irreversible inhibition of human cytochrome p45017alpha by abiraterone (17-(3-pyridyl)androsta-5, 16-dien-3beta-ol) and related steroidal inhibitors. *J Med Chem* 1998; 41: 5375–81

9 **Attard G, Reid AH, A'Hern R et al.** Selective inhibition of CYP17 with abiraterone acetate is highly active in the treatment of castration-resistant prostate cancer. *J Clin Oncol* 2009; 27: 3742–8

10 **Reid AH, Attard G, Danila DC et al.** Significant and sustained antitumor activity in post-docetaxel, castration-resistant prostate cancer with the CYP17 inhibitor abiraterone acetate. *J Clin Oncol* 2010; 28: 1489–95

11 **Danila DC, Morris MJ, de Bono JS et al.** Phase II multicenter study of abiraterone acetate plus prednisone therapy in patients with docetaxel-treated castration-resistant prostate cancer. *J Clin Oncol* 2010; 28: 1496–501

12 **Fizazi K, Scher HI, Molina A et al.** Abiraterone acetate for treatment of metastatic castration-resistant prostate cancer: final overall survival analysis of the COU-AA-301 randomised, double-blind, placebo-controlled phase 3 study. *Lancet Oncol* 2012; 13: 983–92

13 **Logothetis CJ, Basch E, Molina A et al.** Effect of abiraterone acetate and prednisone compared with placebo and prednisone on pain control and skeletal-related events in patients with metastatic castration-resistant prostate cancer: exploratory analysis of data from the COU-AA-301 randomised trial. *Lancet Oncol* 2012; 13: 1210–7

14 **Sternberg CN, Molina A, North S et al.** Effect of abiraterone acetate on fatigue in patients with metastatic castration-resistant prostate cancer after docetaxel chemotherapy. *Ann Oncol* 2013; 24: 1017–25

15 **Harland S, Staffurth J, Molina A et al.** Effect of abiraterone acetate treatment on the quality of life of patients with metastatic castration-resistant prostate cancer after failure of docetaxel chemotherapy. *Eur J Cancer* 2013; 49: 3648–57

16 **Goodman OB, Jr, Flaig TW, Molina A et al.** Exploratory analysis of the visceral disease subgroup in a phase III study of abiraterone acetate in metastatic castration-resistant prostate cancer. *Prostate Cancer Prostatic Dis* 2014; 17: 34–9

17 **Mulders PF, Molina A, Marberger M et al.** Efficacy and safety of abiraterone acetate in an elderly patient subgroup (aged 75 and older) with metastatic castration-resistant prostate cancer after docetaxel-based chemotherapy. *Eur Urol* 2014; 65: 875–83

18 **Procopio G, Grassi P, Testa I et al.** Safety of abiraterone acetate in castration-resistant prostate cancer patients with concomitant cardiovascular risk factors. *Am J Clin Oncol* 2013 [Epub ahead of print]. doi: 10.1097/COC.0b013e3182a790ce

19 **Heck MM, Hoppner M, Horn T et al.** Compassionate use of abiraterone and cabazitaxel: first experiences in docetaxel-pretreated castration-resistant prostate cancer patients. *Urologe A* 2012; 51: 390–7

20 **Azad AA, Eigl BJ, Leibowitz-Amit R et al.** Outcomes with abiraterone acetate in metastatic castration-resistant prostate cancer patients who have poor performance status. *Eur Urol* 2014 [Epub ahead of print]. doi: 10.1016/j.eururo.2014.01.030

21 **Leibowitz-Amit R, Templeton AJ, Omlin A et al.** Clinical variables associated with PSA response to abiraterone acetate in patients with metastatic castration-resistant prostate cancer. *Ann Oncol* 2014; 25: 657–62

22 **Francini E, Fiaschi AI, Petrioli R et al.** Abiraterone in heavily pretreated patients with metastatic castrate-resistant prostate cancer. *Anticancer Drugs* 2014; 25: 472–7

23 **Beardo-Villar P, Ledo-Cepero MJ, Gavira-Moreno R et al.** Initial experience with abiraterone acetate in patients with castration-resistant prostate cancer. *Actas Urol Esp* 2014 [Epub ahead of print]. doi: 10.1016/j.acuro.2013.11.004

24 **Scher HI, Halabi S, Tannock I et al.** Design and end points of clinical trials for patients with progressive prostate cancer and castrate levels of testosterone: recommendations of the Prostate Cancer Clinical Trials Working Group. *J Clin Oncol* 2008; 26: 1148–59

25 **Eisenhauer EA, Therasse P, Bogaerts J et al.** New response evaluation criteria in solid tumours: revised RECIST guideline (version 1.1). *Eur J Cancer* 2009; 45: 228–47

26 **Goodman OB Jr, Flaig TW, Molina A et al.** Exploratory analysis of the visceral disease subgroup in a phase III study of abiraterone acetate in metastatic castration-resistant prostate cancer. *Prostate Cancer Prostatic Dis* 2014; 17: 34–9

27 **Chi KN, Scher HI, Molina A et al.** Exploratory analysis of survival benefit and prior docetaxel (D) treatment in COU-AA-301, a phase III study of abiraterone acetate (AA) plus prednisone (P) in metastatic castration-resistant prostate cancer (mCRPC). *J Clin Oncol* 2012; 30 (Suppl. 5): Abstr 15

28 **Loriot Y, Massard C, Albiges L et al.** Personalizing treatment in patients with castrate-resistant prostate cancer: a study of predictive factors for secondary endocrine therapies activity. *J Clin Oncol* 2012; 30 (Suppl. 5): Abstr 213

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Abbreviations: AA, abiraterone acetate; ECOG, Eastern Cooperative Oncology Group; mCRPC, metastatic castration-resistant prostate cancer; NPP, named patient programme; OS, overall survival; PCWG2, Prostate Cancer Working Group 2; PFS, progression-free survival; ULN, upper limit of normal.