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Urologic Oncology: Seminars and Original Investigations ▮ (2017) ▮▮▮–▮▮▮

UROLOGIC ONCOLOGY

Original article

Prostate-specific antigen response in black and white patients treated with abiraterone acetate for metastatic castrate–resistant prostate cancer

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Received 15 September 2016; received in revised form 15 December 2016; accepted 20 December 2016

Abstract

Purpose: Evidence suggests differences in androgen receptor AR signaling between black (B) and white (W) patients with prostate cancer, but pivotal trials of abiraterone acetate (AA) for patients with metastatic castration–resistant prostate cancer (mCRPC) enrolled few black patients, a population with a higher mortality from prostate cancer. Our primary objective was to determine differences in response to AA between B and W patients.

Methods: We performed a retrospective case-control study of B vs. W patients treated with AA between May 1, 2008 and June 16, 2015 at Duke University Medical Center. Patients were identified (W control patients were matched 2:1 to B patients stratified based on previous docetaxel exposure) through pharmacy records and were eligible if treated with AA for metastatic castration–resistant prostate cancer. Patients with previous enzalutamide use were excluded. The primary objective was to compare the rate of $\geq$90% prostate-specific antigen (PSA) decline from baseline between B vs. W patients. Secondary outcomes included comparing time on therapy, time to PSA progression, and overall survival among groups.

Results: Baseline characteristics among patients (n = 45 B, n = 90 W) were identified; these included Karnofsky performance status, PSA, Gleason score, alkaline phosphatase, albumin, hemoglobin, lactate dehydrogenase, opiate use for pain, and metastatic sites. Baseline characteristics among groups were similar except for median hemoglobin (B = 11.4 g/dl, W = 12.3 g/dl). The proportion of B patients achieving a $\geq$90% PSA level decline was 37.8% vs. 28.9% for W patients (P = 0.296). Statistically significant differences were found in the proportion of patients achieving a $\geq$50% PSA level decline (B = 68.9%, W = 48.9% [P = 0.028]) and $\geq$30% PSA level decline (B = 77.8%, W = 54.4% [P = 0.008]). Rates of primary abiraterone-refractory disease (PSA increase as best response) trended higher in W (31.1%) than in B (15.6%) patients (P = 0.052). Median treatment duration (B = 9.4 mo, W = 8.3 mo) did not differ (Wilcoxon P = 0.444). Median overall survival (B = 27.3 mo [95% CI: 13.9, not estimable], W = 24.8 mo [95% CI: 19, 31.6] [P = 0.669]) and median time to PSA progression (B = 11.0 mo [95% CI: 4.3, 18.0], W = 9.4 mo [95% CI: 6.2, 13.0] [P = 0.917]) did not differ.

Conclusions: Black patients may have a higher PSA response to AA than white patients. An ongoing prospective clinical study (NCT01940276) is evaluating outcomes between black and white patients treated with AA.

Keywords: Prostatic neoplasms; Race; Castration-resistant; Abirterone acetate; Prostate-specific antigen

1. Introduction

Prostate cancer is the most commonly diagnosed cancer in men in the United States [1]. Epidemiologic studies show a higher per capita incidence of prostate cancer among African Americans compared with other racial groups in the

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http://dx.doi.org/10.1016/j.urolonc.2016.12.016
1078-1439/

United States; furthermore, prostate cancer mortality rate in African Americans is more than double than any other ethnic population [1]. Evidence suggests that there may be differences in prostate cancer biology between black and white patients including differences in androgen biosynthesis and metabolism, androgen receptor (AR) expression, and signaling patterns [2–4]. The next generation androgen biosynthesis inhibitor abiraterone acetate (AA) has been approved by the US Food and Drug Administration for treatment of metastatic castration–resistant prostate cancer (mCRPC) based on survival benefits demonstrated in multiple phase III studies [5,6].

However, phase III studies of abiraterone failed to enroll a significant number of black patients. An exploratory analysis of the pivotal COU-AA-302 phase III trial of 1,088 patients randomized to abiraterone/prednisone vs. placebo/prednisone for mCRPC before chemotherapy suggested that prostate-specific antigen (PSA) response, median time to PSA progression (TTP), and radiographic progression-free survival (PFS) were higher in the 15 (54%) of 28 black patients who received AA compared with the 13 (46%) black patients who received placebo [7]. Although the numbers were small, it appeared that ≥90% PSA level decline from baseline after AA treatment was higher in black patients (53.3%, $n = 8/15$) compared with the overall population (30.8%, $n = 168/546$). Another single-institution retrospective study of 74 patients ($n = 20$ African Americans, $n = 54$ white) did not show a significant difference in response rate, duration of response, or time to progression between African Americans and white treated with AA. However, there was a trend toward better responses in African Americans, with >90% PSA level response in 20% of African Americans compared with 9% of white [8]. Early PSA response has been shown to be a potential predictor of survival in patients with mCRPC treated with AA [9]. We hypothesized that black patients treated with AA for mCRPC may have a higher PSA response rate after treatment compared with white patients.

2. Materials and methods

We designed a retrospective case-control study to investigate differences in response to AA between black and white patients treated at Duke University Medical Center between the dates of May 1, 2008 and June 16, 2015. Patients were identified through query of cancer center pharmacy records, and were eligible if progress notes from the electronic medical record indicated they were treated for mCRPC. Pharmacy records contained patient self-identified race; however, patients listed as black or African American and white were included, and patients listed as "unknown" or as "other" races were excluded. Patients treated with enzalutamide before abiraterone were also excluded.

White control patients were identified 2:1 to match black patients based on previous docetaxel exposure (Fig. 1).

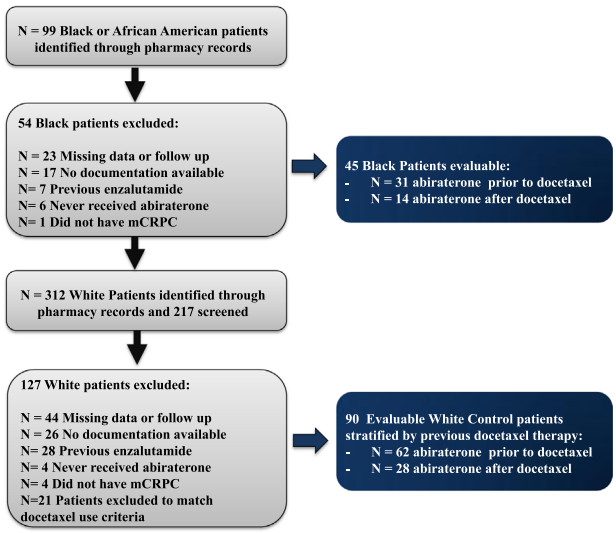

Fig. 1. *Study design*: patients were identified by the above schema. Query of our pharmacy database led to the identification of 99 black and 312 white patients. First, 45 black patients were identified after 54 black patients were excluded for various reasons as shown; 217 white patients were subsequently screened to identify the first 90 evaluable white control patients stratified for prior docetaxel use. (Color version of figure is available online.)

Patients were stratified in this manner as prognosis and survival has been shown to be different in patients with mCRPC before and after docetaxel treatment [5,6]. Baseline prognostic characteristics of the patients related to their disease were identified; these included performance status, PSA, Gleason score, alkaline phosphatase (ALK), albumin, hemoglobin, lactate dehydrogenase (LDH), opiate use for pain, and metastatic sites of disease. The primary objective was to compare the percentage of black patients and the percentage of white patients with a ≥90% PSA decline during initial treatment with AA for mCRPC. The secondary objectives were to compare duration of therapy, PSA progression by prostate cancer working group 2 criteria [10], and overall survival (OS) in black and white patients treated with AA.

2.1. Statistical analysis

Differences in baseline characteristics (Table 1) were assessed using *t*-tests or Wilcoxon rank-sum tests where appropriate. One-sided Chi-square tests were used to compare PSA responses in black and white patients. For the primary objective, we estimated that if we identified 50 black and 100 white control patients, a one-sided Chi-square test would give us 59% power to demonstrate an effect size of 15% difference (40% black vs. 25% white) in ≥90% PSA decline between groups with a significance level of 0.05.

Regarding the secondary objectives, differences in treatment duration among race groups were tested using a Wilcoxon rank-sum tests. Kaplan-Meier methods were used to estimate median 6-month, 1-year, 18-month, and 2-year