Treatment duration and utilization patterns in metastatic castration-resistant prostate cancer patients receiving enzalutamide or abiraterone acetate

Poster L5

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INTRODUCTION

- Castration-resistant prostate cancer (CRPC) is an advanced form of prostate cancer in which the disease has progressed following surgical castration or androgen deprivation therapy.[1,2] Over 84% of CRPC cases demonstrate radiographic findings of metastases.[2] Metastatic CRPC (mCRPC) is characterized by poor prognosis and reduced survival compared with castration-sensitive prostate cancer.[2]
- Enzalutamide (an androgen receptor antagonist) and abiraterone acetate (a CYP17 inhibitor, used in combination with prednisone) are approved oral hormonal therapies for men with mCRPC. With respect to outcomes research, some studies have evaluated treatment duration and dose reduction for patients receiving enzalutamide and abiraterone.[3,4] However, the results reported only discontinuation of mCRPC treatment and did not describe switching to a new treatment; analysis of treatment duration and switching may serve as a proxy for treatment effectiveness.

OBJECTIVE

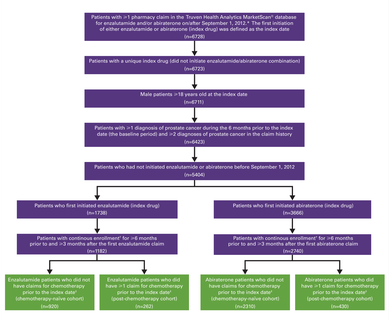
- To describe and compare real-world treatment duration and utilization patterns in patients with mCRPC treated with enzalutamide or abiraterone acetate using administrative claims data in the United States.

METHODS

Data sources

- This study used the MarketScan® commercial claims and Medicare supplemental databases (2012–2015).
- Patients with prostate cancer were identified based on International Classification of Disease, 9th revision (ICD-9-CM) code 185 or ICD-10-CM code C61. At least two diagnoses of prostate cancer were required (see patient selection flow chart; **Figure 1**).

Figure 1. Sample selection flow chart



*September 1, 2012 is the earliest time at which both enzalutamide and abiraterone were commercially available in the United States; †Continuous enrollment was defined as having no gap between periods of enrollment; ‡Chemotherapies included docetaxel, cabazitaxel, mitoxantrone, estramustine, cisplatin, carboplatin, cyclophosphamide, doxorubicin, mitomycin, irinotecan, 5-fluorouracil, gemcitabine, etoposide, paclitaxel, and vinorelbine.

- Patients were categorized into chemotherapy-naïve and post-chemotherapy cohorts based on if they had claims for chemotherapy prior to the index date.
- The baseline period was defined as the 6 months before the index date. All eligible patients were followed until the end of their data availability (with a minimum follow-up of 3 months after the index date).

Study outcomes and statistical analysis

- Patient baseline characteristics included demographics, comorbidities, and medications and procedures received for prostate cancer during the baseline period.
  - Continuous variables were summarized using mean, standard deviation, and median; categorical variables were summarized using counts and proportions.
- Treatment duration was calculated from index treatment initiation to discontinuation. Discontinuation was defined by a gap of at least 45 days between the end of supply of one fill for the index treatment and the date of the next fill. Patients who did not discontinue were censored at the end of continuous enrollment or data availability.
  - Treatment duration was estimated using the Kaplan–Meier method and compared using log-rank tests between the enzalutamide- and abiraterone-treated patients.
- Treatment switching was defined as starting a new line of therapy from 30 days before to 45 days after the date of index treatment discontinuation. The proportions of patients who switched to subsequent therapies were reported.
- Analyses were separately conducted for chemotherapy-naïve and post-chemotherapy patients. Patient subgroups defined according to baseline characteristics were evaluated, including patients with diabetes, cardiovascular disease, and corticosteroid-sensitive comorbidities.

RESULTS

Baseline characteristics

- The study included 3230 chemotherapy-naïve (enzalutamide, 920; abiraterone, 2310) and 692 post-chemotherapy (enzalutamide, 262; abiraterone, 430) patients (**Figure 1**). The majority of patients were chemotherapy-naïve at index date (78% and 84% for enzalutamide and abiraterone, respectively).
- Among chemotherapy-naïve patients, enzalutamide-treated patients were 1 year older than abiraterone-treated patients (mean age, 74.5 years vs. 73.5 years), on average (**Table 1**). A greater proportion of patients treated with abiraterone initiated treatment before 2014, while a greater proportion of enzalutamide-treated patients initiated treatment in 2015.
- With respect to comorbidities, chemotherapy-naïve patients in both cohorts had similar mean Charlson Comorbidity Index scores. However, larger proportions of enzalutamide-treated patients had corticosteroid-sensitive comorbidities, including hypertension and diabetes.
- The mean follow-up time was 12.4 months for enzalutamide- and 15.7 months for abiraterone-treated patients.
- Among the 692 post-chemotherapy patients, the baseline characteristics were similar between the enzalutamide and abiraterone cohorts (data not shown).

Treatment patterns

Treatment duration

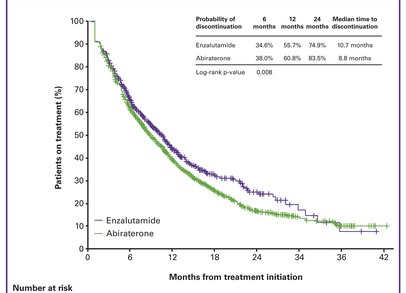
- Among chemotherapy-naïve patients, treatment duration was longer for enzalutamide-treated patients compared with abiraterone-treated patients (log-rank p=0.008; median 10.7 vs. 8.8 months) (**Figure 2**). Within 1 year of initiation, 55.7% of enzalutamide- and 60.8% of abiraterone-treated patients discontinued treatment.

Table 1. Patient baseline characteristics (chemotherapy-naïve patients)

Patient characteristics	Enzalutamide (n=920)	Abiraterone (n=2310)
Demographics		
Age, mean ± SD (median)	74.5 ± 10.7 (75.8)	73.5 ± 10.6 (74.3)
Region, n (%)		
Northeast	224 (24.3)	559 (24.2)
North central	282 (30.7)	638 (27.6)
South	290 (31.5)	685 (29.7)
West	121 (13.2)	418 (18.1)
Unknown	3 (0.3)	10 (0.4)
Year of index date, n (%)		
2012	48 (5.2)	239 (10.3)
2013	159 (17.3)	1096 (47.4)
2014	275 (29.9)	621 (26.9)
2015	438 (47.6)	354 (15.3)
Health insurance type, n (%)		
Comprehensive	348 (37.8)	806 (34.9)
PPO	396 (43.0)	1013 (43.9)
HMO and other capitated plans	73 (7.9)	295 (12.8)
Other	103 (11.2)	196 (8.5)
Comorbidities		
CCI*, mean ± SD (median)	2.7 ± 1.2 (2.0)	2.6 ± 1.1 (2.0)
Prostate cancer-related comorbidities, n (%)		
Bone metastases	564 (61.3)	1481 (64.1)
Hypertension	526 (57.2)	1195 (51.7)
Urinary tract infection	95 (10.3)	245 (10.6)
Glaucoma	81 (8.8)	232 (10.0)
Depression	51 (5.5)	108 (4.7)
Impotence	44 (4.8)	111 (4.8)
Other comorbidities, n (%)		
Diabetes	253 (27.5)	533 (23.1)
Chronic pulmonary disease	124 (13.5)	275 (11.9)
Malignancies (excluding prostate cancer)	131 (14.2)	368 (15.9)
Renal disease	108 (11.7)	272 (11.8)
Peripheral vascular disease	107 (11.6)	245 (10.6)
Congestive heart failure	91 (9.9)	182 (7.9)
Cerebrovascular disease	71 (7.7)	183 (7.9)
Liver disease	44 (4.8)	160 (6.9)
Myocardial infarction	29 (3.2)	61 (2.6)
Treatments received during baseline period, n (%)		
Pharmaceutical treatments		
LHRH agonists/antagonists†	675 (73.4)	1645 (71.2)
Anti-androgen‡	450 (48.9)	1334 (57.7)
Opioids analgesics	394 (42.8)	984 (42.6)
Osteoclast inhibitors§	338 (36.7)	823 (35.6)
Corticosteroids	184 (20.0)	1054 (45.6)
Sipuleucel-T	76 (8.3)	147 (6.4)
Radiopharmaceuticals‖	5 (0.5)	3 (0.1)
Procedures		
Surgical castration¶	15 (1.6)	37 (1.6)
Radiation**	13 (1.4)	9 (0.4)

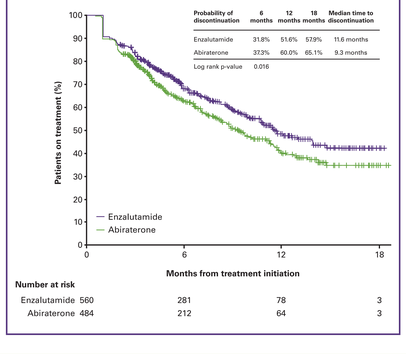
*The CCI has been modified to exclude prostate cancer and metastatic disease; †The following LHRH agonists/antagonists were included: leuprolide, goserelin, triptorelin, histrelin, degarelix, and diethylstilbestrol; ‡Anti-androgens included bicalutamide, nilutamide, and flutamide; §Denosumab and zoledronic acid were included; ‖Radiopharmaceuticals included radium-223 and samarium-153; ¶Surgical castration included both unilateral and bilateral orchiectomy; **Radiation included external beam radiation therapy, stereotactic radiation therapy, and hemibody irradiation.
CCI=Charlson Comorbidity Index; HMO=Health Maintenance Organization; LHRH=luteinizing hormone-releasing hormone; PPO=Preferred Provider Organization; SD=standard deviation.

Figure 2. Treatment duration (chemotherapy-naïve patients)



- Results were consistent in a sensitivity analysis among patients initiating their index therapy after the approval of pre-chemotherapy indication for enzalutamide (September 10, 2014) (**Figure 3**). Treatment duration was significantly longer among enzalutamide-treated patients and 51.6% of enzalutamide- and 60.0% of abiraterone-treated patients discontinued treatment within 1 year of initiation.

Figure 3. Treatment duration (chemotherapy-naïve patients; after pre-chemotherapy indication approval for enzalutamide in September 2014)



- Subgroup analyses for patients with diabetes, cardiovascular disease, and corticosteroid-sensitive comorbidities yielded similar results. Enzalutamide-treated patients had a significantly longer treatment duration and a lower proportion of discontinuations within 1 year of initiation.
- Treatment duration was shorter among post-chemotherapy patients than chemotherapy-naïve patients (median 7.5 vs. 7.1 months for enzalutamide and abiraterone, respectively); the difference between enzalutamide and abiraterone cohorts among post-chemotherapy patients was not statistically significant (log-rank p=0.255).

Treatment switching

- Among chemotherapy-naïve patients within 1 year of treatment initiation, a lower proportion of patients receiving enzalutamide versus abiraterone switched from their index therapy to a different treatment (22.5% vs. 34.7%, respectively).
- Similarly, a greater proportion of post-chemotherapy abiraterone-treated patients switched treatment within 1 year of initiation (enzalutamide, 43.0%; abiraterone, 53.2%).
- Among chemotherapy-naïve patients, the majority of enzalutamide-treated patients who switched therapies switched to abiraterone (65.8%), followed by docetaxel (23.0%), and the majority of abiraterone-treated patients who switched therapies switched to enzalutamide (64.3%), followed by docetaxel (28.9%). A similar trend was observed among post-chemotherapy patients with enzalutamide and abiraterone being the most frequently switched-to therapies, followed by cabazitaxel.

DISCUSSION

- This study is first to evaluate real-world outcomes of mCRPC for chemotherapy-naïve and post-chemotherapy patients separately. These two groups of patients are at different stages of the disease and may have different clinical outcomes; the treatment effect in the two groups may differ as well. Therefore, it is important to evaluate the real-world outcomes for the two groups of patients separately.
- Additionally, this study is the first to examine outcomes in patient subgroups including patients with diabetes, cardiovascular disease, and corticosteroid-sensitive comorbidities.
- The results indicate that there are differences in treatment durations and treatment switching among enzalutamide- and abiraterone-treated patients.
- Enzalutamide-treated patients remained on treatment longer than those initiating abiraterone, and this was consistent across multiple subgroup analyses including various comorbidity populations.
  - The observed treatment durations for both treatments were shorter compared with those reported in the clinical trials of enzalutamide (PREVAIL study)[5] and abiraterone (COU-AA-302 study)[6] at 18.2 versus 13.8 months, respectively. Noticeably, the treatment duration of enzalutamide was longer than that of abiraterone in both the clinical trial setting and real-world clinical practice.
  - Also, enzalutamide-treated patients are less likely to discontinue treatment at 6, 12, and 24 months than abiraterone-treated patients.
  - Since treatment duration is often a reflection of treatment effectiveness in cancer patients, the longer observed duration of treatment in enzalutamide patients might be an indicator of better effectiveness for these patients.[7,8] Future studies should be conducted to confirm this hypothesis.
- This study was the first to examine treatment-switching outcomes in patients with mCRPC initiating enzalutamide or abiraterone. Among chemotherapy-naïve and post-chemotherapy patients within 1 year of treatment initiation, a lower proportion of patients receiving enzalutamide versus abiraterone switched from their index therapy to a different treatment. These findings may reflect higher patient satisfaction and perceived efficacy of treatment.

LIMITATIONS

- This study is subject to the general limitations of using administrative claims data, including potential for incorrectly recoded diagnosis codes and inability to capture medical services or pharmacy dispensing obtained outside of a patient's plan. Furthermore, not all relevant data are collected in claims, such as the reason for discontinuation of treatment.
- Additionally, patients with Medicare supplemental coverage may have received services that were fully covered by Medicare and therefore not captured in this study. However, the proportions of patients with Medicare supplemental coverage were similar between the two cohorts (79% of enzalutamide- and 75% of abiraterone-treated patients at the index date) so the missing service records are not expected to bias the study results.
- The possibility of confounding due to the imbalance of baseline characteristics cannot be excluded in this observational study.

CONCLUSIONS

- This study reveals that differences exist between enzalutamide and abiraterone with respect to treatment duration and utilization patterns.
- The results indicate that chemotherapy-naïve patients initiating enzalutamide stayed on treatment longer and switched to other mCRPC treatments less frequently, despite having a higher comorbidity burden at baseline and being slightly older compared with patients initiating abiraterone. Additionally, the results were consistent across multiple subgroups.

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