# Health care resource utilization and costs in metastatic castration-resistant prostate cancer patients treated with enzalutamide or abiraterone acetate

Poster L8



Vahan Kassabian,[1,*] Scott C. Flanders,[2] Samuel Wilson,[2] Bruce A. Brown,[2,†] Yan Song,[3] Hongbo Yang,[3] Stanislav Lechpammer,[4] Neil M. Schultz[2]

[1]Georgia Urology, Atlanta, Georgia, USA; [2]Astellas Pharma, Inc., Northbrook, IL, USA; [3]Analysis Group, Inc., Boston, MA, USA; [4]Pfizer Inc., San Francisco, California, USA;

[†]An employee of Astellas Pharma Inc. when the research was conducted

## INTRODUCTION

- Castration-resistant prostate cancer (CRPC) accounts for approximately 10–20% of all prostate cancer cases, with over 84% demonstrating radiographic findings of metastases.[1] Metastatic CRPC (mCRPC) is characterized by poor prognosis and reduced survival compared to castration-sensitive prostate cancer.[1]
- The United States Food and Drug Administration approved two second-generation hormonal agents, enzalutamide (an androgen receptor antagonist) and abiraterone acetate (a CYP17 inhibitor, used in combination with prednisone), for mCRPC patients with or without prior chemotherapy.
- Two previous studies evaluated pharmacy costs for the two treatments; however, no studies have examined health care resource utilization (HRU) and costs beyond pharmacy.[2,3]
- Examining the real-world use of these treatments is important from a clinician's perspective as lower HRU burden and related medical service costs may reflect fewer disease monitoring requirements and better real-world effectiveness.

## OBJECTIVE

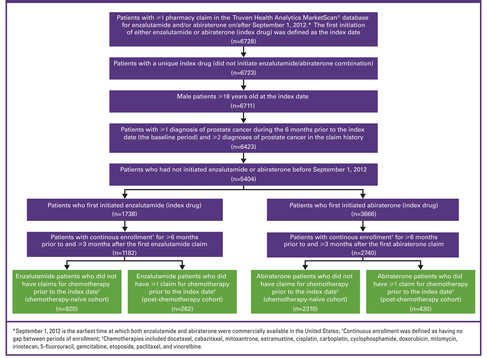
- To compare HRU and costs for patients with mCRPC treated with enzalutamide or abiraterone in the United States.

## METHODS

### Study population and design

- This study used the Truven 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 in the entire claims history were required (see patient selection flow chart; **Figure 1**).
- Patients were categorized into chemotherapy-naïve and post-chemotherapy cohorts based on whether they had claims for chemotherapy in their entire data history prior to the index date.
- The baseline period was defined as the 6 months before the index date. The study period was defined as the period from the index date until the end of data availability (with a minimum follow-up of 3 months after the index date required).

**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; [c]Continuous enrollment was defined as having no gap between periods of enrollment; [d]Chemotherapies included docetaxel, cabazitaxel, mitoxantrone, estramustine, cisplatin, carboplatin, cyclophosphamide, doxorubicin, mitomycin, irinotecan, 5-fluorouracil, gemcitabine, etoposide, paclitaxel, and vinorelbine.

### Study covariates and outcomes

- Patient baseline characteristics included patient age at index date, year of index date, region, health insurance type, comorbidities, and treatments received for prostate cancer during the baseline period.
- Monthly rates of HRU were assessed during the study period and included the following categories: inpatient admissions, total days of hospitalization, and emergency department and outpatient visits. Presence of at least one HRU was also evaluated within the 3-month period after the index date.
- Monthly all-cause medical costs (including inpatient, outpatient, and emergency department costs) and pharmacy costs for the index drug were assessed during the study period. The costs were adjusted to 2015 U.S. dollars.
- Prostate cancer-related HRU and medical costs were estimated based on the claims with a primary or secondary diagnosis of prostate cancer, while pharmacy costs were estimated based on claims for a prostate cancer prescription treatment. The same outcomes as for all-cause HRU and costs were assessed.

### Statistical analyses

- Baseline characteristics were summarized using mean, standard deviation, and median for continuous variables and counts and proportions for categorical variables.
- Incidence rate ratios (IRRs) for HRU outcomes were estimated using generalized linear models with a Poisson distribution and odds ratios (ORs) were estimated using logistic regression. Differences in costs were estimated using generalized linear models with a Tweedie distribution (a compound Poisson–gamma distribution).[4,5] No adjustment for multiple comparisons was performed.
- Adjusted regression comparisons controlled for the following baseline covariates, which were selected based on clinical relevance: patient age at the index date, Charlson Comorbidity Index, year of index date, number of all-cause and prostate cancer-related inpatient and outpatient visits during the baseline period, surgical or chemical castration received during the baseline period, and use of any anti-androgen or androgen synthesis inhibitors during the baseline period.
- All analyses were conducted separately 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

### Patient characteristics

- Overall, 6728 male adult patients were identified with at least one diagnosis of prostate cancer and at least one pharmacy claim for enzalutamide or abiraterone on or after September 1, 2012 (**Figure 1**). The study included 3230 chemotherapy-naïve (enzalutamide, 920; abiraterone, 2310) and 692 post-chemotherapy (enzalutamide, 262; abiraterone, 430) patients.
- The majority of patients were chemotherapy-naïve (78% and 84% for enzalutamide and abiraterone, respectively).
  - Enzalutamide-treated patients were 1 year older than patients treated with abiraterone (mean age, 74.5 vs. 73.5 years), on average (**Table 1**).
  - With respect to comorbidities, 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.
  - Larger proportions of abiraterone-treated patients received anti-androgen therapies (including bicalutamide and nilutamide) and corticosteroids during the baseline period.
- In total, 262 enzalutamide-treated patients and 430 abiraterone-treated patients were post-chemotherapy. These patients were typically younger than the chemotherapy-naïve patients. The baseline characteristics were similar between the enzalutamide and abiraterone cohorts among post-chemotherapy patients and in patient subgroups (data not shown).

### HRU

- Among chemotherapy-naïve patients, enzalutamide-treated patients had fewer all-cause inpatient admissions and days of hospitalization (adjusted IRRs [95% confidence interval (CI)]: 0.87 [0.76, 0.99] and 0.84 [0.70, 1.02]) and outpatient visits (adjusted IRR [95% CI]: 0.94 [0.90, 0.98]) compared with abiraterone-treated patients (**Table 2**).
  - Within 3 months of the index date, enzalutamide-treated patients were 25% less likely to have any all-cause inpatient admission (adjusted OR [95% CI] 0.75 [0.57, 0.97]; data not shown).

**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) |
| 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) |
| Diabetes | 253 (27.5) | 533 (23.1) |
| 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) |
| Treatments received during baseline period, n (%) | | |
| 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) |
| Surgical castration[¶] | 15 (1.6) | 37 (1.6) |

*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; [¶]Surgical castration included both unilateral and bilateral orchiectomy.
CCI=Charlson Comorbidity Index; HMO=Health Maintenance Organization; LHRH=luteinizing hormone-releasing hormone; PPO=Preferred Provider Organization; SD=standard deviation.

**Table 2. Health care resource utilization during the study period (chemotherapy-naïve patients)**

| | Monthly incidence rate | | Incidence rate ratios[†] | | | |
|---|---|---|---|---|---|---|
| | | | Unadjusted | | Adjusted | |
| | Enzalutamide (n=920) | Abiraterone (n=2310) | IRR (95% CI) | P-value | IRR (95% CI) | P-value |
| All-cause resource use | | | | | | |
| Inpatient admissions | 0.05 | 0.06 | 0.86 (0.75, 0.97) | 0.018* | 0.87 (0.76, 0.99) | 0.033* |
| Days of hospitalization[‡] | 0.76 | 0.72 | 1.05 (0.88, 1.25) | 0.615 | 0.92 (0.77, 1.10) | 0.357 |
| Days of hospitalization | 0.33 | 0.40 | 0.83 (0.69, 1.00) | 0.047* | 0.84 (0.70, 1.02) | 0.084 |
| Emergency department visits | 0.14 | 0.13 | 1.02 (0.91, 1.14) | 0.789 | 1.00 (0.89, 1.12) | 0.949 |
| Outpatient visits | 3.14 | 3.32 | 0.95 (0.90, 0.99) | 0.023* | 0.94 (0.90, 0.98) | 0.004* |
| Prostate cancer-related resource use | | | | | | |
| Inpatient admissions | 0.04 | 0.04 | 0.86 (0.74, 0.99) | 0.043* | 0.86 (0.74, 1.01) | 0.059 |
| Days of hospitalization[‡] | 0.78 | 0.71 | 1.11 (0.91, 1.35) | 0.316 | 0.96 (0.79, 1.18) | 0.722 |
| Days of hospitalization | 0.27 | 0.32 | 0.84 (0.68, 1.03) | 0.100 | 0.85 (0.69, 1.06) | 0.155 |
| Emergency department visits | 0.04 | 0.04 | 0.94 (0.79, 1.12) | 0.508 | 0.93 (0.78, 1.11) | 0.403 |
| Outpatient visits | 1.78 | 1.93 | 0.92 (0.87, 0.97) | 0.003* | 0.92 (0.87, 0.96) | <0.001* |

*p<0.05; [†]IRRs comparing enzalutamide versus abiraterone, their 95% CIs, and p-values were estimated using generalized linear model with a Poisson distribution, with an offset to account for varying follow up times between patients; [‡]Calculated among patients with an inpatient admission.
CI=confidence interval; IRR=incidence rate ratio.

- Enzalutamide-treated patients had fewer prostate cancer-related inpatient admissions and outpatient visits (adjusted IRRs [95% CI] 0.86 [0.74, 1.01] and 0.92 [0.87, 0.96]).
  - Within 3 months of the index date, the enzalutamide-treated patients were 28% and 24% less likely to have a prostate cancer-related emergency department visit or inpatient admission, respectively (adjusted OR [95% CI]: 0.72 [0.53, 0.98] and 0.76 [0.57, 1.02], respectively; data not shown).
- Subgroup analyses for patients with diabetes, corticosteroid-sensitive comorbidities, and cardiovascular disease yielded similar results (data not shown).
- No significant differences in HRU were observed between the enzalutamide and abiraterone cohorts among post-chemotherapy patients (data not shown).

### Costs

- Among chemotherapy-naïve patients, enzalutamide-treated patients had lower all-cause and prostate cancer-related emergency department costs (adjusted difference of monthly cost: -$51; p=0.018 and -$26; p=0.009, respectively) but higher pharmacy costs than the abiraterone cohort (**Table 3**).

**Table 3. Health care costs (2015 U.S. dollars) during the study period (chemotherapy-naïve patients)**

| | Monthly cost, mean ± SD[†] | | Difference in monthly cost (enzalutamide – abiraterone)[‡] | | | |
|---|---|---|---|---|---|---|
| | | | Unadjusted | | Adjusted | |
| | Enzalutamide (n=847) | Abiraterone (n=2018) | Difference | P-value | Difference | P-value |
| Total health care cost (all cause) | 14,002 ± 11,618 | 13,774 ± 15,090 | 228 | 0.529 | 204 | 0.574 |
| Medical service cost | 6894 ± 11,360 | 7699 ± 15,144 | -805 | 0.014* | -84 | 0.801 |
| Inpatient admissions | 1666 ± 4207 | 2068 ± 5442 | -402 | 0.008* | -253 | 0.117 |
| Emergency department visits | 267 ± 921 | 297 ± 1191 | -30 | 0.176 | -51 | 0.018* |
| Outpatient visits | 4961 ± 9654 | 5334 ± 13,128 | -373 | 0.112 | 189 | 0.406 |
| Pharmacy cost | 7108 ± 3166 | 6075 ± 2746 | 1033 | <0.001* | 511 | <0.001* |
| Total health care cost (prostate cancer-related) | 10,874 ± 7476 | 10,290 ± 11,299 | 584 | 0.025 | 430 | 0.093 |
| Medical service cost | 4129 ± 7169 | 4533 ± 11,307 | -404 | 0.056 | 54 | 0.785 |
| Inpatient admissions | 432 ± 1570 | 524 ± 1696 | -92 | 0.083 | -114 | 0.024* |
| Emergency department visits | 79 ± 608 | 104 ± 685 | -25 | 0.050 | -26 | 0.009* |
| Outpatient visits | 3617 ± 6873 | 3905 ± 10,948 | -288 | 0.126 | 228 | 0.197 |
| Pharmacy cost | 6745 ± 2957 | 5758 ± 2499 | 987 | <0.001* | 454 | <0.001* |
| Index drug | 6293 ± 3098 | 4847 ± 2682 | 1446 | <0.001* | 782 | <0.001* |

*p<0.05; [†]This analysis was restricted to patients who were not on capitated insurance plans – patients with mixed insurance types were excluded if the plan type they held longest during their period of continuous enrollment was capitated; [‡]Differences and p-values were estimated using generalized linear models with a Tweedie distribution – outcomes were standardized as monthly costs to account for varying follow up times between patients.
SD=standard deviation.

- Prostate cancer-related costs for inpatient admissions were also lower for enzalutamide-treated patients compared with abiraterone-treated patients (adjusted difference of monthly cost: -$114; p=0.024).
- Results were similar in subgroups among patients with diabetes, corticosteroid-sensitive comorbidities, and cardiovascular disease (data not shown).
- No significant differences were observed in medical costs among post-chemotherapy patients (data not shown).

## DISCUSSION

- Enzalutamide-treated patients without prior chemotherapy treatment had less frequent all-cause inpatient and emergency department visits compared with abiraterone-treated patients. The higher HRU among abiraterone-treated patients could be due to monitoring of concomitant corticosteroid use (since abiraterone label requires co-administration of prednisone[6]) or occurrence of more serious adverse events associated with abiraterone, including fluid retention, hypertension, and hypokalemia.
- The most frequently reported procedure codes for inpatient and emergency department visits were explored for the two cohorts to try to explain the reasons behind the higher hospitalization burden and the more frequent emergency department visits among abiraterone-treated patients. The most frequent procedure code descriptions were non-specific (e.g. "subsequent hospital care" or "emergency department visit") and therefore the differences need to be further explored in future studies.
- The total monthly all-cause and prostate cancer-related health care costs among chemotherapy-naïve patients initiating enzalutamide and abiraterone were not significantly different in adjusted analyses, due to a cost offset from the lower medical costs of enzalutamide-treated patients.
- This is the first analysis of real-world HRU and medical costs associated with enzalutamide and abiraterone. The study results provide important information for clinicians as lower HRU and related medical-service costs may reflect fewer disease monitoring requirements and better real-world effectiveness.

## LIMITATIONS

- 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-treated patients 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. To the extent possible, this study has controlled for observed baseline imbalance between the study cohorts, including some proxies of disease severity, using multivariable regression modelling.

## CONCLUSIONS

- This is the first study to assess HRU and medical costs among enzalutamide- and abiraterone-treated patients, adding a comprehensive comparison to the current knowledge base.
- Chemotherapy-naïve patients initiating enzalutamide incurred fewer inpatient and outpatient visits and had lower prostate cancer-related inpatient and emergency department costs. The lower HRU burden may reflect the better real-world effectiveness of enzalutamide.
- Despite the higher drug acquisition cost of enzalutamide compared with abiraterone, the lower medical costs of enzalutamide-treated patients offset the incremental pharmacy cost among these patients.

## ACKNOWLEDGMENTS

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*VKassabian@gaurology.com