Patient and Provider Variables Associated with Variation in the Systemic Treatment of Advanced Prostate Cancer

Supplementary Materials - Online Content

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1.0 Overview

Supplementary Materials have been provided by the authors to give readers additional information about their work.

We first present a general overview of the methods and then describe details of each step in separate sections. The database used in this analysis is the Clinformatics ™ Data Mart comprised of administrative health claims for members of a large national managed care company affiliated with OptumInsight.

2.0 Preprocessing

2.1 Cohort Definition and Disease Diagnosis

We had access to fully de-identified data on all beneficiaries who have prostate cancer from May 1, 2001, through June 30, 2016, as identified by at least one International Classification of Diseases (ICD-9-CM and ICD-10-CM) code for any prostate cancer diagnosis. The presence of a comorbid condition was defined as at least two diagnosis codes within the two years before receipt of the first-line treatment, in order to identify pre-existing conditions rather than a comorbid condition that may have resulted from the treatment. We used codes from the Elixhauser Comorbidity Index to identify a diagnosis of diabetes, hypertension, cardiac arrhythmia, and congestive heart failure.[1] We used codes from the Clinical Classification Software to identify a diagnosis of osteoporosis.[2] In the Medical Claims table, we used ICD_FLAG to indicate whether the version of the claim is ICD-9 or ICD-10. ICD codes for prostate cancer, metastatic disease, and each comorbid condition are as follows:

1) Prostate cancer
   a. **ICD-9:** 185
   b. **ICD-10:** C61
2) Metastatic
   a. **ICD-9:** 196x, 197x, 198x, 19880, 19881, 19882, 19889
   b. **ICD-10:** C770, C772, C773, C774, C775, C778, C7800, C781, C782, C783, C784, C785, C786, C787, C7889, C7981, C7982, C7989
3) Hypertension
   a. **ICD-9:** 4011, 4019, 6420, 4010, 6421, 6422, 6427, 6429, 402x, 403x, 404x
   b. **ICD-10:** I10x, I11x, I12x, I13x, I15x
4) Diabetes
   a. **ICD-9:** 6480, 7751, 250x
   b. **ICD-10:** E10, E11, E13
5) Cardiac arrhythmia
   a. **ICD-9:** 42610, 42611, 42613, 4262, 4263, 4264, 42650, 42651, 42652, 42653, 4266, 4267, 42681, 42682, 42689, 4270, 4272, 42731, 42760, 4279, 7850, V450, V533
   b. **ICD-10:** I441, I442, I4430, I4439, I456, I459, ROOO, ROO1, ROO8, T821, Z450, Z951, I47x, I48x
6) Congestive heart failure
   a. **ICD-9:** 39891, 40201, 40211, 40291, 40401, 40403, 40411, 40413, 40491, 40493, 428x
   b. **ICD-10:** I099, I110, I130, I132, I255, I420, 1425, I427, I428, I429, P290, I43x, I50x
7) Osteoporosis
   a. **ICD-9:** 73300, 73301, 73302, 73303, 73309
   b. **ICD-10:** M810, M816, M818, M80x

2.2 Treatment Definition

We identified use of a study treatment from medical claims and prescription claims data using National Coverage Determination (NDC) codes, which are the unique codes that identify a drug product as defined by the National Drug Data File, and Current Procedural Terminology (CPT) / Healthcare Common Procedure

Coding System (HCPCS) codes, which describe the service provided. One treatment may have multiple names under which it is listed. Treatments are defined as follows:

1) Docetaxel
   a. Name: DOCETAXEL, TAXOTERE, DOCEFREZ, DOCEDAD
   b. NDC: 00069914111, 00069914122, 00069914211, 00069914222, 00069914411, 00409020102, 00409020110, 00409020120, 00409020125, 00409020126, 00409020127, 00703572001, 00703573001, 00955102001, 00955102104, 16714046501, 16714050001, 16729012049, 16729022850, 16729023163, 16729023164, 16729023165, 16729026763, 16729026764, 16729026765, 25021022201, 25021022204, 25021022207, 42367012121, 42367012125, 42367012129, 43598025811, 43598025940, 45963073452, 45963073454, 45963073474, 45963076552, 45963078174, 45963079056, 63739093211, 63739097117, 66758005001, 66758005002, 66758005003, 66758095002, 66758095003, 66758095004,00075800301, 00075800404
   c. HCPCS: J9170, J9171
2) Abiraterone
   a.   Name: ZYTIGA, ABIRATAS, ABRETONE, ABIRAPRO, ABIRATERONE ACETATE, ABIRATERONE
   b.   NDC: 57894015012
3) Enzalutamide
   a.   Name: XTANDI, ENZALUTAMIDE
   b.   NDC: 00469012599
4) Sipuleucel-T
   a.   Name: PROVENGE, APC8015, SIPULEUCEL T, SIPULEUCEL, SIPULEUCELT
   b.   NDC: 30237890006
   c.   HCPCS: Q2043, C9273
5) Cabazitaxel
   a.   Name: JEVTANA, CABAZITAXEL, XRP-6258, XRP6258
   b.   NDC: 00024582411, 00024582315, 00024582201
   c.   HCPCS: J9043
6) Radium-223
   a. Name: XOFIGO, RADIUM-223, RADIUM223, RADIUM RA223, RA223,RADIUM-RA223
   b. NDC: 50419020801
   c. HCPCS: A9606

2.3 Provider definition

We used DEA (Drug Enforcement Agency), NPI (National Provider Identifier), PROV (A unique system-generated number that identified the provider) and SERVICE_PROV (Rendering Provider on Non-Facility Claim Attending Provider on Facility Claim) codes to identify unique providers. There were 5,575 patients in the final cohort associated with first-line prescription records, among which 2,780 patients had their prescribing provider identified from pharmacy claims data and 2,795 patients had their prescribing provider identified from medical claims data. The variables linking prescribing providers from pharmacy claims are DEA and NPI numbers, and the variables linking prescribing providers from medical claims are SERVICE_PROV and PROV. We use DEA, NPI, PROV and SERVICE_PROV codes to identify unique providers of the first-line therapy. In summary, there are 19 patients for whom the providers prescribing their initial treatment cannot be identified. The algorithm for identifying providers is shown below. We use the term "record" to describe a unique patient in the below algorithm:

1) Pharmacy claims:
   a) For records with both NPI and DEA;
      1. Match on unique NPI and DEA;
      2. Among the remaining records, match unique NPI or unique DEA;
      3. Among the remaining records, combine partially identical columns;

b) For records with only NPI (85 records), match on unique NPI;

c) For records with only DEA (25 records), match on unique DEA;

2) Medical claim: match on unique SERVICE_PROV or PROV;

We used Prov_Unique, a unique system-generated number that identified the provider, to identify unique providers. The final cohort has 2,981 unique providers, among which 1,981 (65.4%) are medical oncologists, 298 (10.0%) are urologists, 32 (1.1%) are radiation oncologists, 679 (22.8%) are other providers, and 22 (0.7%) have unknown provider types.

2.4 Provider Specialty

We defined the provider specialty based on self-reported taxonomy. Medical oncologist taxonomy codes include: 207RH0000X, 207RH0003X, 207RX0202X, 2080P0207X; Urologist taxonomy codes include: 208800000X, 2088F0040X, 2088P0231X; Radiation oncologist taxonomy codes include: 2085R0001X. There were 69 taxonomies that identified other individuals that could not be assigned to either medical oncology, urology, or radiation oncology, including nurse practitioners, physician assistants, primary care providers, allopathic & osteopathic physicians from other specialties, dietary & nutritional service providers, emergency medical service providers, nursing service providers, and others. Taxonomies related to a facility category included hospitals, laboratories, agencies, and others (39 taxonomies in our analysis). There were also several taxonomies that could not be identified and thus we included those under unknown. Due to the large number of taxonomies included for other individuals, facilities, and unknown, we grouped them together into a final category of "Others." It is possible that some of these providers would have been categorized as a medical oncologist, urologist, or radiation oncologist, but it was essential to the analysis that we not misclassify a provider.

Explicitly, "other individuals" taxonomy codes in our analysis include: 207R00000X, 174400000X, 363A00000X, 363L00000X, 208800000X, 363AM0700X, 207P00000X, 208C00000X, 207Q00000X, 282N00000X, 363LA2200X, 207RA0201X, 207PE0004X, 363AS0400X, 2085R0203X, 163W00000X, 207L00000X, 363LF0000X, 152W00000X, 252Y00000X, 261QM0801X, 225100000X, 282NC0060X, 363LA2100X, 207RP1001X, 103T00000X, 146L00000X, 225700000X, 208D00000X, 133V00000X, 207RG0100X, 207Y00000X, 363LG0600X, 207LP2900X, 207VG0400X, 364S00000X, 2085R0202X, 390200000X, 207ZP0105X, 103G00000X, 367500000X, 2085N0904X, 207ZP0102X, 207RR0500X, 207XX0801X, 207V00000X, 101YM0800X, 207RS0012X, 207VM0101X, 2085R0001X, 208100000X, 207RG0300X, 207VX0201X, 208M00000X, 2080P0203X, 2084P0800X, 207RC0000X, 2085B0100X, 207T00000X, 225X00000X, 104100000X, 364SP0808X, 207QA0505X, 111N00000X, 208600000X, 171100000X, 2086S0127X, 1223G0001X, 207U00000X.

"Facility" taxonomy codes in our analysis include: 261Q00000X, 282N00000X, 3336S0011X, 302F00000X, 302R00000X, 282NR1301X, 273Y00000X, 261QE0700X, 261QM1300X, 282E00000X, 251F00000X, 332B00000X, 261QU0200X, 251G00000X, 291U00000X, 315D00000X, 282NC0060X, 333600000X, 273R00000X, 3336C0003X, 332900000X, 314000000X, 284300000X, 3416L0300X, 3416A0800X, 341600000X, 261QX0200X, 3336C0002X, 251E00000X, 282NC2000X, 3336I0012X, 261QR1300X, 261QA1903X, 261QA0600X, 332BX2000X, 283X00000X, 261QS1000X, 261QR0200X, 275N00000X.

The proportion details are shown in Figure 2 and in Supplementary Table 1, which show the association between provider type and the six treatments.

3.0 Building Treatment-Covariate Association Models

The main factors of interest included some categorical variables (race, education, income, region, insurance product, metastatic, ASO, year, comorbidities, provider type) and one more variable that we initially considered continuous (age). After our initial model building exploration, we chose to categorize age by 10 year increments. The age variable was used for adjustment (which we defined in four categories: <55, 55-64, 65-74, ≥75).

The first model is a polytomous/multinomial logistic model for the association between first-line treatment and 15 potential predictors. The response Y is docetaxel (Y=0), abiraterone or enzalutamide (Y=1), others (Y=2) and docetaxel is treated as the reference category. The model can be expressed in the following form:

$$\eta_j = \log\left(\frac{P(Y=j|x)}{P(Y=0|x)}\right) = \alpha_j + \beta_j^T x$$

$$= \alpha_j + \beta_{j1}Age + \beta_{j2}Race + \beta_{j3}Education + \beta_{j4}Income + \beta_{j5}Region + \beta_{j6}Product$$
$$+\beta_{j7}Met + \beta_{j8}ASO + \beta_{j9}Year + \beta_{j,10}Diabetes + \beta_{j,11}Hypertension$$
$$+\beta_{j,12}Arrhythmia + \beta_{j,13}CHF + \beta_{j,14}Osteoporosis + \beta_{j,15}Provider, j = 1,2$$

The second model is a dichotomous/binomial logistic model for the association between first-line drug prescription and 15 potential predictors. The response Z is abiraterone (Z=0) or enzalutamide (Z=1), and abiraterone is considered as the reference. The model is

$$\mu = \log\left(\frac{P(Z=1|x)}{P(Z=0|x)}\right) = \delta + \gamma^T x$$

$$= \delta + \gamma_1 Age + \gamma_2 Race + \gamma_3 Education + \gamma_4 Income + \gamma_5 Region + \gamma_6 Product$$
$$+\gamma_7 Met + \gamma_8 ASO + \gamma_9 Year + \gamma_{10}Diabetes + \gamma_{11}Hypertension$$
$$+\gamma_{12}Arrhythmia + \gamma_{13}CHF + \gamma_{14}Osteoporosis + \gamma_{15}Provider$$

We ran the first model by R package VGAM,[3] and the second model by R default package stats.

4.0 Missing Data

Missingness in covariates was handled using multiple imputation by chained equations (MICE).[4] Sensitivity analyses were carried out by comparing with a complete case data analysis, and by treating missing covariate data as a separate category, "unknown" for each variable. (Supplementary Tables 4 and 5)

Missingness patterns in the covariates used in our models are as follows. Out of the 2,696 observations from 2014 to mid-2016, 82.37% have no missing values, and this subset is used for our complete case analysis. Among these 557 subjects with partial missingness, 361 (13.39%) had one missing value, 23 (0.85%) had two missing values, 167 (6.19%) had three missing values, and 6 (0.22%) had four missing values. The missing values were present in five different variable categories: Geographic division (0.14% missing), provider type (3.97% missing), education level (6.64% missing), race (9.12% missing) and household income range (14.69% missing). To avoid discarding a large number of subjects who had missing data in at least one of the variables, we carried out multiple imputation by chained equations (MICE). We used the R package MICE with a polytomous logistic regression[4] to impute the 5 categorical variables conditional on others. Ten imputed datasets were created by MICE, each of which consisted of 2,696 observations.

We compared regression coefficients and their standard errors and associated confidence intervals corresponding to each covariate from post multiple imputation combined analysis (see below) and complete case analysis and noticed they are very similar in terms of the final inferential conclusion. We also compared the inferential results with "unknown" treated as a separate category for each variable, often a standard way to run models on a common set of subjects. The results are fairly robust across all three methods with multiple imputation being the most justifiable one with enhanced precision and narrower confidence intervals.

5.0 Combining Multiple Imputation Results

We imputed variables with missing data. To account for uncertainty in the values that were imputed, we created ten datasets generated post imputation. We then estimated the associations using each of the ten datasets, yielding ten sets of log odds ratio estimates corresponding to the multinomial/binomial logistic regression models described in Section 3.0. We combined these results using the well-known Rubin's rule[5] to produce a single overall estimate and accompanying confidence interval, which appropriately accounts for the variability in multiple imputations. Specifically, we applied the following formulas with D=10 imputations, and where U_m denotes the standard error associated with the log odds ratio estimate $\hat{\beta}_m$ in the m-th imputed dataset. M=1 …, 10.

The pooled estimate is given by $\bar{\beta} = \frac{1}{D}\sum_{m=1}^{D}\hat{\beta}_m$, and its variance estimate is given by $T = \bar{U} + \left(1 + \frac{1}{D}\right)B$, where $\bar{U} = \frac{1}{D}\sum_{m=1}^{D}U_m$, $B = \frac{1}{D-1}\sum_{m=1}^{D}\left(\hat{\beta}_m - \bar{\beta}\right)^2$. The 95% confidence interval is $\bar{\beta} \pm 1.96 \times \sqrt{T}$.

Though the exact test statistic and confidence interval using the pooled estimate and standard error has a t-distribution, in our analysis, as the sample size is over 2,000 and the number of covariates in each model is small, we approximate the t-confidence intervals by a z-confidence interval.

The resulting overall odds ratios and confidence intervals from applying these formulas are presented in Table 2 of the main text.

6.0 Geographic Variation

The geographic region for each patient was determined based on the patient's address. In member eligibility details for patients, OptumInsight provides census level regional division based on state.

Figure 3 was generated based on proportions of patients who received a treatment over the total number of patients in that region with prostate cancer during the timeframe of interest, 2014-mid-2016. The top panel shows the proportion of patients who received one of the six treatments as first-line therapy among all patients with prostate cancer during the years 2014 through mid-2016 in each region. The bottom left panel shows the difference of proportions between oral drug (abiraterone or enzalutamide) and docetaxel for first-line treatment among all patients with prostate cancer during the years 2014 through mid-2016 in each region. [(#patients receiving abiraterone or enzalutamide / total patients with prostate cancer) – (#patients receiving docetaxel / total patients with prostate cancer)] Therefore, the darker blue indicates more prescriptions for an oral therapy than docetaxel. The bottom right panel shows the difference of proportion between abiraterone and enzalutamide for first-line treatment among all patients with prostate cancer during the years 2014 through mid-2016 in each region. [(#patients receiving abiraterone / total patients with prostate cancer) – (#patients receiving enzalutamide / total patients with prostate cancer)] Therefore, the darker green indicates more prescriptions for abiraterone than enzalutamide. Patients with prostate cancer were defined as patients with at least one diagnostic code as a medical claim during the years 2014 and mid-2016. The results of this summary graphic mirror the results of the logistic regression analyses

7.0 Stability of the Cohort

Our cohort includes patients who are enrolled in an insurance plan through a private insurer that is linked to OptumInsight. The stability of the cohort is essential to the validity of this investigation. From our previous definition, 328,989 patients were identified as having at least one diagnosis of prostate cancer from 2010 to 2016. There were 3,891 (1.2%) patients who had continuous coverage (5,996 days) from 2001 to 2016. There were 39.0% patients who entered the cohort at an intermediate time point and were continuously enrolled until 2016. It is not rare that patients who entered the cohort at an intermediate time point dropped out before 2016. (36.7%), or left the cohort and then returned (23.1%). In the entire prostate cancer cohort, the average length of continuous coverage is 4.75 years. In the final treatment cohort, 5,575 patients who received the studied treatments had an average length of stay of 5.75 years.

It is important to note that in our final cohort (n=5,575), the majority of patients (81.2%) had no gap in coverage and were therefore continuously enrolled until censored. (Supplementary Table 8)

8.0 Tables and Figures

8.1 Supplementary Table 1. Characteristics of Available Treatments for Metastatic Castration-Resistant Prostate Cancer

Drug	Comparator	Survival Benefit (months)	Side Effect Risk	Infrastructure	Cost	Year of Approval
Docetaxel + prednisone[6]	Mitoxantrone + prednisone	2.5	+++	++	+	2004
Cabazitaxel + prednisone[7]	Mitoxantrone + prednisone	2.4	+++	++	+++	2010
Sipuleucel-T[8]	Placebo	4.1	+	+++	+++	2010
Abiraterone + prednisone[9-11]	Prednisone	4.6	+	+	++	2011
Enzalutamide[12]	Placebo	4.8	+	+	++	2012
Radium-223[13]	Placebo	3.6	++	++	+++	2013

Supplementary Table 1 Legend: Survival benefit is based on referenced studies. It is important to note that each study had a different treatment used in the comparator arm. None of the comparators have demonstrated an improvement in overall survival in metastatic castration-resistant prostate cancer. Docetaxel and cabazitaxel were tested against mitoxantrone, abiraterone was tested against single-agent prednisone, and enzalutamide, sipuleucel-T, and radium-223 were tested against a placebo. Ratings for side effect risk and infrastructure are the median results of a survey of five experts who treat patients with advanced prostate cancer at the University of Michigan. Cost is based on Average Wholesale Price; + is < $5,000 a month, ++ is $5,000-$10,000 a month, and +++ is > $10,000 a month.

8.2 Supplementary Table 2. (Complementary to Figure 1 from the text): Frequencies and Rates of Therapy Use from January 2010 through June 2016

First Treatment Used

	Docetaxel		Cabazitaxel		Sipuleucel-T		Radium-223		Enzalutamide		Abiraterone		Total	
2010	523	(96.5)	15	(2.8)	4	(0.7)	0	(0.0)	0	(0.0)	0	(0.0)	542	(100)
2011	392	(62.2)	13	(2.1)	62	(9.8)	0	(0.0)	0	(0.0)	163	(25.9)	630	(100)
2012	371	(49.0)	7	(0.9)	111	(14.7)	0	(0.0)	23	(3.0)	245	(32.4)	757	(100)
2013	200	(21.1)	4	(0.4)	105	(11.1)	3	(0.3)	85	(8.9)	553	(58.2)	950	(100)
2014	254	(24.0)	3	(0.3)	95	(9.0)	8	(0.8)	207	(19.6)	491	(46.4)	1,058	(100)
2015	313	(29.0)	3	(0.3)	79	(7.3)	29	(2.6)	275	(25.5)	380	(35.2)	1,079	(100)
2016*	161	(28.8)	5	(0.9)	48	(9.6)	20	(3.5)	157	(28.1)	168	(30.1)	559	(100)
Total	2,214	(39.7)	50	(0.9)	504	(9.0)	60	(1.1)	747	(13.4)	2,000	(35.9)	5,575	(100)

Total treatment Used

	Docetaxel		Cabazitaxel		Sipuleucel-T		Radium-223		Enzalutamide		Abiraterone		Total	
2010	620	(90.8)	59	(8.6)	4	(0.6)	0	(0.0)	0	(0.0)	0	(0.0)	683	(100)
2011	616	(54.5)	99	(8.8)	78	(6.9)	0	(0.0)	0	(0.0)	337	(29.8)	1,130	(100)
2012	699	(39.1)	134	(7.5)	148	(8.3)	0	(0.0)	171	(9.6)	638	(35.6)	1,790	(100)
2013	469	(20.4)	137	(6.0)	139	(6.0)	26	(1.1)	474	(20.6)	1,057	(45.9)	2,302	(100)
2014	555	(19.4)	115	(4.0)	159	(5.6)	29	(1.0)	814	(28.5)	1,187	(41.5)	2,859	(100)
2015	715	(20.7)	147	(4.3)	142	(4.1)	176	(5.1)	1,131	(32.7)	1,144	(33.1)	3,455	(100)
2016*	544	(19.5)	134	(4.8)	101	(3.6)	141	(5.1)	933	(33.5)	934	(33.5)	2,787	(100)
Total	4,218	(28.1)	825	(5.5)	771	(5.1)	372	(2.5)	3,523	(23.5)	5,297	(35.3)	15,006	(100)

*2016 only includes data through June.

Supplementary Figure 2 Legend: Frequencies of patients prescribed one of the six treatments as first-line treatment with proportions in parentheses. Patients are only included once in the top panel since they represent first treatment used. Frequencies of any time a treatment was started in the bottom panel each year. Thus, patients may be counted more than once since a patient could receive more than one treatment in a given year.

8.3 Supplementary Table 3. (Complementary to Figure 2 from the text): Provider Specialty for Providers Who Prescribed One of the Six Treatments as First-Line Therapy from January 2010 through June 2016

Provider specialty	Docetaxel		Cabazitaxel		Sipuleucel-T		Radium-223		Enzalutamide		Abiraterone		Total	
	Counts (row %)	(col %)	Counts (row %)	(col %)	Counts (row %)	(col %)	Counts (row %)	(col %)	Counts (row %)	(col %)	Counts (row %)	(col %)	Counts (row %)	(col %)
Medical oncologist	1,424 (39.6)	(64.3)	32 (0.9)	(64.0)	199 (5.5)	(39.5)	0 (0.0)	(0.0)	450 (12.5)	(60.2)	1,491 (41.5)	(74.6)	3,596 (100)	(64.5)
Urologist	4 (0.8)	(0.2)	0 (0.0)	(0.0)	167 (34.2)	(33.1)	0 (0.0)	(0.0)	156 (31.9)	(20.9)	153 (31.3)	(7.7)	489 (100)	(8.8)
Radiation oncologist	11 (22.0)	(0.5)	1 (2.0)	(2.0)	12 (24.0)	(2.4)	18 (36.0)	(30.0)	3 (6.0)	(0.4)	5 (10.0)	(0.3)	50 (100)	(0.9)
Others	775 (53.8)	(35)	17 (1.2)	(34.0)	126 (8.8)	(25.0)	42 (2.9)	(70.0)	167 (11.6)	(22.4)	351 (24.4)	(17.6)	1,440 (100)	(25.8)
Total	2,214 (39.7)	(100)	50 (0.9)	(100)	504 (9.0)	(100)	60 (1.1)	(100)	747 (13.4)	(100)	2,000 (35.9)	(100)	5,575 (100)	(100)

Supplementary Table 3 Legend: This table shows the counts and column/row proportions of the provider specialty that was associated with the prescription for each of the 5,575 patients who received a focus treatment from 2010 to mid-2016. The "row %" indicates the proportion of the treatment prescribed among all six treatments within that particular specialty, which corresponds to the left panel of Figure 2. The "col %" indicates the proportion of providers within a particular specialty who prescribed a particular treatment, which corresponds to the right panel of Figure 2.

8.4 Supplementary Table 4. (Continuation of Table 3 from the text): Multinomial Logistic Regression of First-Line Treatment Among Patients Treated January 2014 through June 2016

Variable	Others[α] (n=290) Count(%)	Unadjusted OR OR	Unadjusted OR 95% CI	Multivariable Analysis OR	Multivariable Analysis 95% CI
Age					
<55	4 (1.4)	1.00		1.00	
55-64	38 (13.1)	**3.54**	**(1.18,10.64)**	**3.64**	**(1.15,11.50)**
65-74	100 (34.5)	2.46	(0.86,7.10)	1.84	(0.59,5.70)
≥75	148 (51.0)	**5.31**	**(1.85,15.23)**	**3.64**	**(1.16,11.42)**
Race					
White	196 (67.6)	1.00		1.00	
Black	41 (14.1)	**1.52**	**(1.01,2.28)**	1.33	(0.82,2.16)
Asian	3 (1.0)	0.60	(0.16,2.28)	0.48	(0.11,2.03)
Hispanic	14 (4.8)	0.80	(0.45,1.43)	0.66	(0.34,1.29)
Unknown	36 (12.4)				
Education level					
Less than 12th Grade	3 (1.0)	1.00		1.00	
High School Diploma	71 (24.5)	0.27	(0.04,1.74)	0.19	(0.02,1.57)
Less than Bachelor Degree	142 (49.0)	0.29	(0.05,1.89)	0.21	(0.03,1.78)
Bachelor Degree Plus	41 (14.1)	0.29	(0.04,1.94)	0.27	(0.03,2.38)
Unknown	33 (11.4)				
Household income range					
< $50,000	85 (29.3)	1.00		1.00	
$50,000-$99,000	97 (33.4)	1.05	(0.73,1.51)	1.07	(0.69,1.67)
> $99,000	58 (20.0)	0.74	(0.51,1.08)	0.83	(0.49,1.40)
Unknown	50 (17.2)				
Geographic Region*					
South Atlantic	55 (19.0)	1.00		1.00	
New England	8 (2.8)	0.48	(0.21,1.08)	0.45	(0.19,1.05)
Middle Atlantic	29 (10.0)	1.01	(0.59,1.72)	0.62	(0.35,1.12)
East North Central	59 (20.3)	1.31	(0.84,2.04)	1.23	(0.75,2.01)
East South Central	16 (5.5)	1.48	(0.74,2.97)	1.02	(0.46,2.24)
West North Central	31 (10.7)	**0.58**	**(0.35,0.95)**	0.68	(0.38,1.21)
West South Central	30 (10.3)	1.14	(0.67,1.93)	1.45	(0.78,2.71)
Mountain	45 (15.5)	1.49	(0.92,2.41)	1.55	(0.87,2.77)
Pacific	17 (5.9)	0.74	(0.40,1.39)	1.36	(0.66,2.80)
Unknown	- (0.0)				
Product[π]					
HMO	60 (20.7)	1.00		1.00	
PPO	16 (5.5)	1.15	(0.61,2.18)	1.85	(0.86,3.99)
Other	214 (73.8)	**1.47**	**(1.06,2.05)**	**1.68**	**(1.09,2.57)**
Metastatic[€]					
Yes	256 (88.3)	1.00		1.00	
No	34 (11.7)	**0.61**	**(0.41,0.92)**	**0.33**	**(0.21,0.52)**
ASO					
No	256 (88.3)	1.00		1.00	
Yes	34 (11.7)	1.05	(0.68,1.60)	1.36	(0.81,2.28)
Year[∞]					
2014	106 (36.6)	1.00		1.00	
2015	111 (38.3)	0.85	(0.62,1.16)	0.76	(0.54,1.08)
2016	73 (25.2)	1.09	(0.76,1.55)	1.10	(0.74,1.65)
Comorbid Conditions[‡]					
Hypertension	225 (77.6)	**1.55**	**(1.13,2.13)**	1.27	(0.88,1.84)
Diabetes	93 (32.1)	**1.37**	**(1.01,1.84)**	**1.47**	**(1.04,2.07)**
Arrhythmia	62 (21.4)	0.97	(0.70,1.36)	0.71	(0.48,1.03)
CHF	34 (11.7)	**1.66**	**(1.05,2.61)**	1.61	(0.97,2.68)
Osteoporosis	49 (16.9)	**3.41**	**(2.19,5.29)**	**2.95**	**(1.81,4.79)**
Provider Type					
Medical oncologist	69 (23.8)	1.00		1.00	
Urologist	97 (33.4)	**95.61**	**(35.23,259.49)**	**109.70**	**(39.76,302.70)**
Others	118 (40.7)	**2.50**	**(1.80,3.48)**	**3.00**	**(2.11,4.27)**
Unknown	6 (2.1)				

Abbreviations: OR, Odds Ratio; CI, Confidence Interval; HMO, health maintenance organization; PPO, preferred provider organization; ASO, administrative services only (self-funded health plan); CHF, Congestive Heart Failure

Supplementary Table 4 Legend: This is continuation of Table 3 from the text. Multinomial Logistic Regression of first-line drugs among patients prescribed one of the three categories of treatments: oral (abiraterone or enzalutamide), docetaxel, or other (sipuleucel-T, radium-223, cabazitaxel) from 2014 to mid-2016. The regression results for abiraterone or enzalutamide versus docetaxel can be found in the text, Table 3.

[α]Others includes cabazitaxel, sipuleucel-T, and radium-223
*Geographic region:
- New England (NE): Connecticut (CT), Maine (ME), Massachusetts (MA), New Hampshire (NH), Rhode Island (RI), Vermont (VT)
- Middle Atlantic (MA): New Jersey (NJ), New York (NY), Pennsylvania (PA)
- East North Central (ENC): Illinois (IL), Indiana (IN), Michigan (MI), Ohio (OH), Wisconsin (WI)
- West North Central (WNC): Iowa (IA), Kansas (KS), Minnesota (MN), Missouri (MO), Nebraska (NE), North Dakota (ND), South Dakota (SD)
- South Atlantic (SA): Delaware (DE), Washington D.C. (DC), Florida (FL), Georgia (GA), Maryland (MD), North Carolina (NC), South Carolina (SC), Virginia (VA), West Virginia (WV)
- East South Central (ESC): Alabama (AL), Kentucky (KY), Mississippi (MS), Tennessee (TN)
- West South Central (WSC): Arkansas (AR), Louisiana (LA), Oklahoma (OK), and Texas (TX)
- Mountain (M): Arizona (AZ), Colorado (CO), Idaho (ID), Montana (MT), Nevada (NV), New Mexico (NM), Utah (UT), Wyoming (WY)
- Pacific (PAC): Alaska (AK), California (CA), Hawaii (HI), Oregon (OR), Washington (WA)

[π]The insurance product is the product they are enrolled in when their first treatment is prescribed. For those few patients who did not have a product at the time of their first prescription, their insurance product was designated as the plan prior to receipt of the treatment. [€]Patients were classified as metastatic if a medical claim with metastatic ICD-9 codes or ICD-10 codes were observed at any point during follow up.

[∞]Year indicates the year that the patient was started on the first-line therapy.

[‡]Patients were classified to have comorbid conditions if a medical claim with at least 2 corresponding ICD-9 codes or ICD-10 codes were observed at any point within the two years before first-line treatments. Details of the ICD codes are in Supplementary Materials, Section 2.1.

8.5 Supplementary Table 5. (Complementary to Table 3 from the text): Multinomial Logistic Regression of First-Line Treatment Among Patients Treated January 2014 through June 2016 ("unknowns" coded as categories)

| | Abiraterone or Enzalutamide vs Docetaxel | | | | Others[α] vs Docetaxel | | | |
| | Unadjusted OR | | Multivariable Analysis | | Unadjusted OR | | Multivariable Analysis | |
Variable	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
Age								
<55	1.00		1.00		1.00		1.00	
55-64	**2.14**	**(1.24,3.68)**	**2.15**	**(1.20,3.87)**	**3.54**	**(1.18,10.64)**	**3.89**	**(1.22,12.40)**
65-74	1.43	(0.87,2.37)	1.48	(0.84,2.60)	2.46	(0.86,7.10)	1.87	(0.60,5.86)
≥75	**4.71**	**(2.85,7.79)**	**4.25**	**(2.39,7.56)**	**5.31**	**(1.85,15.23)**	**3.71**	**(1.18,11.72)**
Race								
White	1.00		1.00		1.00		1.00	
Black	**1.42**	**(1.06,1.90)**	**1.49**	**(1.06,2.10)**	**1.53**	**(1.01,2.33)**	1.42	(0.87,2.33)
Asian	1.51	(0.81,2.84)	1.44	(0.71,2.91)	0.59	(0.17,2.11)	0.44	(0.11,1.75)
Hispanic	**1.46**	**(1.05,2.03)**	1.00	(0.68,1.47)	0.71	(0.38,1.31)	0.58	(0.28,1.17)
Unknown	0.60	(0.45,0.80)	1.03	(0.59,1.77)	1.03	(0.68,1.57)	0.49	(0.20,1.20)
Education level								
Less than 12th Grade	1.00		1.00		1.00		1.00	
High School Diploma	0.42	(0.09,1.87)	0.63	(0.12,3.17)	0.24	(0.04,1.45)	0.14	(0.02,1.02)
Less than Bachelor Degree	0.40	(0.09,1.79)	0.63	(0.13,3.18)	0.27	(0.04,1.61)	0.16	(0.02,1.22)
Bachelor Degree Plus	0.39	(0.09,1.79)	0.73	(0.14,3.77)	0.27	(0.04,1.68)	0.23	(0.03,1.78)
Unknown	0.19	(0.04,0.86)	0.37	(0.06,2.13)	0.32	(0.05,2.00)	0.70	(0.07,6.86)
Household income range								
< $50,000	1.00		1.00		1.00		1.00	
$50,000-$99,000	0.83	(0.66,1.03)	0.95	(0.73,1.24)	1.04	(0.73,1.48)	1.06	(0.71,1.59)
> $99,000	**0.50**	**(0.39,0.64)**	**0.66**	**(0.48,0.93)**	0.72	(0.49,1.06)	0.78	(0.46,1.30)
Unknown	**0.55**	**(0.42,0.72)**	0.79	(0.53,1.17)	0.91	(0.60,1.37)	0.60	(0.31,1.18)
Geographic Region*								
South Atlantic	1.00		1.00		1.00		1.00	
New England	0.87	(0.57,1.33)	1.07	(0.66,1.72)	0.48	(0.21,1.08)	0.45	(0.19,1.06)
Middle Atlantic	1.13	(0.80,1.59)	0.94	(0.64,1.38)	1.01	(0.59,1.72)	0.63	(0.35,1.12)
East North Central	1.13	(0.84,1.52)	1.09	(0.77,1.53)	1.31	(0.84,2.04)	1.24	(0.75,2.04)
East South Central	0.98	(0.60,1.62)	0.76	(0.44,1.34)	1.49	(0.74,2.97)	1.07	(0.49,2.34)
West North Central	**0.28**	**(0.20,0.39)**	**0.29**	**(0.20,0.43)**	**0.58**	**(0.35,0.95)**	0.68	(0.38,1.22)
West South Central	1.16	(0.82,1.64)	1.03	(0.69,1.54)	1.14	(0.67,1.94)	1.47	(0.79,2.74)
Mountain	1.22	(0.88,1.70)	1.08	(0.72,1.62)	1.49	(0.92,2.41)	1.53	(0.85,2.73)
Pacific	**2.61**	**(1.85,3.69)**	**2.80**	**(1.82,4.31)**	0.75	(0.40,1.40)	1.34	(0.65,2.75)
Unknown	0.46	(0.06,3.28)	0.45	(0.05,3.89)	-		-	
Product[π]								
HMO	1.00		1.00		1.00		1.00	
PPO	0.94	(0.65,1.38)	1.28	(0.79,2.09)	1.15	(0.61,2.18)	1.78	(0.82,3.87)
Other	**0.81**	**(0.67,0.98)**	1.00	(0.75,1.32)	**1.47**	**(1.06,2.05)**	**1.64**	**(1.07,2.52)**
Metastatic[∈]								
Yes	1.00		1.00		1.00		1.00	
No	1.18	(0.94,1.48)	0.86	(0.65,1.12)	**0.61**	**(0.41,0.92)**	**0.31**	**(0.20,0.51)**
ASO								
No	1.00		1.00		1.00		1.00	
Yes	1.13	(0.86,1.49)	**1.85**	**(1.33,2.59)**	1.05	(0.68,1.60)	1.45	(0.87,2.44)
Year[∞]								
2014	1.00		1.00		1.00		1.00	
2015	**0.76**	**(0.63,0.93)**	**0.79**	**(0.63,0.98)**	0.85	(0.62,1.16)	0.77	(0.55,1.08)
2016	**0.73**	**(0.58,0.93)**	0.78	(0.59,1.03)	1.09	(0.76,1.55)	1.09	(0.72,1.63)
Comorbid Conditions[‡]								
Hypertension	**1.25**	**(1.04,1.52)**	1.10	(0.87,1.39)	**1.55**	**(1.13,2.13)**	1.28	(0.89,1.86)
Diabetes	**1.27**	**(1.04,1.55)**	1.12	(0.89,1.41)	**1.37**	**(1.01,1.84)**	**1.46**	**(1.04,2.07)**
Arrhythmia	**1.26**	**(1.02,1.55)**	1.00	(0.78,1.28)	0.97	(0.70,1.36)	0.71	(0.49,1.04)
CHF	**2.12**	**(1.56,2.89)**	**1.67**	**(1.17,2.39)**	**1.66**	**(1.05,2.61)**	1.57	(0.94,2.61)
Osteoporosis	**1.57**	**(1.10,2.25)**	1.50	(1.00,2.23)	**3.41**	**(2.19,5.29)**	**3.14**	**(1.93,5.12)**
Provider Type								
Medical oncologist	1.00		1.00		1.00		1.00	
Urologist	48.84	(12.10,197.09)	47.34	(11.64,192.46)	293.11	(70.67,1215.68)	355.51	(84.75,1491.24)
Others	**0.30**	**(0.24,0.37)**	**0.33**	**(0.26,0.42)**	**2.59**	**(1.86,3.62)**	**3.10**	**(2.17,4.43)**
Unknown	0.73	(0.48,1.12)	**0.56**	**(0.35,0.89)**	1.07	(0.43,2.64)	1.17	(0.46,2.97)

Abbreviations: OR, Odds Ratio; CI, Confidence Interval; HMO, health maintenance organization; PPO, preferred provider organization; ASO, administrative services only (self-funded health plan); CHF, Congestive Heart Failure

Supplementary Table 5 Legend: (n=2,696) Multinomial Logistic Regression of first-line drugs among patients prescribed one of the three categories of treatments: oral (abiraterone or enzalutamide), docetaxel, or other (sipuleucel-T, radium-223, cabazitaxel) from 2014 to mid-2016. This table is complementary to Table 3 from the text and includes the regression results treating unknown variables as an unknown category. Docetaxel is the reference so is not included as a column. In addition, the "Total" number of patients column is not included as it is in Table 3 from the text. Odds ratios with confidence intervals that do not cross 0 are bolded.

αOther therapies include cabazitaxel, sipuleucel-T, and radium-223.
*Geographic region:
- New England (NE): Connecticut (CT), Maine (ME), Massachusetts (MA), New Hampshire (NH), Rhode Island (RI), Vermont (VT)
- Middle Atlantic (MA): New Jersey (NJ), New York (NY), Pennsylvania (PA)
- East North Central (ENC): Illinois (IL), Indiana (IN), Michigan (MI), Ohio (OH), Wisconsin (WI)
- West North Central (WNC): Iowa (IA), Kansas (KS), Minnesota (MN), Missouri (MO), Nebraska (NE), North Dakota (ND), South Dakota (SD)
- South Atlantic (SA): Delaware (DE), Washington D.C. (DC), Florida (FL), Georgia (GA), Maryland (MD), North Carolina (NC), South Carolina (SC), Virginia (VA), West Virginia (WV)
- East South Central (ESC): Alabama (AL), Kentucky (KY), Mississippi (MS), Tennessee (TN)
- West South Central (WSC): Arkansas (AR), Louisiana (LA), Oklahoma (OK), and Texas (TX)
- Mountain (M): Arizona (AZ), Colorado (CO), Idaho (ID), Montana (MT), Nevada (NV), New Mexico (NM), Utah (UT), Wyoming (WY)
- Pacific (PAC): Alaska (AK), California (CA), Hawaii (HI), Oregon (OR), Washington (WA)

πThe insurance product the product they are enrolled in when their first treatment is prescribed. For those few patients who did not have a product at the time of their first prescription, their insurance product was designated as the plan prior to receipt of the treatment.
€Patients were classified as metastatic if a medical claim with metastatic ICD-9 codes or ICD-10 codes were observed at any point during follow up.
∞Year indicates the year that the patient was started on the first-line therapy.
‡Patients in were classified to have comorbid conditions if a medical claim with at least 2 corresponding ICD-9 codes or ICD-10 codes were observed at any point within the two years before first-line treatments. Details of the ICD codes are in the Supplementary Materials, Section 2.1.

8.6 Supplementary Table 6. (Complementary to Table 3 from the text): Multinomial Logistic Regression of First-Line Treatment Among Patients Treated January 2014 through June 2016 (Complete case analysis with "unknowns" excluded)

Variable	Abiraterone or Enzalutamide vs Docetaxel				Others[α] vs Docetaxel			
	Unadjusted OR		Multivariable Analysis		Unadjusted OR		Multivariable Analysis	
	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
Age								
<55	1.00		1.00		1.00		1.00	
55-64	**2.16**	**(1.19,3.91)**	**2.09**	**(1.10,3.98)**	**4.23**	**(1.21,14.83)**	**4.60**	**(1.23,17.20)**
65-74	1.50	(0.87,2.60)	1.40	(0.75,2.61)	2.87	(0.85,9.68)	1.90	(0.52,6.99)
≥75	**5.28**	**(3.05,9.14)**	**4.16**	**(2.20,7.85)**	**6.58**	**(1.96,22.02)**	**4.03**	**(1.08,14.96)**
Race								
White	1.00		1.00		1.00		1.00	
Black	**1.40**	**(1.02,1.91)**	**1.45**	**(1.00,2.11)**	**1.64**	**(1.06,2.55)**	1.53	(0.90,2.59)
Asian	1.43	(0.76,2.68)	1.25	(0.61,2.56)	0.57	(0.16,2.03)	0.37	(0.09,1.49)
Hispanic	1.37	(0.95,1.97)	0.82	(0.54,1.27)	0.77	(0.40,1.46)	0.61	(0.29,1.29)
Unknown								
Education level								
Less than 12th Grade	1.00		1.00		1.00		1.00	
High School Diploma	0.55	(0.12,2.56)	0.79	(0.14,4.51)	0.38	(0.05,2.72)	0.24	(0.03,2.29)
Less than Bachelor Degree	0.54	(0.12,2.50)	0.81	(0.14,4.60)	0.43	(0.06,3.06)	0.30	(0.03,2.83)
Bachelor Degree Plus	0.55	(0.12,2.60)	0.98	(0.17,5.75)	0.48	(0.06,3.50)	0.52	(0.05,5.12)
Unknown								
Household income range								
< $50,000	1.00		1.00		1.00		1.00	
$50,000-$99,000	0.84	(0.67,1.07)	0.94	(0.71,1.25)	1.06	(0.74,1.52)	1.08	(0.71,1.64)
> $99,000	**0.49**	**(0.38,0.64)**	**0.63**	**(0.44,0.90)**	0.71	(0.48,1.06)	0.76	(0.44,1.31)
Unknown								
Geographic Region*								
South Atlantic	1.00		1.00		1.00		1.00	
New England	1.05	(0.64,1.73)	1.21	(0.69,2.12)	0.59	(0.24,1.45)	0.53	(0.20,1.38)
Middle Atlantic	1.18	(0.80,1.73)	1.04	(0.67,1.61)	1.10	(0.62,1.96)	0.65	(0.34,1.24)
East North Central	1.19	(0.85,1.67)	1.09	(0.74,1.60)	1.20	(0.73,1.97)	1.11	(0.63,1.96)
East South Central	0.97	(0.56,1.68)	0.79	(0.43,1.45)	1.34	(0.62,2.87)	1.01	(0.42,2.41)
West North Central	**0.28**	**(0.19,0.41)**	**0.31**	**(0.20,0.48)**	0.66	(0.39,1.11)	0.87	(0.46,1.62)
West South Central	1.40	(0.94,2.09)	1.34	(0.85,2.12)	1.06	(0.57,1.97)	1.48	(0.72,3.07)
Mountain	**1.59**	**(1.09,2.34)**	1.41	(0.89,2.23)	1.46	(0.83,2.55)	1.58	(0.81,3.08)
Pacific	**3.17**	**(2.10,4.80)**	**3.20**	**(1.93,5.30)**	0.70	(0.33,1.50)	1.36	(0.57,3.22)
Unknown								
Product[π]								
HMO	1.00		1.00		1.00		1.00	
PPO	0.79	(0.51,1.22)	1.13	(0.65,1.96)	1.25	(0.62,2.52)	2.18	(0.93,5.13)
Other	**0.76**	**(0.60,0.95)**	1.01	(0.73,1.39)	**1.48**	**(1.01,2.18)**	**1.86**	**(1.14,3.04)**
Metastatic[€]								
Yes	1.00		1.00		1.00		1.00	
No	1.14	(0.88,1.47)	0.85	(0.63,1.16)	**0.52**	**(0.33,0.84)**	**0.27**	**(0.16,0.47)**
ASO								
No	1.00		1.00		1.00		1.00	
Yes	0.93	(0.70,1.25)	**1.65**	**(1.15,2.37)**	0.80	(0.50,1.29)	1.09	(0.62,1.94)
Year[∞]								
2014	1.00		1.00		1.00		1.00	
2015	**0.72**	**(0.58,0.90)**	**0.71**	**(0.55,0.92)**	0.84	(0.59,1.20)	0.73	(0.49,1.08)
2016	**0.68**	**(0.52,0.90)**	**0.69**	**(0.50,0.94)**	1.03	(0.69,1.54)	1.05	(0.66,1.67)
Comorbid Conditions[‡]								
Hypertension	**1.33**	**(1.08,1.66)**	1.16	(0.89,1.51)	**1.67**	**(1.17,2.39)**	1.39	(0.91,2.12)
Diabetes	**1.34**	**(1.07,1.68)**	1.16	(0.89,1.51)	**1.48**	**(1.06,2.07)**	**1.66**	**(1.12,2.46)**
Arrhythmia	**1.32**	**(1.04,1.67)**	1.03	(0.78,1.38)	1.00	(0.69,1.45)	0.71	(0.46,1.10)
CHF	**2.22**	**(1.56,3.15)**	**1.70**	**(1.13,2.56)**	**1.71**	**(1.03,2.85)**	1.57	(0.88,2.80)
Osteoporosis	**1.85**	**(1.19,2.86)**	1.60	(0.99,2.61)	**4.35**	**(2.59,7.31)**	**3.72**	**(2.09,6.61)**
Provider Type								
Medical oncologist	1.00		1.00		1.00		1.00	
Urologist	38.54	(9.53,155.91)	36.47	(8.94,148.76)	255.11	(60.95,1067.79)	308.05	(72.61,1306.91)
Others	**0.32**	**(0.25,0.40)**	**0.37**	**(0.28,0.47)**	**2.78**	**(1.91,4.04)**	**3.50**	**(2.34,5.24)**
Unknown								

Abbreviations: OR, Odds Ratio; CI, Confidence Interval; HMO, health maintenance organization; PPO, preferred provider organization; ASO, administrative services only (self-funded health plan); CHF, Congestive Heart Failure

Supplementary Table 6 Legend: (n=2,139) This table includes the odds ratios for the multinomial regression that is complementary to Table 3 from the text and the Supplementary Table 4 above. Table 3 in the text shows results of the regression using data that went through multiple imputation, Supplementary Table 4 shows results of the regression using a dataset that coded "unknowns" as a separate category for each variable included and this Supplementary Table 6 shows results of the regression that excluded patients who had an unknown variable. Therefore, for this complete case analysis, we only include 2,139 patients, among which 1,354 used abiraterone or enzalutamide, 553 used docetaxel, and 232 used an "other" therapy. Of note, the reference for these odds ratios was patients receiving docetaxel as first-line. Odds ratios with confidence intervals that do not cross 0 are bolded.

α Other therapies include cabazitaxel, sipuleucel-T, and radium-223.
*Geographic region:
- New England (NE): Connecticut (CT), Maine (ME), Massachusetts (MA), New Hampshire (NH), Rhode Island (RI), Vermont (VT)
- Middle Atlantic (MA): New Jersey (NJ), New York (NY), Pennsylvania (PA)
- East North Central (ENC): Illinois (IL), Indiana (IN), Michigan (MI), Ohio (OH), Wisconsin (WI)
- West North Central (WNC): Iowa (IA), Kansas (KS), Minnesota (MN), Missouri (MO), Nebraska (NE), North Dakota (ND), South Dakota (SD)
- South Atlantic (SA): Delaware (DE), Washington D.C. (DC), Florida (FL), Georgia (GA), Maryland (MD), North Carolina (NC), South Carolina (SC), Virginia (VA), West Virginia (WV)
- East South Central (ESC): Alabama (AL), Kentucky (KY), Mississippi (MS), Tennessee (TN)
- West South Central (WSC): Arkansas (AR), Louisiana (LA), Oklahoma (OK), and Texas (TX)
- Mountain (M): Arizona (AZ), Colorado (CO), Idaho (ID), Montana (MT), Nevada (NV), New Mexico (NM), Utah (UT), Wyoming (WY)
- Pacific (PAC): Alaska (AK), California (CA), Hawaii (HI), Oregon (OR), Washington (WA)

π The insurance product is the product they are enrolled in when their first treatment is prescribed. For those few patients who did not have a product at the time of their first prescription, their insurance product was designated as the plan prior to receipt of the treatment.
€ Patients were classified as metastatic if a medical claim with metastatic ICD-9 codes or ICD-10 codes were observed at any point during follow up.
∞ Year indicates the year that the patient was started on the first-line therapy.
‡ Patients were classified to have comorbid conditions if a medical claim with at least 2 corresponding ICD-9 codes or ICD-10 codes were observed at any point within the two years before first-line treatments. Details of the ICD codes are in Supplementary Materials, Section 2.1.

8.7 Supplementary Table 7. Logistic Regression of Abiraterone Versus Enzalutamide Among Patients Prescribed an Oral Therapy First-Line January 2014 through June 2016 (MICE imputed)

Variable	Abiraterone or Enzalutamide (n=1,678) Mean range / Count(%)		Abiraterone (n=1,039) Mean range / Count(%)		Enzalutamide (n=639) Mean range / Count(%)		P-value	Enzalutamide vs Abiraterone Unadjusted OR OR	95% CI	Multivariable Analysis OR	95% CI
Age							0.102				
<55	31	(1.8)	10	(1.6)	21	(2.0)		1.00		1.00	
55-64	178	(10.6)	54	(8.5)	124	(11.9)		0.91	(0.40,2.07)	0.94	(0.40,2.19)
65-74	451	(26.9)	171	(26.8)	280	(26.9)		1.28	(0.59,2.79)	1.19	(0.52,2.70)
≥75	1,018	(60.7)	404	(63.2)	614	(59.1)		1.38	(0.64,2.96)	1.25	(0.55,2.82)
Race							0.637				
White	1,129	(67.3)	428	(67.0)	701	(67.5)		1.00		1.00	
Black	219	(13.1)	90	(14.1)	129	(12.4)		1.18	(0.88,1.59)	1.11	(0.80,1.55)
Asian	44	(2.6)	18	(2.8)	26	(2.5)		1.12	(0.61,2.04)	1.03	(0.54,1.96)
Hispanic	166	(9.9)	58	(9.1)	108	(10.4)		0.89	(0.63,1.24)	0.85	(0.58,1.24)
Unknown	120	(7.2)	45	(7.0)	75	(7.2)					
Education level							0.583				
Less than 12th Grade	12	(0.7)	5	(0.8)	7	(0.7)		1.00		1.00	
High School Diploma	499	(29.7)	177	(27.7)	322	(31.0)		0.71	(0.22,2.29)	0.62	(0.19,2.08)
Less than Bachelor Degree	851	(50.7)	330	(51.6)	521	(50.1)		0.82	(0.26,2.57)	0.74	(0.22,2.45)
Bachelor Degree Plus	239	(14.2)	95	(14.9)	144	(13.9)		0.84	(0.26,2.75)	0.83	(0.24,2.88)
Unknown	77	(4.6)	32	(5.0)	45	(4.3)					
Household income range							0.061				
< $50,000	613	(36.5)	223	(34.9)	390	(37.5)		1.00		1.00	
$50,000-$99,000	555	(33.1)	229	(35.8)	326	(31.4)		1.25	(1.00,1.56)	1.17	(0.91,1.51)
> $99,000	292	(17.4)	98	(15.3)	194	(18.7)		0.91	(0.67,1.24)	0.90	(0.60,1.36)
Unknown	218	(13.0)	89	(13.9)	129	(12.4)					
Geographic Region*							0.015				
South Atlantic	302	(18.0)	121	(18.9)	181	(17.4)		1.00		1.00	
New England	80	(4.8)	27	(4.2)	53	(5.1)		0.77	(0.46,1.28)	0.73	(0.42,1.25)
Middle Atlantic	178	(10.6)	88	(13.8)	90	(8.7)		**1.47**	**(1.01,2.13)**	1.40	(0.94,2.10)
East North Central	279	(16.6)	110	(17.2)	169	(16.3)		0.98	(0.70,1.36)	0.91	(0.63,1.31)
East South Central	58	(3.5)	20	(3.1)	38	(3.7)		0.79	(0.44,1.42)	0.73	(0.39,1.37)
West North Central	83	(4.9)	22	(3.4)	61	(5.9)		**0.54**	**(0.32,0.93)**	**0.51**	**(0.29,0.90)**
West South Central	167	(10.0)	61	(9.5)	106	(10.2)		0.86	(0.58,1.27)	0.84	(0.54,1.31)
Mountain	203	(12.1)	80	(12.5)	123	(11.8)		0.97	(0.68,1.40)	0.90	(0.58,1.40)
Pacific	326	(19.4)	110	(17.2)	216	(20.8)		0.76	(0.55,1.06)	0.81	(0.53,1.26)
Unknown	2	(0.1)	-	(0.0)	2	(0.2)					
Productπ							0.033				
HMO	527	(31.4)	186	(29.1)	341	(32.8)		1.00		1.00	
PPO	115	(6.9)	35	(5.5)	80	(7.7)		0.80	(0.52,1.24)	0.65	(0.38,1.11)
Other	1,036	(61.7)	418	(65.4)	618	(59.5)		1.24	(1.00,1.54)	1.22	(0.88,1.69)
Metastatic€							0.013				
Yes	1,335	(79.6)	488	(76.4)	847	(81.5)		1.00		1.00	
No	343	(20.4)	151	(23.6)	192	(18.5)		**1.37**	**(1.07,1.74)**	1.06	(0.81,1.39)
ASO							0.462				
No	1,467	(87.4)	564	(88.3)	903	(86.9)		1.00		1.00	
Yes	211	(12.6)	75	(11.7)	136	(13.1)		0.88	(0.65,1.19)	1.00	(0.71,1.43)
Year∞							**<0.001**				
2014	698	(41.6)	207	(32.4)	491	(47.3)		1.00		1.00	
2015	655	(39.0)	275	(43.0)	380	(36.6)		**1.72**	**(1.37,2.15)**	**1.66**	**(1.31,2.11)**
2016	325	(19.4)	157	(24.6)	168	(16.2)		**2.22**	**(1.69,2.91)**	**2.01**	**(1.50,2.68)**
Comorbid Conditions‡											
Hypertension	1,237	(73.7)	483	(75.6)	754	(72.6)	0.191	1.17	(0.93,1.47)	0.95	(0.74,1.23)
Diabetes	512	(30.5)	213	(33.3)	299	(28.8)	0.055	1.24	(1.00,1.53)	1.19	(0.94,1.51)
Arrhythmia	437	(26.0)	171	(26.8)	266	(25.6)	0.640	1.06	(0.85,1.33)	0.90	(0.70,1.16)
CHF	244	(14.5)	107	(16.7)	137	(13.2)	0.053	**1.32**	**(1.01,1.74)**	1.28	(0.94,1.74)
Osteoporosis	144	(8.6)	63	(9.9)	81	(7.8)	0.169	1.29	(0.92,1.83)	1.19	(0.83,1.72)
Provider Type							**<0.001**				
Medical oncologist	1,127	(67.2)	371	(58.1)	756	(72.8)		1.00		1.00	
Urologist	264	(15.7)	158	(24.7)	106	(10.2)		**2.93**	**(2.23,3.85)**	**2.64**	**(1.97,3.52)**
Others	220	(13.1)	87	(13.6)	133	(12.8)		1.31	(0.97,1.77)	1.23	(0.90,1.68)
Unknown	67	(4.0)	23	(3.6)	44	(4.2)					

Abbreviations: OR, Odds Ratio; CI, Confidence Interval; HMO, health maintenance organization; PPO, preferred provider organization; ASO, administrative services only (self-funded health plan); CHF, Congestive Heart Failure

Supplementary Table 7 Legend: This table shows results of a bivariate logistic regression that models the odds of a patient receiving enzalutamide versus abiraterone (reference) based on different covariates. This Supplementary Table 7 uses a dataset for which multiple imputation (MICE) was used when a patient had a missing or unknown variable. Odds ratios with confidence intervals that do not cross 0 are bolded.

*Geographic region:
- New England (NE): Connecticut (CT), Maine (ME), Massachusetts (MA), New Hampshire (NH), Rhode Island (RI), Vermont (VT)
- Middle Atlantic (MA): New Jersey (NJ), New York (NY), Pennsylvania (PA)
- East North Central (ENC): Illinois (IL), Indiana (IN), Michigan (MI), Ohio (OH), Wisconsin (WI)
- West North Central (WNC): Iowa (IA), Kansas (KS), Minnesota (MN), Missouri (MO), Nebraska (NE), North Dakota (ND), South Dakota (SD)
- South Atlantic (SA): Delaware (DE), Washington D.C. (DC), Florida (FL), Georgia (GA), Maryland (MD), North Carolina (NC), South Carolina (SC), Virginia (VA), West Virginia (WV)
- East South Central (ESC): Alabama (AL), Kentucky (KY), Mississippi (MS), Tennessee (TN)
- West South Central (WSC): Arkansas (AR), Louisiana (LA), Oklahoma (OK), and Texas (TX)
- Mountain (M): Arizona (AZ), Colorado (CO), Idaho (ID), Montana (MT), Nevada (NV), New Mexico (NM), Utah (UT), Wyoming (WY)
- Pacific (PAC): Alaska (AK), California (CA), Hawaii (HI), Oregon (OR), Washington (WA)

πThe insurance product is the product they are enrolled in when their first treatment is prescribed. For those few patients who did not have a product at the time of their first prescription, their insurance product was designated as the plan prior to receipt of the treatment.

€Patients were classified as metastatic if a medical claim with metastatic ICD-9 codes or ICD-10 codes were observed at any point during follow up.

∞Year indicates the year that the patient was started on the first-line therapy

‡Patients were classified to have comorbid conditions if a medical claim with at least 2 corresponding ICD-9 codes or ICD-10 codes were observed at any point within the two years before first-line treatments. Details of the ICD codes are in the Supplementary Materials, Section 2.1.

8.8 Supplementary Table 8. (Complimentary to Supplementary Table 7) Logistic Regression of Abiraterone Versus Enzalutamide Among Patients Prescribed an Oral Therapy First-Line January 2014 through June 2016 ("Unknowns" coded as a category; complete case analysis with "unknowns" excluded)

	"unknowns" coded as a category (n=1,678)				Complete case analysis (n=1,354)			
	Unadjusted OR		Multivariable Analysis		Unadjusted OR		Multivariable Analysis	
Variable	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
Age								
<55	1.00		1.00		1.00		1.00	
55-64	0.91	(0.41,2.15)	0.93	(0.41,2.26)	0.84	(0.36,2.11)	0.87	(0.35,2.23)
65-74	1.28	(0.60,2.90)	1.18	(0.53,2.78)	1.14	(0.50,2.75)	1.08	(0.46,2.71)
≥75	1.38	(0.66,3.09)	1.25	(0.56,2.92)	1.24	(0.56,2.93)	1.18	(0.50,2.95)
Race								
White	1.00		1.00		1.00		1.00	
Black	1.14	(0.85,1.53)	1.10	(0.79,1.52)	1.10	(0.80,1.51)	1.05	(0.73,1.50)
Asian	1.13	(0.61,2.08)	1.05	(0.54,2.00)	1.23	(0.65,2.30)	1.15	(0.58,2.23)
Hispanic	0.88	(0.62,1.23)	0.84	(0.57,1.23)	0.90	(0.61,1.31)	0.89	(0.58,1.36)
Unknown	0.98	(0.66,1.44)	0.69	(0.36,1.25)				
Education level								
Less than 12th Grade	1.00		1.00		1.00		1.00	
High School Diploma	0.77	(0.24,2.63)	0.67	(0.20,2.44)	0.69	(0.18,2.84)	0.62	(0.15,2.69)
Less than Bachelor Degree	0.89	(0.28,3.02)	0.82	(0.24,2.97)	0.80	(0.21,3.27)	0.76	(0.18,3.30)
Bachelor Degree Plus	0.92	(0.29,3.20)	0.93	(0.27,3.48)	0.80	(0.20,3.30)	0.84	(0.20,3.75)
Unknown	1.00	(0.29,3.63)	1.12	(0.26,5.03)				
Household income range								
< $50,000	1.00		1.00		1.00		1.00	
$50,000-$99,000	1.23	(0.97,1.56)	1.15	(0.89,1.50)	1.19	(0.94,1.53)	1.11	(0.85,1.46)
> $99,000	0.88	(0.66,1.18)	0.86	(0.60,1.24)	0.93	(0.69,1.26)	0.91	(0.62,1.33)
Unknown	1.21	(0.88,1.65)	1.16	(0.77,1.74)				
Geographic Region*								
South Atlantic	1.00		1.00		1.00		1.00	
New England	0.76	(0.45,1.27)	0.73	(0.42,1.25)	0.73	(0.40,1.30)	0.68	(0.37,1.23)
Middle Atlantic	1.46	(1.01,2.13)	1.43	(0.96,2.13)	1.33	(0.87,2.02)	1.24	(0.80,1.95)
East North Central	0.97	(0.70,1.36)	0.91	(0.63,1.31)	0.91	(0.62,1.31)	0.86	(0.58,1.30)
East South Central	0.79	(0.43,1.40)	0.73	(0.38,1.36)	0.75	(0.39,1.41)	0.74	(0.37,1.45)
West North Central	**0.54**	**(0.31,0.91)**	**0.51**	**(0.28,0.90)**	**0.45**	**(0.24,0.82)**	**0.43**	**(0.22,0.81)**
West South Central	0.86	(0.58,1.27)	0.85	(0.54,1.32)	0.75	(0.48,1.15)	0.72	(0.44,1.16)
Mountain	0.97	(0.68,1.40)	0.89	(0.58,1.39)	0.82	(0.55,1.23)	0.72	(0.44,1.16)
Pacific	0.76	(0.55,1.05)	0.81	(0.52,1.25)	0.66	(0.45,0.95)	0.64	(0.39,1.04)
Unknown								
Product^π								
HMO	1.00		1.00		1.00		1.00	
PPO	0.80	(0.51,1.23)	0.65	(0.38,1.11)	0.94	(0.56,1.52)	0.68	(0.37,1.24)
Other	1.24	(1.00,1.54)	1.21	(0.87,1.68)	**1.29**	**(1.01,1.64)**	1.14	(0.80,1.64)
Metastatic^€								
Yes	1.00		1.00		1.00		1.00	
No	**1.37**	**(1.07,1.74)**	1.05	(0.80,1.38)	**1.35**	**(1.03,1.76)**	1.07	(0.79,1.44)
ASO								
No	1.00		1.00		1.00		1.00	
Yes	0.88	(0.65,1.19)	1.03	(0.72,1.46)	0.95	(0.68,1.32)	1.10	(0.74,1.61)
Year^∞								
2014	1.00		1.00		1.00		1.00	
2015	**1.72**	**(1.37,2.15)**	**1.66**	**(1.32,2.11)**	**1.65**	**(1.29,2.12)**	**1.64**	**(1.26,2.13)**
2016	**2.22**	**(1.69,2.91)**	**2.04**	**(1.53,2.73)**	**2.12**	**(1.57,2.86)**	**1.95**	**(1.41,2.69)**
Comorbid Conditions^‡								
Hypertension	1.17	(0.93,1.47)	0.94	(0.73,1.22)	1.09	(0.85,1.40)	0.89	(0.67,1.18)
Diabetes	1.24	(1.00,1.53)	1.20	(0.95,1.51)	1.23	(0.97,1.56)	1.15	(0.89,1.49)
Arrhythmia	1.06	(0.85,1.33)	0.9	(0.69,1.15)	1.02	(0.80,1.31)	0.86	(0.65,1.14)
CHF	1.32	(1.00,1.74)	1.29	(0.94,1.76)	1.28	(0.95,1.74)	1.27	(0.90,1.78)
Osteoporosis	1.29	(0.91,1.82)	1.21	(0.84,1.74)	1.43	(0.97,2.11)	1.32	(0.88,1.98)
Provider Type								
Medical oncologist	1.00		1.00		1.00		1.00	
Urologist	**3.04**	**(2.31,4.01)**	**2.72**	**(2.04,3.65)**	**2.66**	**(1.97,3.60)**	**2.43**	**(1.77,3.34)**
Others	1.33	(0.99,1.79)	1.26	(0.92,1.71)	1.29	(0.93,1.77)	1.20	(0.86,1.67)
Unknown	1.07	(0.62,1.77)	1.06	(0.61,1.81)				

Abbreviations: OR, Odds Ratio; CI, Confidence Interval; HMO, health maintenance organization; PPO, preferred provider organization; ASO, administrative services only (self-funded health plan); CHF, Congestive Heart Failure

Supplementary Table 8 Legend: This table is complementary to Supplementary Table 7 and shows results of a bivariate logistic regression that models the odds of a patient receiving enzalutamide versus abiraterone (reference) based on different covariates. The first analysis on the left side of this Table shows the results of the regression that codes unknown variables as a separate category. The second analysis on the right side of the Table shows results of the regression that is a complete case analysis that excludes observations for which there are variables with unknown values. Odds ratios with confidence intervals that do not cross 0 are bolded.

*Geographic region:
- New England (NE): Connecticut (CT), Maine (ME), Massachusetts (MA), New Hampshire (NH), Rhode Island (RI), Vermont (VT)
- Middle Atlantic (MA): New Jersey (NJ), New York (NY), Pennsylvania (PA)
- East North Central (ENC): Illinois (IL), Indiana (IN), Michigan (MI), Ohio (OH), Wisconsin (WI)
- West North Central (WNC): Iowa (IA), Kansas (KS), Minnesota (MN), Missouri (MO), Nebraska (NE), North Dakota (ND), South Dakota (SD)
- South Atlantic (SA): Delaware (DE), Washington D.C. (DC), Florida (FL), Georgia (GA), Maryland (MD), North Carolina (NC), South Carolina (SC), Virginia (VA), West Virginia (WV)
- East South Central (ESC): Alabama (AL), Kentucky (KY), Mississippi (MS), Tennessee (TN)
- West South Central (WSC): Arkansas (AR), Louisiana (LA), Oklahoma (OK), and Texas (TX)
- Mountain (M): Arizona (AZ), Colorado (CO), Idaho (ID), Montana (MT), Nevada (NV), New Mexico (NM), Utah (UT), Wyoming (WY)
- Pacific (PAC): Alaska (AK), California (CA), Hawaii (HI), Oregon (OR), Washington (WA)

πThe insurance product is the product they are enrolled in when their first treatment is prescribed. For those few patients who did not have a product at the time of their first prescription, their insurance product was designated as the plan prior to receipt of the treatment.

€Patients were classified as metastatic if a medical claim with metastatic ICD-9 codes or ICD-10 codes were observed at any point during follow up.

∞Year indicates the year that the patient was started on the first-line therapy

‡Patients were classified to have comorbid conditions if a medical claim with at least 2 corresponding ICD-9 codes or ICD-10 codes were observed at any point within the two years before first-line treatments. Details of the ICD codes are in the Supplementary Materials, Section 2.1.

8.9 Supplementary Table 9. Stability of Cohort Summary Statistics

Variables	Total (N=328,989; 2010-2016) Median/mean [min,max] / count(%)		Final Cohort (n=5,575; 2010-2016) Median/mean [min,max] / count(%)	
Length of stay (years)*	4.75	[0.1,16.4]	5.75	[0.6,16.4]
Number of gaps				
0	258,050	(78.4)	4,528	(81.2)
1	59,755	(18.2)	905	(16.2)
2	9,603	(2.9)	130	(2.3)
3	1,319	(0.4)	10	(0.2)
4	208	(0.1)	2	(0.0)
>4	54	(0.0)	0	(0.0)
Mean number of gaps**	1.18	[1,8]	1.14	[1,4]
Median length of gap (days)	1105	[28,5510]	857.4	[28,4810]

*median length of stay
**mean number of gaps among patients who have at least one gap. Patients with at least one gap in the total Cohort n=70,939 (21.6%); patients with at least one gap in the Final Cohort n=1,047 (18.8%).

Supplementary Table 9 Legend: This table shows the summary statistics of enrollment in insurance plan from 2001 to 2016 for patients in total and final cohort. Length of stay is the total years a patient is enrolled in the insurance plan. Number of gaps is the frequency of changing insurance plans of a patient. A gap is defined as being disenrolled for more than 30 days.

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