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

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Abstract

Purpose: Six treatments have improved overall survival in men with metastatic castration-resistant prostate cancer (mCRPC), each differing in toxicities and cost. This study identified patient and provider factors associated with variation in treatment of men with mCRPC to identify potential barriers to treatments.

Methods: A claims database of commercially insured patients was used to identify patients with prostate cancer treated with abiraterone, enzalutamide, docetaxel, cabazitaxel, sipuleucel-T, or radium-223 between 2010 and 2016. Multinomial and binomial logistic regressions were conducted to determine patient and provider factors associated with treatment patterns.

Results: Among 5,575 patients identified, patients with a household income >$99,000 were less likely to receive an expensive oral androgen signaling inhibitor (abiraterone or enzalutamide) as first-line treatment versus docetaxel compared to patients with a household income <$50,000 (odds ratio, OR, 0.66, 95% confidence interval, CI, 0.48–0.92). Patients who are Black (OR 1.43, 95% CI 1.02–2.01), live in the Pacific region versus the South Atlantic (OR 2.68, 95% CI 1.74–4.11), received treatment from a urologist versus a medical oncologist (OR 16.05, 95% CI 6.01–42.86), or had pre-existing heart failure (OR 1.69, 95% CI 1.18–2.42) were more likely to receive

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first-line oral androgen signaling inhibitors over docetaxel, independent of other factors on multivariable analysis.

Conclusion: Clinicians and policy makers should be aware of the potential barriers and provider factors that influence use of novel therapies among patients with advanced prostate cancer, including the paradoxical effect of income and the substantial effect of provider specialty on first-line treatment rendered to patients with mCRPC.

Keywords

prostate cancer; novel agents; variation; care delivery; claims data

Introduction

Several treatments have demonstrated an improvement in overall survival for men with metastatic castration-resistant prostate cancer (mCRPC). Since docetaxel was approved by the Food and Drug Administration (FDA) in 2004,[1] five more therapies have demonstrated a survival benefit and are FDA-approved to treat mCRPC,[2–8] each unique with respect to administration, cost, and side effects. Docetaxel and cabazitaxel are intravenous chemotherapies, each associated with neuropathy, fatigue, and the potential for life-threatening myelosuppression. Abiraterone and enzalutamide are secondary oral androgen signaling inhibitors with fewer and less life-threatening side effects such as hypertension and hypokalemia for abiraterone and fatigue for enzalutamide, but higher potential out-of-pocket costs. Radium-223 and sipuleucel-T are relatively well-tolerated but require specialized infrastructure for treatment delivery (nuclear medicine for radium-223 and a pheresis center for sipuleucel-T). Guidelines from specialty societies, the American Society of Clinical Oncology and the American Urologic Association, recommend starting with abiraterone or enzalutamide in treatment-naïve mCRPC.[9,10] Beyond first-line treatment, sipuleucel-T can be considered in patients with minimal to no symptoms, radium-223 in patients with symptomatic bone-only metastatic disease, and docetaxel and cabazitaxel reserved for patients with a good performance status. However, despite these recommendations, there is still tremendous room for uncertainty and variation at the hands of the treating provider and little is known about optimal treatment sequences and whether providers are prescribing treatments concordant with guidelines. Supplementary Table 1 describes key factors that may affect prescribing patterns.

Considering that some of these treatments were approved before others, their use will vary over time as additional treatments enter the market, as we have demonstrated in previous work.[11,12] There will also be warranted variation in treatment according to a patient's site of disease (e.g. radium-223 used for patients with bone-only metastases), symptoms (e.g. sipuleucel-T for asymptomatic patients), and preference. However, there is still a potential for significant unwarranted variation due to non-clinical patient and physician factors, such as race, income, and place of residence, similar to other conditions.[13–18]

In this context, we sought to evaluate variation in prescription patterns at the level of the patient, provider, and region. We hypothesized that nonclinical patient factors such as race and income would affect receipt of expensive oral androgen signaling inhibitors (abiraterone

or enzalutamide) versus a less expensive but more toxic therapy (docetaxel) as first-line treatment. We also expected to find geographic variability, and substantial variation in use of these treatments depending on whether a patient was treated by a urologist or a medical oncologist.

Materials and Methods

Data Source and Sample Selection

We used the Clinformatics TM Data Mart Database (OptumInsight, Eden Prairie, Minnesota) to identify a cohort of men over the age of 18 with prostate cancer. This database includes patients who are insured through a national private commercial payer and is representative of privately insured patients with prostate cancer in the general US population by age, and socioeconomic variables.[19] We further restricted our study cohort to include patients with prostate cancer who received at least one of the six focus treatments (abiraterone, enzalutamide, sipuleucel-T, docetaxel, cabazitaxel, radium-223) between January 2010 and June 2016 and were enrolled continuously for 180 days before the first focus treatment claim.

We identified prescription records of the six focus treatments by national drug codes, brand names, and Healthcare Common Procedure Coding System codes and matched to respective fields within the medical claims and pharmacy claims data. (Supplementary Materials 2.1–2.2.)

Patient and Provider Variables

Sociodemographic variables were derived from a demographic-based analytical model using a major data syndicator, Knowledge-Based Marketing Solutions (KBM, Richardson, TX). Pre-existing comorbid diseases known to affect treatment decisions and common to patients with advanced prostate cancer (i.e. diabetes, hypertension, cardiac arrhythmias, congestive heart failure, and osteoporosis) were assessed for each patient (Supplementary Materials 2.1).

The specialty of provider who prescribed patients their first-line treatment was determined by self-reported taxonomy and categorized as medical oncologist, urologist, radiation oncologist, or other (Supplementary Materials 2.3–2.4).

Outcomes

The first objective was to identify the temporal pattern of first-line treatment choices from January 2010 through June 2016. First-line treatment was defined as the first focus treatment for a patient during the study period with no receipt of any other focus treatments during the preceding 12 months. Our second objective was to determine the association of patient sociodemographic and provider variables with first-line treatments. To minimize the effect of market availability and insurance coverage on use of treatments, we restricted our analysis to January 2014 through June 2016 since the last of the six focus treatments (radium-223) was FDA-approved in 2013 (Supplementary Materials 2.2).

Statistical Analysis

Patients were classified into one of the three categories of treatment prescribed as first-line: oral therapy (abiraterone or enzalutamide), docetaxel, or other treatment (sipuleucel-T, radium-223, cabazitaxel) during the timeframe January 2014 through June 2016. Using overall χ^2 tests for independence and unadjusted odds ratios (ORs) from a simple multinomial logistic regression (with three categories), patients across treatment categories were compared. Among those patients who received an oral therapy first-line during that same 30-month time period, patients who received abiraterone versus enzalutamide were compared using a simple binomial logistic regression model. We then used corresponding multivariable multinomial and binomial logistic regression models to analyze the adjusted associations between first-line treatment and patient and provider characteristics.

Missing data was assumed to be missing at random. Supplementary Materials 3.0–6.0 detail methods used to handle missing, sensitivity analyses, and the stability of the cohort.

Results

Table 1 demonstrates the characteristics of patients with prostate cancer and the characteristics of those in the final cohort (n=5,575) who received one of the six focus treatments.

Figure 1 illustrates the frequencies and proportions of the different treatments used over time with the top panel demonstrating an increasing total number of patients treated each year as newer agents came onto the market. The number of patients in the cohort was relatively similar each year (Table 1), so the increased number of treated patients cannot be explained by an increasing insured cohort. The number of patients treated with first-line docetaxel declined initially, but then stayed relatively stable while the use of other therapies increased, indicating both a substitution effect of the newer therapies for docetaxel and an expansion of treatment for patients with mCRPC. Furthermore, as the number of patients prescribed enzalutamide first-line increased from 2013 to 2015, there was an apparent substitution effect of enzalutamide for abiraterone as the use of first-line abiraterone declined at a similar rate. The use of sipuleucel-T and cabazitaxel did not substantially rise throughout the entire study period. Supplementary Table 2 includes the corresponding values for Figure 1.

The frequency of and proportion of different treatments prescribed also varied by provider type (Figure 2). Medical oncologists prescribed the majority (64.5%) of first-line treatments for patients, abiraterone in 41.5%, docetaxel in 39.6%, enzalutamide in 12.5%, and sipuleucel-T in 5.5% of patients. In contrast, urologists prescribed 8.8% of the first-line treatments, using sipuleucel-T, enzalutamide, and abiraterone, each in a third of patients.

Table 2 shows the results of a multinomial logistic regression model demonstrating the odds of receiving an oral therapy versus docetaxel. The odds of receiving an “other” treatment versus docetaxel as first-line was also calculated and is reported in Supplementary Table 4. Race, income, geography, and provider type were factors significantly associated with choice of first-line therapy in multivariable analysis. Black patients had greater odds of receiving an oral therapy over docetaxel first-line (OR 1.43, 95% CI 1.02–2.01) compared to

white patients. Paradoxically, those with household income >$99,000 had a lower odds of receiving the more expensive oral agents over docetaxel (OR 0.66, 95% CI 0.48–0.92) compared to those with a household income <$50,000, a finding that was independent of other factors such as education, provider type, and year of treatment. In addition, patients who received first-line treatment by a urologist versus a medical oncologist had a substantially greater odds of receiving an oral therapy over docetaxel (OR 16.05, 95% CI 6.01–42.86). The results from the regressions that were done treating the “unknown” category as a separate category and the complete case analysis where unknowns were excluded are numerically similar to the findings that we report using multiple imputed dataset and combined inference (Supplementary Tables 5 and 6).

Standard binomial logistic regression was also conducted to demonstrate variables associated with the odds of receiving abiraterone versus enzalutamide (Supplementary Tables 7 and 8). Compared to 2014, patients prescribed first-line treatment in 2015 (OR 1.66, 95% CI 1.31–2.11) and 2016 (OR 2.01, 95% CI 1.50–2.68) had greater odds of being prescribed enzalutamide than abiraterone. In addition, patients treated by a urologist versus a medical oncologist were more likely to receive enzalutamide than abiraterone (OR 2.64, 95% CI 1.97–3.52), independent of other variables.

For all regression analyses, we observed geographic variability. Considering patients in the South Atlantic as a reference, patients in the West North Central region had substantially lower odds of being prescribed an oral therapy as first-line versus docetaxel (OR 0.30, 95% CI 0.20–0.45), and patients in the Pacific region had a greater odds of being prescribed an oral therapy as first-line (OR 2.68, 95% CI 1.74–4.11). Among patients who received an oral first-line therapy, patients in the West North Central region had lower odds of receiving enzalutamide than abiraterone (OR 0.51, 95% CI 0.29–0.90). These findings were independent of other factors such as age, race, education, income, and provider specialty. Using methods described in Supplementary Materials 6.1, Figure 3 demonstrates the observed geographic variability.

Discussion

Throughout the study period, we observed both an expansion of total treatment use to more patients than would otherwise have been treated and a substitution effect of oral therapies for docetaxel and enzalutamide for abiraterone. Not surprisingly, patients treated by urologists were more likely to receive an oral therapy first-line than docetaxel, and more likely to receive enzalutamide. In addition, urologists prescribed a disproportionate amount of sipuleucel-T and enzalutamide for the number of patients they treated. An unexpected finding was the paradoxical effect that patients with higher incomes were more likely to receive the less expensive docetaxel than secondary androgen signaling inhibitors, independent of other factors.

Similar to studies in other clinical conditions, we were not surprised to find race and geographic region to influence prescribing.[13–18] The association of Black race with receiving first-line oral androgen signaling inhibitors over docetaxel could be due to patient preference or other factors we were unable to measure, such as rural/urban distribution. To

explain the unexpected association of patients with higher income being more likely to receive docetaxel first-line over an oral androgen signaling inhibitor, we considered a landmark study (CHAARTED) published in August 2015, as a possible explanation. CHAARTED demonstrated a benefit to using docetaxel in an earlier phase of disease (hormone-naïve setting).[20] With our methods, patients treated with docetaxel per CHAARTED would be identified as receiving docetaxel first-line, and one would expect that patients with higher income might be the patients to seek out groundbreaking care concordant with the latest evidence. However, the paradoxical income effect we observed did not extinguish in multivariable analysis. Thus, one can infer that there must be another explanation for the association of higher income and receipt of docetaxel first-line than the guideline changes as a result of CHAARTED. Another possible explanation for this paradoxical effect of income on receipt of docetaxel may be due to the high out-of-pocket costs faced by some patients for oral medications since oral therapies are typically covered through a different insurance benefit than intravenous medications. Patients with lower incomes are commonly eligible to receive patient assistance through pharmaceutical companies or through other grant mechanisms, while patients with higher incomes, who may still have prohibitive cost sharing requirements, may not qualify for patient assistance.[21,22]

To explain why urologists were responsible for a disproportionate number of sipuleucel-T treatments, we considered that patients treated for mCRPC by urologists may have less aggressive and asymptomatic disease. There is also increasing interest among urologists in treating patients with advanced prostate cancer since therapies that do not involve cytotoxic chemotherapy have become available.[23–25] Investing in the infrastructure to be able to offer sipuleucel-T could potentially give patients treated by urologists an additional treatment option. We expected patients treated by urologists to be more likely to receive an oral agent over docetaxel, since urologists are not typically trained to deliver cytotoxic chemotherapy, but were not expecting urologists to have a preference for enzalutamide over abiraterone. It is possible this preference may stem from the fact that abiraterone, while on the market longer and arguably better tolerated in patients, requires concurrent use of prednisone and frequent blood pressure and laboratory monitoring that may not be feasible for some urology practices.

There are limitations to this study. First, regarding cohort identification, we included all patients with a claim for one of the focus treatments, regardless of having a diagnosis code for metastatic disease, since methods to identify metastatic disease through claims are known to be insensitive.[26] We were also not able to identify whether a patient had castration-resistant disease. Since the objective was to compare patterns and preferences of treatments among treated patients, this limitation is not germane to the present study. Fortunately, all of the focus treatments, except docetaxel, were FDA-approved for use only in mCRPC during the proposed years of analysis, so we were confident that treatments prescribed were being used for mCRPC and not another cancer. Among patients who received docetaxel, very few patients (3.9%) had a diagnosis of a co-occurring cancer for which docetaxel is used. Another limitation to this study is the generalizability of our findings since all patients in this study had private insurance. Thus, greater disparities are likely to exist in treatment patterns with a more inclusive cohort of patients. Finally, there

were limitations inherent to the claims database for identifying sociodemographic variables, several of which were generated from a composite of public records, purchase transactions, census data, and consumer surveys, and for identifying provider specialty. However, our algorithm for identifying providers was conservative and our “other” category that was primarily associated with docetaxel was large, suggesting that our findings may be underestimating the difference between medical oncologists and urologists.

Conclusion

A patient’s race, income level, geographic area of residence, and specialty of provider caring for them all significantly influence the treatment they will receive for mCRPC. In particular, whether a patient follows with medical oncology or urology may substantially influence the treatment that a patient receives. Once we have more evidence on sequences of therapy that lead to best outcomes for patients, the discrepancy between the treatments patients receive depending on their provider specialty could have tremendous implications for patients. In addition, the finding that higher income may be a barrier to novel oral therapies has implications for patient care that mandate further consideration regarding assistance programs, which may very well account for our findings.[27] Effectively improving access to tolerable and available treatments hinges on the understanding of current practices. Future work will use knowledge of drivers of variation in treatment to develop targeted implementation strategies for current and future therapies.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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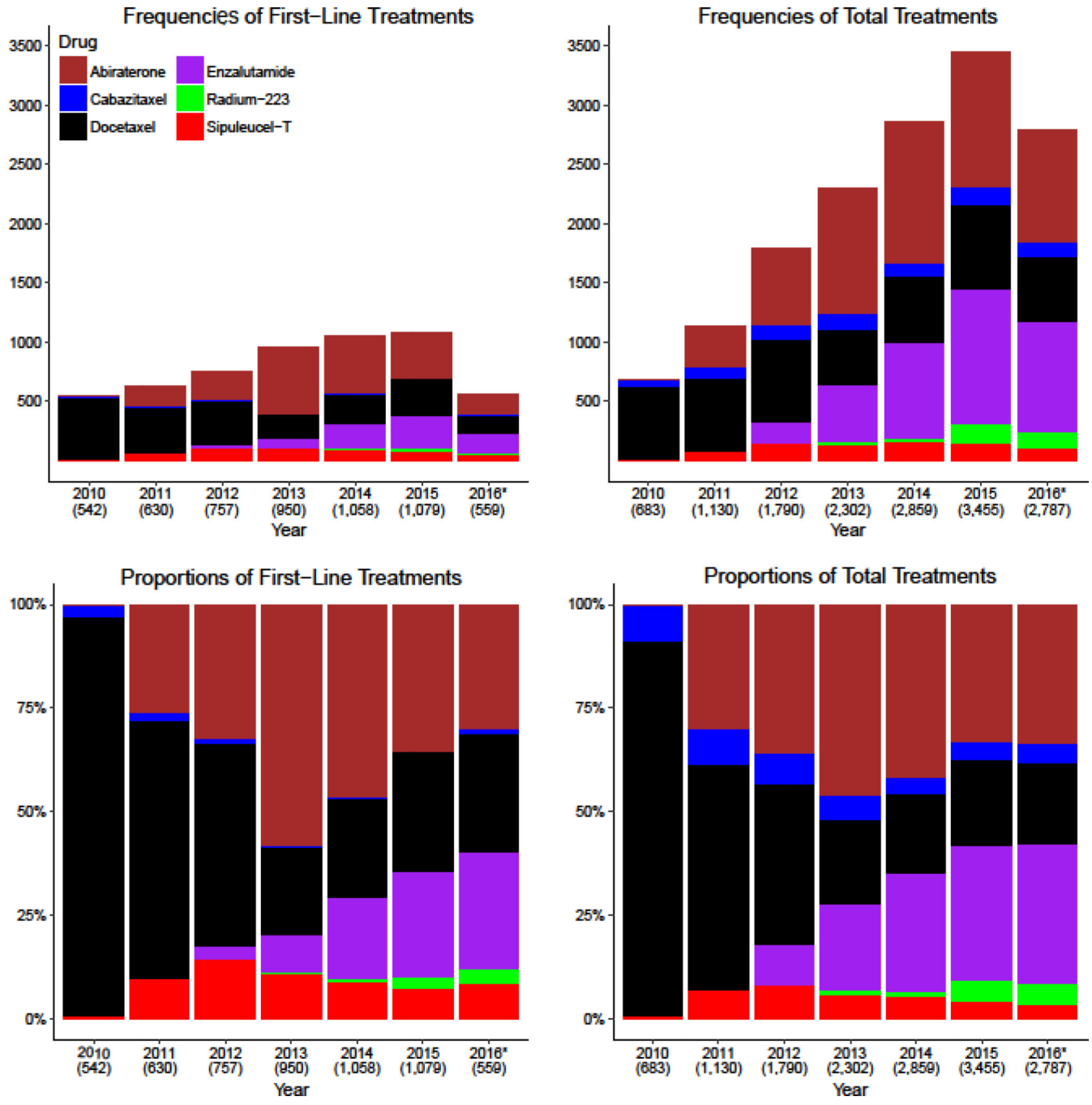

Figure 1. Frequencies and Rates of Therapy Use

The top panels show the frequency of treatments used: the top left panel shows the frequency of patients who were started on a treatment as first-line therapy each year, and the top right panel shows the total use of treatment each year. The bottom panels show proportions of treatments used in relation to the other available treatments: the bottom left panel shows proportions of patients who started a first-line therapy each year and the bottom right panel shows the total proportions of the different therapies used each year. The proportions in the bottom panels sum to 100%. *2016 only includes data from the first six

months of the year. The number of patients included in each column is included beneath the year on the X-axis of each bar graph.

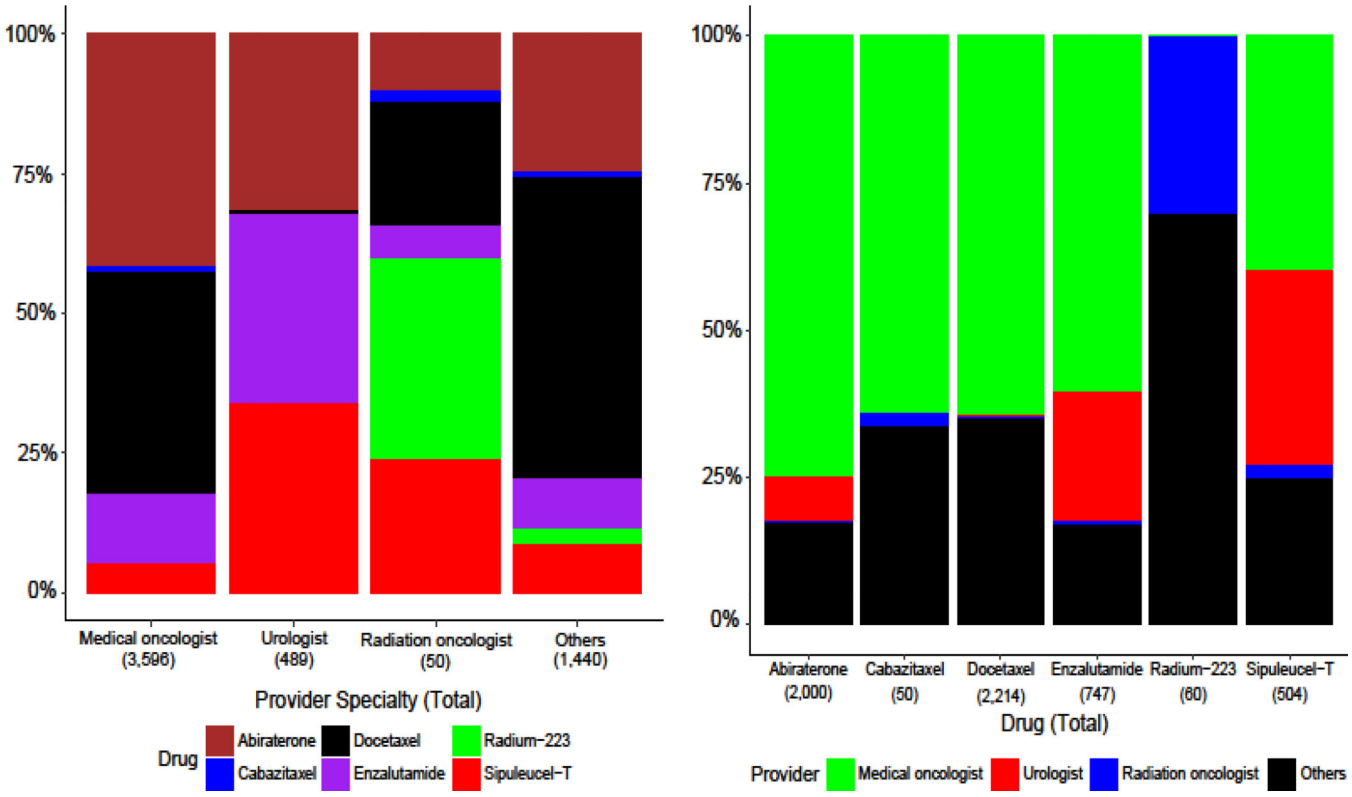

Figure 2. Provider Type and First-Line Treatment

The top panel shows the proportions of first-line treatments prescribed by different provider specialties and the bottom panel shows the proportions of providers that prescribe the different studied treatments. These proportions include all patients started on a treatment between January 2010 and June 2016. “Others” includes other providers such as advanced practice providers, primary care providers, pharmacies, facilities such as hospitals, and other taxonomies for which we could not confirm that the provider was a medical oncologist, urologist, or radiation oncologist. Details for the classification of providers are in Sections 2.3–2.4 of the Supplementary Materials.

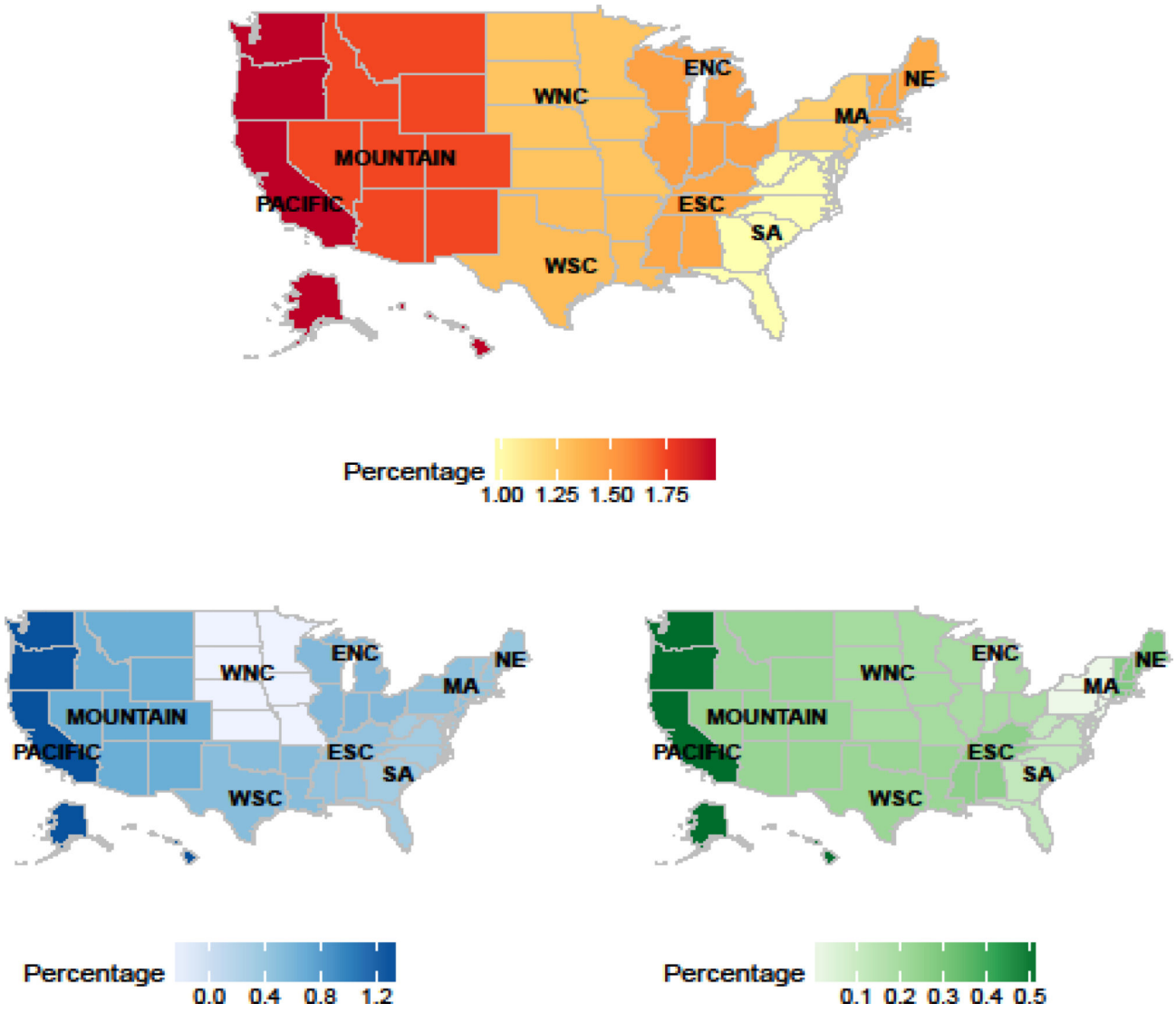

Figure 3. Geographic variation of drug patterns by region

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. 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. 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. Methods to generate this figure are in Supplementary Materials, Section 6.1.

Abbreviations: 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)

Table 1.

Patient Characteristics: Total cohort includes all patients ≥18 years with prostate cancer (N=328,989) and study cohort includes patients with prostate cancer who received any of the six treatments and were continuously enrolled for ≥ 180 days before receipt of their first treatment (n = 5,575) over the study period years 2010 through mid-2016

	Total Cohort (N=328,989)		Final Cohort (n=5,575)	
Variable	**Mean [Range]/Count (%)**		**Mean range/Count (%)**	
Age	71.44	[18,90]	73.62	[32,90]
Race				
White	223,035	(67.8)	3,888	(69.7)
Black	37,567	(11.4)	737	(13.2)
Asian	6,239	(1.9)	108	(1.9)
Hispanic	23,091	(7.0)	410	(7.4)
Unknown	39,057	(11.9)	432	(7.8)
Education level				
Less than 12th Grade	1,530	(0.5)	37	(0.7)
High School Diploma	89,140	(27.1)	1,621	(29.1)
Less than Bachelor Degree	162,252	(49.3)	2,858	(51.3)
Bachelor Degree Plus	45,880	(13.9)	785	(14.1)
Unknown	30,187	(9.2)	274	(4.9)
Household income range				
<$50,000	98,244	(29.9)	1,985	(35.6)
$50,000-$99,000	96,987	(29.5)	1,721	(30.9)
>$99,000	76,551	(23.3)	1,091	(19.6)
Unknown	57,207	(17.4)	778	(14.0)
Net worth				
<$25,000	18,347	(5.6)	334	(6.0)
$25,000-$149,000	47,045	(14.3)	891	(16.0)
$150,000-$249,000	42,972	(13.1)	773	(13.9)
$250,000-$499,000	81,771	(24.9)	1,393	(25.0)
>$500,000	85,002	(25.8)	1,454	(26.1)
Unknown	53,852	(16.4)	730	(13.1)
Geographic Region*				
South Atlantic	89,340	(27.2)	1,291	(23.1)
New England	17,999	(5.5)	285	(5.1)
Middle Atlantic	32,045	(9.7)	440	(7.9)
East North Central	46,568	(14.2)	806	(14.5)
East South Central	11,747	(3.6)	202	(3.6)

	Total Cohort (N=328,989)		Final Cohort (n=5,575)	
Variable	**Mean [Range]/Count (%)**		**Mean range/Count (%)**	
West North Central	32,548	(9.9)	604	(10.8)
West South Central	32,775	(10.0)	539	(9.7)
Mountain	31,429	(9.6)	609	(10.9)
Pacific	33,078	(10.1)	771	(13.8)
Unknown	1,460	(0.4)	28	(0.5)
Metastatic				
Yes	28,451	(8.6)	4,890	(87.7)
No	300,538	(91.4)	685	(12.3)
Year				
2010	97,410	(29.6)	2,365	(42.4)
2011	101,968	(31.0)	2,743	(49.2)
2012	110,243	(33.5)	3,071	(55.1)
2013	117,544	(35.7)	3,237	(58.1)
2014	115,297	(35.0)	3,132	(56.2)
2015	122,555	(37.3)	2,872	(51.6)
2016	99,292	(30.2)	1,992	(35.7)
Comorbid condition				
Hypertension	223,777	(68.0)	3,842	(68.9)
Diabetes	94,275	(28.7)	1,584	(28.4)
Arrhythmia	71,897	(21.9)	1,151	(20.4)
Congestive heart failure	39,342	(12.0)	597	(10.7)
Osteoporosis	13,374	(4.1)	385	(6.9)

OR, Odds Ratio; CI, Confidence Interval

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- South Atlantic: Delaware, Washington D.C., Florida, Georgia, Maryland, North Carolina, South Carolina, Virginia, West Virginia
- East South Central: Alabama, Kentucky, Mississippi, Tennessee
- West South Central: Arkansas, Louisiana, Oklahoma, and Texas
- Mountain: Arizona, Colorado, Idaho, Montana, Nevada, New Mexico, Utah, Wyoming
- Pacific: Alaska, California, Hawaii, Oregon, Washington

Table 2.

Multinomial Logistic Regression of First-Line Treatment Among Patients Treated 2014–2016: 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. Multivariable analyses also adjusted for net worth, insurance product, and whether the insurance plan was administrative services only. The regression results for the category of other (sipuleucel-T, cabazitaxel, and radium-223) were not included in this Table, but are in Supplementary Materials, Section 8.3.

	Total (n=2,696)		Docetaxel (n=728)		Abiraterone or Enzalutamide (n=1,678)			Abiraterone or Enzalutamide vs Docetaxel			
								Unadjusted OR		Multivariable Analysis	
Variable	**Count (%)**		**Count (%)**		**Count (%)**		**P-value**	**OR**	**95% CI**	**OR**	**95% CI**
Age							**<0.01**				
<55	70	(2.6)	35	(4.8)	31	(1.8)		1.00		1.00	
55–64	310	(11.5)	94	(12.9)	178	(10.6)		**2.14**	**(1.24,3.68)**	**2.12**	**(1.18,3.80)**
65–74	906	(33.6)	355	(48.8)	451	(26.9)		1.43	(0.87,2.37)	1.37	(0.78,2.41)
≥75	1,410	(52.3)	244	(33.5)	1,018	(60.7)		**4.71**	**(2.85,7.79)**	**4.06**	**(2.28,7.22)**
Race							**<0.01**				
White	1,830	(67.9)	505	(69.4)	1,129	(67.3)		1.00		1.00	
Black	329	(12.2)	69	(9.5)	219	(13.1)		**1.40**	**(1.05,1.87)**	**1.43**	**(1.02,2.01)**
Asian	60	(2.2)	13	(1.8)	44	(2.6)		1.40	(0.74,2.63)	1.38	(0.68,2.82)
Hispanic	231	(8.6)	51	(7.0)	166	(9.9)		1.39	(0.99,1.95)	0.95	(0.65,1.40)
Unknown	246	(9.1)	90	(12.4)	120	(7.2)					
Education level							0.72				
Less than 12th Grade	17	(0.6)	2	(0.3)	12	(0.7)		1.00		1.00	
High School Diploma	770	(28.6)	200	(27.5)	499	(29.7)		0.43	(0.10,1.90)	0.66	(0.13,3.46)
Less than Bachelor Degree	1,349	(50.0)	356	(48.9)	851	(50.7)		0.42	(0.09,1.85)	0.68	(0.13,3.58)
Bachelor Degree Plus	381	(14.1)	101	(13.9)	239	(14.2)		0.41	(0.09,1.85)	0.79	(0.15,4.28)
Unknown	179	(6.6)	69	(9.5)	77	(4.6)					
Household income range							**<0.01**				
<$50,000	895	(33.2)	197	(27.1)	613	(36.5)		1.00		1.00	
$50,000-$99,000	868	(32.2)	216	(29.7)	555	(33.1)		0.82	(0.66,1.03)	0.94	(0.72,1.23)
>$99,000	537	(19.9)	187	(25.7)	292	(17.4)		**0.51**	**(0.41,0.65)**	**0.66**	**(0.48,0.92)**
Unknown	396	(14.7)	128	(17.6)	218	(13.0)					
Geographic Region*							**<0.01**				
South Atlantic	495	(18.4)	138	(19.0)	302	(18.0)		1.00		1.00	
New England	130	(4.8)	42	(5.8)	80	(4.8)		0.87	(0.57,1.33)	1.06	(0.65,1.70)
Middle Atlantic	279	(10.3)	72	(9.9)	178	(10.6)		1.13	(0.80,1.58)	0.96	(0.65,1.41)
East North Central	451	(16.7)	113	(15.5)	279	(16.6)		1.13	(0.84,1.52)	1.09	(0.78,1.53)
East South Central	101	(3.7)	27	(3.7)	58	(3.5)		0.98	(0.59,1.61)	0.81	(0.46,1.41)

	Total (n=2,696)		Docetaxel (n=728)		Abiraterone or Enzalutamide (n=1,678)			Abiraterone or Enzalutamide vs Docetaxel			
								Unadjusted OR		Multivariable Analysis	
Variable	**Count (%)**		**Count (%)**		**Count (%)**		**P-value**	**OR**	**95% CI**	**OR**	**95% CI**
West North Central	249	(9.2)	135	(18.5)	83	(4.9)		**0.28**	**(0.20,0.39)**	**0.30**	**(0.20,0.45)**
West South Central	263	(9.8)	66	(9.1)	167	(10.0)		1.15	(0.81,1.63)	1.04	(0.70,1.55)
Mountain	324	(12.0)	76	(10.4)	203	(12.1)		1.22	(0.87,1.70)	1.08	(0.73,1.62)
Pacific	400	(14.8)	57	(7.8)	326	(19.4)		**2.60**	**(1.84,3.67)**	**2.68**	**(1.74,4.11)**
Unknown	4	(0.1)	2	(0.3)	2	(0.1)					
Metastatic							**<0.01**				
Yes	2,189	(81.2)	598	(82.1)	1,335	(79.6)		1.00		1.00	
No	507	(18.8)	130	(17.9)	343	(20.4)		1.18	(0.94,1.48)	0.85	(0.65,1.11)
Year							**0.03**				
2014	1,058	(39.2)	254	(34.9)	698	(41.6)		1.00		1.00	
2015	1,079	(40.0)	313	(43.0)	655	(39.0)		**0.76**	**(0.63,0.93)**	**0.77**	**(0.62,0.97)**
2016	559	(20.7)	161	(22.1)	325	(19.4)		**0.73**	**(0.58,0.93)**	0.77	(0.58,1.02)
Comorbid Conditions											
Hypertension	1,965	(72.9)	503	(69.1)	1,237	(73.7)	**<0.01**	**1.25**	**(1.04,1.52)**	1.11	(0.88,1.40)
Diabetes	792	(29.4)	187	(25.7)	512	(30.5)	**0.03**	**1.27**	**(1.04,1.55)**	1.12	(0.89,1.41)
Arrhythmia	658	(24.4)	159	(21.8)	437	(26.0)	**0.04**	**1.26**	**(1.02,1.55)**	0.97	(0.76,1.25)
Congestive heart failure	332	(12.3)	54	(7.4)	244	(14.5)	**<0.01**	**2.12**	**(1.56,2.89)**	**1.69**	**(1.18,2.42)**
Osteoporosis	234	(8.7)	41	(5.6)	144	(8.6)	**<0.01**	**1.57**	**(1.10,2.25)**	1.44	(0.97,2.14)
Provider Type							**<0.01**				
Medical oncologist	1,613	(59.8)	417	(57.3)	1,127	(67.2)		1.00		1.00	
Urologist	363	(13.5)	2	(0.3)	264	(15.7)		**16.66**	**(6.34,43.79)**	**16.05**	**(6.01,42.86)**
Others	613	(22.7)	275	(37.8)	220	(13.1)		**0.31**	**(0.25,0.38)**	**0.35**	**(0.28,0.44)**
Unknown	107	(4.0)	34	(4.7)	67	(4.0)					

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