Physician Dispensing Among Urology Practices and the Use of Abiraterone or Enzalutamide for Men With Advanced Prostate Cancer

Lillian Y. Lai, MD, MS,1* Samuel R. Kaufman, MA,1 Mary K. Oerline, MS,1 Megan E.V. Caram, MD, MS1,2 Avinash Maganty, MD,1 Brent K. Hollenbeck, MD, MS1, Vahakn B. Shahinian, MD, MS1,2

1Department of Urology, University of Michigan, Ann Arbor, MI, USA; 2Department of Internal Medicine, University of Michigan, Ann Arbor, MI, USA; and 3VA Health Services Research & Development, Center for Clinical Management and Research, VA Ann Arbor Healthcare System, Ann Arbor, MI, USA

*Correspondence to: Lillian Y. Lai, MD, MS, Department of Urology, University of Michigan, 2800 Plymouth Road, Bldg 16, Ann Arbor, MI 48109-2800, USA (e-mail: lillianla67@gmail.com).

Abstract

Urologists are increasingly prescribing oral targeted therapies to patients with advanced prostate cancer. Concurrent with this trend, urology practices are allowing patients to fill their prescription onsite or through a pharmacy established by the practice. We examined prescription patterns for abiraterone or enzalutamide between eventually dispensing single-specialty urology practices, nondispensing single-specialty urology practices, and multispecialty practices using a 20% random sample of the 2013-2017 national Medicare claims. We determined physician dispensing through manual search of publicly available information. From 2015 through 2017, higher percentages of patients managed by eventually dispensing single-specialty urology practices had a filled prescription of abiraterone or enzalutamide compared with patients managed in nondispensing single-specialty urology practices (eg, in 2017, 8.9%, 95% confidence interval = 7.3% to 10.9%, vs 5.9%, 95% confidence interval = 5.0% to 7.0%, respectively; 2-sided P < .001). Insofar as physician dispensing is associated with higher use of abiraterone or enzalutamide, it may represent a means to improve treatment access.

Traditionally, patients with advanced prostate cancer were treated with docetaxel, an intravenous cytotoxic chemotherapy, under the care of medical oncologists. With the introduction of abiraterone and enzalutamide—oral agents with similar efficacy and improved toxicity profiles relative to docetaxel (1-4)—men with advanced prostate cancer can now receive treatment at home. Both abiraterone and enzalutamide have since surpassed docetaxel in the rate of use among patients with advanced prostate cancer (5) and are increasingly prescribed by urologists (6).

Concurrent with this trend, urology practices are offering an alternative dispensing model where patients fill their prescriptions onsite or through a pharmacy established by the practice (collectively referred to as physician dispensing) (7). This streamlined delivery model, coupled with the longstanding urologist–patient relationship, has the potential to reduce care fragmentation and improve access. To understand the scope of this delivery model, we examined prescription patterns for abiraterone or enzalutamide across a range of practice contexts.

We used claims from a 20% national random sample of fee-for-service Medicare beneficiaries from 2013 to 2017 to identify patients with advanced prostate cancer, defined as patients with a diagnosis of prostate cancer who were undergoing chronic androgen deprivation therapy (ADT). The use of chronic ADT was defined as a history of bilateral orchiectomy or at least 6 months of continuous coverage of leuprolide, goserelin, degarelix, or triptorelin. To exclude patients who received androgen deprivation therapy as an adjunct to localized treatment, we eliminated patients who had undergone prostatectomy or radiation therapy in the period beginning 12 months prior to the initiation of ADT and ending 6 months after. Only patients with continuous enrollment in Medicare Parts A and B in the 12 months prior to the initiation of ADT were included in the study to allow for assessment of baseline patient characteristics.

Each patient was assigned to the urologist responsible for his prostate cancer management, defined as the urologist who provided the plurality of claims for evaluation and management services associated with the diagnosis code for prostate cancer in the given year. The urologist was then linked to the corresponding group practice based on the tax identification number using data from the Medicare data on provider practice and special file. Each practice was characterized as a single-specialty urology practice or a multispecialty practice. The dispensing status of single-specialty...
urology practices was determined using a manual search of practice websites and other publicly available information (Supplementary Methods, available online) and held constant throughout the study period. Prescription fills were assessed at the patient-level using Medicare Part D claims. All prescription fills for each patient were included in the analysis, even if prescribed by providers outside the practice or non-urologists.

To standardize the study population, we limited our analysis to patients who initiated ADT within a 3-year period, inclusive of the index year, for each year of the study (ie, creating 5 cross-sectional cohorts). In each cohort, patient age; race (Black, Other [Asian, Hispanic, North American Native, other, and unknown], or White) as reported in Medicare data; comorbidity (8); socioeconomic status (9); and days since ADT initiation were compared according to practice type (eventually dispensing single-specialty urology practice, nondispensing single-specialty urology practice, multispecialty practice) using $\chi^2$ statistics. The adjusted percentages of patients with advanced prostate cancer who had a filled prescription of abiraterone or enzalutamide by practice type were derived from multivariable logistic models, with adjustments for clustering at the patient level, and compared using the least squares means procedure. All statistical tests were 2-sided, and a $P$ value of less than .05 was considered statistically significant. This study was exempt from review by the institutional review board.

Patients with advanced prostate cancer were similar in age and comorbidity across practice types (Table 1). Eventually dispensing single-specialty urology practices managed the highest percentages of patients with advanced prostate cancer who were Black and patients of higher socioeconomic status. Patients with advanced prostate cancer managed by eventually dispensing single-specialty urology practices were, on average, 26 days closer to their ADT initiation than those managed by nondispensing single-specialty urology practices and 34 days further from their ADT initiation than those managed by multispecialty practices (606 days for patients managed by eventually dispensing single-specialty urology practices vs 632 days for patients managed by nondispensing single-specialty urology practices vs 571 days for patients managed by multispecialty practices; $P < .001$).

As illustrated in Figure 1, from 2015 to 2017, eventually dispensing single-specialty urology practices had higher percentages of patients with advanced prostate cancer who had a filled prescription of abiraterone or enzalutamide compared with nondispensing single-specialty urology practices. For instance, in 2017, 8.9% (95% confidence interval [CI] = 7.3% to 10.9%) of patients with advanced prostate cancer managed by eventually dispensing single-specialty urology practices had a filled prescription of abiraterone or enzalutamide compared with 5.9% (95% CI = 5.0% to 7.0%) of patients with advanced prostate cancer managed by nondispensing single-specialty urology practices ($P < .001$).

The observed differences in the use of abiraterone or enzalutamide may partially be explained by the differences in volume of patients with advanced prostate cancer managed by practices with or without dispensing. Eventually dispensing single-specialty urology practices, on average, had the highest volume of patients with advanced prostate cancer, which could translate into increased familiarity with the use of abiraterone or enzalutamide among physicians in such practices. However, as observed in 2015, eventually dispensing single-specialty urology practices had an even higher percentage of patients with advanced prostate cancer with a filled prescription of abiraterone or enzalutamide than multispecialty practices, which often involved medical oncologists who also have specialized experience with these agents.

This study has several limitations. First, the method used to identify physician dispensing was specific but lacked sensitivity, which might have caused some dispensing practices to be misclassified as nondispensing practices. However, such misclassification would bias the findings toward the null, underestimating the influence of physician dispensing. Second, because of the use of Medicare claims, cancer severity and nuances of comorbidity were

Table 1. Characteristics of patients with advanced prostate cancer, according to practice type

| Characteristics               | Eventually dispensing single-specialty urology practices | Nondispensing single-specialty urology practices | Multispecialty practices | $P^a$ |
|------------------------------|---------------------------------------------------------|--------------------------------------------------|----------------------------|------|
| Number of practices          | 72                                                      | 1597                                             | 765                        | —    |
| Number of patients           | 3697                                                   | 10 564                                           | 4606                       |      |
| Age at ADT initiation, No. (%) |                                                          |                                                  |                             |      |
| 66-69                        | 293 (7.9)                                               | 745 (7.1)                                        | 360 (7.8)                  | .12  |
| 70-74                        | 692 (18.7)                                              | 1882 (17.8)                                      | 869 (18.9)                 |      |
| 75-79                        | 872 (23.6)                                              | 2532 (24.0)                                      | 1139 (24.7)                |      |
| 80-84                        | 967 (26.2)                                              | 2800 (26.5)                                      | 1166 (25.3)                |      |
| 85 or older                  | 873 (23.6)                                              | 2605 (24.7)                                      | 1072 (23.3)                |      |
| Race, No. (%)                |                                                         |                                                  |                             |      |
| Black                        | 488 (13.2)                                              | 1182 (11.3)                                      | 488 (10.6)                 | <.001|
| Otherb                       | 108 (2.9)                                               | 450 (4.3)                                        | 121 (2.6)                  |      |
| White                        | 3099 (83.9)                                             | 8836 (84.4)                                      | 3991 (86.8)                |      |
| Socioeconomic status, No. (%)|                                                         |                                                  |                             | <.001|
| Low                          | 967 (26.2)                                              | 3568 (33.8)                                      | 1459 (31.7)                |      |
| Medium                       | 1219 (33.0)                                             | 3759 (35.6)                                      | 1748 (38.0)                |      |
| High                         | 1511 (40.9)                                             | 3237 (30.6)                                      | 1399 (30.4)                |      |
| Comorbidity score, No. (%)   |                                                         |                                                  |                             |      |
| 0                            | 1645 (44.5)                                             | 4659 (44.1)                                      | 2067 (44.9)                | .62  |
| 1                            | 875 (23.7)                                              | 2466 (23.3)                                      | 1032 (22.4)                |      |
| 2                            | 458 (12.4)                                              | 1408 (13.3)                                      | 620 (13.5)                 |      |
| $\geq$3                      | 719 (19.5)                                              | 2031 (19.2)                                      | 887 (19.3)                 |      |
| Days since ADT initiation, mean (SD) | 606 (313)                                    | 632 (310)                                        | 572 (318)                  | <.001|

*Statistical differences (2-sided $P$ values) were estimated using $\chi^2$ statistics. ADT = androgen deprivation therapy.

**Other** includes Asian, Hispanic, North American Native, other, and unknown, as reported in Medicare data.
not captured. However, given the generally similar patient characteristics (e.g., age at ADT initiation, comorbidity score), the observed differences in the use of abiraterone or enzalutamide at the practice level are likely not attributable to differences in disease trajectory or overall health status of the patient.

Insofar as physician dispensing may facilitate treatment access, it can represent a means to mitigate disparities in prostate cancer treatment and outcomes (10). However, the financial incentives associated with self-referral may foster overutilization in circumstances of clinical uncertainty. Future research should explore the effects of physician dispensing on prescribing appropriateness, treatment compliance, and out-of-pocket cost to comprehensively understand the implications of this delivery model.

Data Availability
The Medicare claims data underlying this article were provided by the Centers for Medicare & Medicaid Services (CMS) under license/by permission. Data will be shared on request to the corresponding author with permission of CMS.

References
1. Ryan CJ, Smith MR, de Bono JS, et al. Abiraterone in metastatic prostate cancer without previous chemotherapy. N Engl J Med. 2013;368(2):138–148. doi:10.1056/NEJMoa1209096.
2. Beer TM, Armstrong AJ, Rathkopf DE, et al. Enzalutamide in metastatic prostate cancer before chemotherapy. N Engl J Med. 2014;371(5):424–433. doi:10.1056/NEJMoa1405095.
3. de Bono JS, Logothetis CJ, Molina A, et al. Abiraterone and increased survival in metastatic prostate cancer. N Engl J Med. 2011;364(21):1995–2005. doi:10.1056/NEJMoa1014618.
4. Scher HI, Fizazi K, Saad F, et al. Increased survival with enzalutamide in prostate cancer after chemotherapy. N Engl J Med. 2012;367(13):1187–1197. doi:10.1056/NEJMoa1207506.
5. Caram MEV, Estes JP, Griggs JJ, Lin P, Mukherjee B. Temporal and geographic variation in the systemic treatment of advanced prostate cancer. BMC Cancer. 2019;20(1):1–10. doi:10.1186/s12885-018-4166-3.
6. Caram MEV, Kaufman SR, Modi PK, et al. Adoption of abiraterone and enzalutamide by urologists. Urology. 2019;131:176–183. doi:10.1016/j.urology.2019.05.012.
7. Sellinger SB, Shore ND. Member census shows LUGPA practices exhibit high level of innovation, sophistication, and growth. Rev Urol. 2018;20(2):94–97. doi:10.3909/riu0805.
8. Klabunde CN, Potosky AL, Legler JM, Warren JL. Development of a comorbidity index using physician claims data. J Clin Epidemiol. 2000;53(12):1258-1267. doi:10.1016/S0895-4356(00)00256-0.
9. Drez Roux AV, Merkin SS, Arnett D, et al. Neighborhood of residence and incidence of coronary heart disease. N Engl J Med. 2001;345(2):99–106. doi:10.1056/NEJM2000101213450205.
10. Kريمпхове MJ, Cole AP, Fletcher SA, et al. Evaluation of the contribution of demographics, access to health care, treatment, and tumor characteristics to racial differences in survival of advanced prostate cancer. Prostate Cancer Prostatic Dis. 2019;22(1):125–136. doi:10.1038/s41391-018-0083-4.

Funding
This work was supported by AHRQ R01 HS025707 to VBS and BKH. LYL and AM are supported by the National Cancer Institute (T32 CA180984).

Notes
Role of the funders: The funders had no role in the study design, in the collection, analysis, or interpretation of the data; the writing of the study; or the decision to submit the manuscript for publication.

Disclosures: The authors have no conflict of interest to declare.

Author contributions: Conceptualization and Methodology: LYL, SRK, MEC, BKH, VBS. Data curation and Resources: LYL, SRK, BKH, VBS. Formal analysis and Visualization: LYL, SRK, BKH, VBS. Writing—original draft: LYL, BKH, VBS. Writing—review & editing: All authors. Supervision: BKH, VBS.