Management of Patients with Metastatic Castration-Sensitive Prostate Cancer in the Real-World Setting in the United States

Charles J. Ryan, Xuehua Ke, Marie-Hélène Lafeuille et al.

Correspondence: Charles J. Ryan (ryanc@umn.edu).

Full-length article available at www.auajournals.org/doi/10.1097/JU.0000000000002121.

Study Need and Importance: As more effective therapies become available for patients with metastatic castration-sensitive prostate cancer (mCSPC) in the U.S., a deeper understanding of the current treatment patterns and burden of these patients for the health care system is warranted. This study assessed real-world treatment patterns, health care resource utilization (HRU) and costs of patients with mCSPC using 2 large U.S. administrative health claim databases covering commercially, Medicare Advantage and Medicare Fee-for-Service-insured patients.

What We Found: This retrospective analysis of men diagnosed with mCSPC in 2015–2019 demonstrates that despite level 1 evidence and updated guideline recommendations, only 2%–13% of patients used abiraterone acetate and docetaxel, while 45%–46% of patients used only androgen deprivation therapy, and 38%–48% of patients remained untreated or deferred treatment. HRU increased after onset of metastasis, resulting in 4–5 times higher health plan-paid costs in the mCSPC period versus the 12 months prior to the metastasis diagnosis.

Limitations: As the study period predated the approvals and inclusion of apalutamide and enzalutamide for mCSPC in evidence-based guidelines, the use of these 2 agents was not assessed. The patients included in this study may not be representative of the general U.S. population or patients without health insurance. Nonetheless, administrative claims data remain a valuable source of information, comprising valid and large data reflecting patient management in the real-world setting.

Interpretation for Patient Care: This retrospective analysis of men with mCSPC found the majority are still treated with androgen deprivation therapy alone, an approach discordant with current guidelines and shown to be inferior to advanced oral therapies in slowing progression and overall survival. The substantial clinical and economic burden in patients with mCSPC highlights the importance of earlier and more effective treatment, although the impact of increased use of newer agents on real-world outcomes was not assessed.

Table. Therapy received in patients with mCSPC

| Therapy                                                                 | Database 1 (Commercially Insured and Medicare Advanced Pts, 2014–2019 [6,517]) | Database 2 (Medicare Fee-for-Service Pts, 2014–2017 [13,324]) |
|------------------------------------------------------------------------|----------------------------------------------------------------------------------|------------------------------------------------------------------|
| Duration of mCSPC period (mos), mean ± SD [median, IQR]               | 13.3 ± 12.0 [9.6, 15.6]                                                        | 12.8 ± 9.9 [10.5, 15.6]                                          |
| No. pts with no mCSPC medication or bilateral orchiectomy (%)        | 2,450 (37.6)                                                                   | 6,367 (47.8)                                                    |
| No. pts with mCSPC therapy (%)                                        | 4,067 (62.4)                                                                   | 6,957 (52.2)                                                    |
| Androgen deprivation therapy (monotherapy)*                          | 2,960 (45.4)                                                                   | 6,105 (45.8)                                                   |
| First-generation androgen signaling inhibitors only                   | 269 (4.1)                                                                     | 536 (4.0)                                                        |
| Abiraterone acetate or docetaxel:                                     | 838 (12.9)                                                                    | 316 (2.4)                                                      |
| Abiraterone acetate                                                   | 471 (7.2)                                                                     | 109 (0.8)                                                      |
| Docetaxel                                                             | 364 (5.6)                                                                     | 207 (1.6)                                                      |

* Androgen deprivation therapy medications or bilateral orchiectomy.
Management of Patients with Metastatic Castration-Sensitive Prostate Cancer in the Real-World Setting in the United States

Charles J. Ryan,1,* Xuehua Ke,2 Marie-Hélène Lafeuille,3 Hela Romdhani,3 Frederic Kinkead,3 Patrick Lefebvre,3 Allison Petrilla,4 Zul Pulungan,4 Seung Kim,4 Denise M. D’Andrea,2 Peter Francis5 and Stephen J. Freedland6,7

1Division of Hematology, Oncology and Transplantation, Department of Medicine, University of Minnesota, Minneapolis, Minnesota
2Janssen Scientific Affairs, LLC, Horsham, Pennsylvania
3Analysis Group, Inc., Montreal, Quebec, Canada
4Avalere Health, Washington, District of Columbia
5Janssen Pharmaceuticals, Inc., Raritan, New Jersey
6Division of Urology, Department of Surgery, Cedars-Sinai Medical Center, Los Angeles, California
7Urology Section, Durham VA Medical Center, Durham, North Carolina

Purpose: This study provides a contemporary assessment of the treatment patterns, health care resource utilization (HRU) and costs among metastatic castration-sensitive prostate cancer (mCSPC) patients in the U.S.

Materials and Methods: Adults with mCSPC were selected from Optum’s de-identified Clinformatics® Data Mart Database (Commercial insurance/Medicare Advantage [COM/MA]; January 1, 2014–July 31, 2019) or Medicare Fee-for-Service (FFS; January 1, 2014–December 31, 2017). The index date was the first metastatic disease diagnosis date on/after the first prostate cancer diagnosis (without prior evidence of castration resistance). Patients were observed for 12 months pre-index (baseline) through their mCSPC period (from index until castration resistance or followup end). First-line (1L) mCSPC therapy was assessed during the mCSPC period; all...

Abbreviations and Acronyms
1L = first-line
ADT = androgen deprivation therapy
CCI = Charlson Comorbidity Index
COM/MA = Commercial insurance/Medicare Advantage
ER = emergency room
HRU = health care resource utilization
mCRC = metastatic castration-resistant prostate cancer
mCSPC = metastatic castration-sensitive prostate cancer
Medicare-FFS = Medicare Fee-for-Service
NCCN® = National Comprehensive Cancer Network®
OP = outpatient
PC = prostate cancer
PPPY = per-patient-per-year
SNF = skilled nursing facility
Patients with metastatic prostate cancer are typically initially responsive to surgical or medical (androgen deprivation therapy [ADT]) castration, characterized as metastatic castration-sensitive prostate cancer (mCSPC). Patients who develop metastases without being exposed to ADT are also considered as having mCSPC (primary progressive mCSPC). Patients who no longer respond to ADT in the mCSPC setting, typically after 18 to 24 months, are diagnosed with metastatic castration-resistant prostate cancer (mCRPC). Since mCSPC and mCRPC have vastly different prognoses (mCSPC being less advanced than mCRPC), appropriate early intervention is warranted in mCSPC patients to delay disease progression and increase overall survival. Clinical trials have shown that men with mCSPC can achieve a median overall survival of 34-81 months when treated appropriately with ADT with either androgen signaling inhibitors or docetaxel.

In the last 5 years, randomized placebo-controlled clinical trials of novel agents for mCSPC have demonstrated superior survival benefits when used in combination with ADT versus ADT monotherapy. Notably, a meta-analysis of clinical trials showed a reduction in risk of death of 37% and 25% with ADT plus abiraterone acetate with prednisone/methylprednisolone and with ADT plus docetaxel versus ADT monotherapy, respectively. Similar evidence from more recent trials led to the approvals of apalutamide and enzalutamide for the treatment of mCSPC in 2019. Based on these practice-changing findings, the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) added ADT with abiraterone acetate, docetaxel, apalutamide, or enzalutamide as category 1 (ie based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate) treatment options for mCSPC, in addition to ADT monotherapy (category 2A, ie based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate).

In light of these recent additions to the mCSPC treatment options, there is a need to assess how the updated guideline recommendations have translated to real-world clinical practice in the United States. Therefore, the present study aimed to provide a comprehensive and contemporary (until mid-2019) assessment of the real-world treatment patterns, health care resource utilization (HRU), and associated costs of mCSPC patients using large U.S. administrative health claim databases.

**METHODS**

**Data Sources**

Administrative health claims and laboratory test data from 2 large U.S. databases were used separately to identify insured patients with mCSPC: 1) Optum’s de-identified Clinformatics® Data Mart Database (COM/MA; January 1, 2014—July 31, 2019), which include claims from commercial and Medicare Advantage plans for 13 million annual lives across all U.S. census regions; and 2) Centers for Medicare & Medicaid Services-sourced Medicare Fee-for-Service (FFS) Research Identifiable Files 100% Sample (January 1, 2014—December 31, 2017), including institutional (Part A), non-institutional (Part B), and drug (Part D) claim types.

For both databases, patient data include demographics, date of death, and claims/costs for medical services and prescription drugs. Laboratory test results are available for ~10% of patients. All data were de-identified and complied with the patient requirements of the Health Insurance Portability and Accountability Act (HIPAA).

**Study Design and Population**

A retrospective observational cohort study was conducted. The index date was defined as the date of the first medical claim with a diagnosis for metastatic disease on or after the first observed prostate cancer (PC) diagnosis during the study period.

**Sample Selection.** This study used a comprehensive algorithm to identify patients with mCSPC using claims...
Observation Period. The baseline period comprised the 12 months pre-index date. The mCSPC period spanned from the index date until the first observed evidence of castration resistance post-index (supplementary information, https://www.jurology.com), or, for mCSPC patients with no observed evidence of castration resistance, the earliest date among death or end of data availability/insurance coverage.

Study Measures and Statistical Analysis

Patient Characteristics. Patient demographics were assessed on the index date. Clinical characteristics included Quan Charlson Comorbidity Index (CCI), comorbidities, laboratory tests and results, and imaging tests during baseline, as well as presence of visceral metastases on the index date. Primary progressive mCSPC was defined as the presence of the first PC diagnosis >60 days pre-index date; de novo mCSPC as the first PC diagnosis within 60 days prior to or on the index date. The threshold of 60 days was selected in collaboration with clinical experts and was supported by sensitivity analyses using other periods.

Treatment Patterns. First-line (1L) therapy during the mCSPC period was assessed among COM/MA and Medicare-FFS patients separately. The 1L therapies for mCSPC were determined by review of evidence-based guidelines at the time the study was conducted and were further refined based on expert clinical opinion. These included ADT (ie bilateral orchectomy or ADT medication), first-generation androgen signaling inhibitors, abiraterone acetate, and docetaxel. Apalutamide and enzalutamide were added to evidence-based guidelines as mCSPC treatments after the end of the study period (July 31, 2019) and were not considered as mCSPC therapy in the current study. The supplementary information (https://www.jurology.com) includes additional details regarding the definition of 1L therapy.

The proportion of patients receiving a 1L therapy for mCSPC, time from index date to start of 1L therapy, 1L therapy duration, and the 1L therapy received were reported. The proportion of patients who received ADT only during the entire mCSPC period was also reported. The type of 1L mCSPC therapy received was stratified by year of index date (2015–2017, 2018–2019) for the COM/MA database; data for 2018 onwards were not available in the Medicare-FFS database.

HRU and Health Plan-Paid Costs. All-cause HRU and health plan-paid costs were analyzed during both the baseline and mCSPC periods. HRU and costs were reported per-patient-per-year (PPPY) and included acute hospitalizations, rehabilitation/skilled nursing facility (SNF) stays, emergency room (ER) visits, outpatient (OP) services, other services, and pharmacy claims. Costs were adjusted to 2019 USD using the medical care component of the consumer price index.

Statistical Analysis. Study measures were described using means, medians, standard deviations (SDs), and interquartile ranges (IQRs) for continuous variables, and frequencies and percentages for categorical variables.

RESULTS

Patient Characteristics

A total of 6,517 COM/MA and 13,324 Medicare-FFS patients with mCSPC were identified (supplementary figure 1, https://www.jurology.com). Mean±SD (median) age was 75±9 (75) years and 75±8 (74) years, respectively (table 1). The mean±SD (median) Quan-CCI was 3.5±2.2 (3) and 3.8±2.3 (3), respectively. The most common comorbidities were hypertension (COM/MA: 72%; Medicare-FFS: 78%) and diabetes (COM/MA: 32%; Medicare-FFS: 34%). Visceral metastases were present in 14% of patients from both databases. Most patients had primary progressive mCSPC (COM/MA: 64%; Medicare-FFS: 66%) vs de novo metastatic disease.

Treatment Patterns

During a median mCSPC period of 9.6 months (COM/MA) and 10.5 months (Medicare-FFS), 62% and 52% of patients received a 1L mCSPC therapy, for a median duration of 9.4 and 8.1 months, respectively (table 2). Among all patients, 38% of COM/MA and 48% of Medicare-FFS patients remained untreated or deferred treatment, while 45% and 46%, respectively, were treated with 1L ADT monotherapy. Abiraterone acetate or docetaxel were used as 1L therapy in 13% (COM/MA) and 2% (Medicare-FFS) of patients. Approximately 43% and 38% of patients, respectively, only received ADT monotherapy (with or without first-generation androgen signaling inhibitors) during the entire mCSPC period despite the availability of other more potent therapies.

When stratified by year of index date, in the COM/MA database, treatment with 1L ADT monotherapy decreased numerically from 48% to 43% among patients diagnosed with mCSPC in 2015–2017 vs 2018–2019 (fig. 1). While the overall use of abiraterone or docetaxel remained similar in the 2 periods (12%–14%), the use of abiraterone acetate increased among patients diagnosed in 2018–2019 (10%) vs 2015–2017 (5%), whereas the use of docetaxel decreased in 2018–2019 (4%) compared with 2015–2017 (7%).

HRU and Health Plan-Paid Costs

When evaluating the trends in HRU from the baseline to the mCSPC periods, the mean number of days of acute hospitalizations PPPY increased from 1.1 to 12.0 for COM/MA and from 3.0 to 15.8 for Medicare-FFS patients; the mean number of days of rehabilitation/SNF PPPY increased from 1.0 to 8.6 and from 2.6 to 13.8, respectively (table 3). The
mean number of ER visits PPPY increased from 1.0 to 2.7 for COM/MA and from 1.7 to 3.3 for Medicare-FFS patients, and the mean number of OP service claims PPPY increased from 48.7 to 134.7 and from 37.7 to 97.6, respectively. The mean number of other service claims PPPY increased from 21.1 to 37.6 and from 0.3 to 2.1, respectively.

Accordingly, mean all-cause medical health plan-paid costs PPPY increased from $18,401 in the baseline period to $98,177 in the mCSPC period.

### Table 1. Demographic and clinical characteristics of patients with mCSPC evaluated during the 12-month baseline period

|                                                                 | COM/MA Database (6,517 pts) | Medicare-FFS Database (13,324 pts) |
|-----------------------------------------------------------------|-----------------------------|-----------------------------------|
| **Demographics**                                               |                             |                                   |
| Mean age at index date±SD (median, IQR)                        | 74.8±8.9 (75, 13)           | 75.4±8.0 (74, 12)                 |
| No. yr of index date (%)                                       |                             |                                   |
| 2015                                                            | 634 (9.7)                   | 4,632 (34.8)                      |
| 2016                                                            | 1,305 (20.0)                | 4,381 (32.9)                      |
| 2017                                                            | 1,638 (25.1)                | 4,311 (32.4)                      |
| 2018                                                            | 1,942 (29.8)                | Not available                     |
| 2019                                                            | 998 (15.3)                  | Not available                     |
| **No. race (%)**                                               |                             |                                   |
| White                                                           | Not available               | 9,952 (74.7)                      |
| Black                                                           | Not available               | 2,348 (17.6)                      |
| Asian                                                           | Not available               | 235 (1.8)                         |
| Hispanic                                                        | Not available               | 271 (2.0)                         |
| North American Native                                          | Not available               | 63 (0.5)                          |
| Other*                                                          | Not available               | 455 (3.4)                         |
| **No. region (%)**                                            |                             |                                   |
| South                                                           | 2,331 (35.8)                | 4,657 (35.0)                      |
| West                                                            | 1,760 (27.0)                | 2,538 (19.0)                      |
| Midwest                                                         | 1,470 (22.6)                | 3,271 (24.5)                      |
| Northeast                                                       | 939 (14.4)                  | 2,824 (21.2)                      |
| Unknown                                                         | 17 (0.3)                    | 34 (0.3)                          |
| **No. insurance plan type (%)**                                |                             |                                   |
| Medicare Advantage                                              | 5,370 (82.4)                | Not available                     |
| Medicare-FFS                                                     | Not available               | 13,324 (100.0)                    |
| Commercial                                                      | 1,147 (17.6)                | Not available                     |
| **Clinical characteristics**                                   |                             |                                   |
| Mean Quan CCI±SD (median, IQR)$^{17}$                          | 3.5±2.2 (3, 3)              | 3.6±2.3 (3, 3)                    |
| Hypertension                                                    | 4,696 (72.1)                | 10,415 (72.8)                     |
| Diabetes                                                        | 2,086 (32.0)                | 4,465 (33.5)                      |
| Obesity                                                         | 1,066 (16.4)                | 1,850 (13.9)                      |
| Depression                                                      | 609 (9.3)                   | 1,647 (12.4)                      |
| Falls                                                           | 554 (8.5)                   | 265 (2.0)                         |
| Fractures                                                       | 385 (5.9)                   | 273 (2.0)                         |
| **No. pts with presence of visceral metastases (%)$^†$**        | 906 (13.9)                  | 1,878 (14.1)                      |
| Digestive system                                               | 422 (6.5)                   | 828 (6.2)                         |
| Respiratory system                                             | 311 (4.8)                   | 601 (4.5)                         |
| Brain                                                           | 131 (2.0)                   | 214 (1.6)                         |
| Retroperitoneum                                                 | 99 (1.5)                    | 141 (1.1)                         |
| Adrenal glands                                                  | 28 (0.4)                    | 55 (0.4)                          |
| Excretory system                                                | 23 (0.4)                    | 199 (1.5)                         |
| Reproductive system                                             | 1 (0.0)                     | 16 (0.1)                          |
| **Laboratory tests and results:**                              |                             |                                   |
| No. pts with PSA (%)                                           | 4,940 (75.8)                | 10,588 (79.5)                     |
| No. pts with PSA test result available (%)                     | 2,535 (38.9)                | 212 (1.6)                         |
| Mean ng/ml test result±SD (median, IQR)$^†$                     | 113.9±549.6 (8, 32)         | 11.8±17.2 (5, 12)                 |
| No. pts with testosterone test (%)                             | 1,006 (15.4)                | 1,908 (13.6)                      |
| No. pts with testosterone test result available (%)            | 501 (7.7)                   | Not available                     |
| Mean ng/dl test result±SD (median, IQR)$^†$                     | 244.6±232.5 (232, 403)      | Not available                     |
| No. pts with use of imaging tests (%):                         |                             |                                   |
| Computerized tomography                                        | 3,554 (54.5)                | 7,860 (59.0)                      |
| Bone scan                                                      | 2,195 (33.7)                | 3,906 (29.3)                      |
| Magnetic resonance imaging                                     | 1,553 (23.8)                | 3,609 (27.1)                      |
| Positron emission tomography                                   | 468 (7.2)                   | 704 (5.3)                         |
| No. pts with presence of first PC diagnosis (%)                |                             |                                   |
| >60 days prior to index date (proxy for primary progressive mCSPC) | 4,168 (64.0)               | 8,777 (65.9)                      |
| ≤60 days prior to or on index date (proxy for de novo mCSPC)    | 2,349 (36.0)                | 4,547 (34.1)                      |

* Other refers to other races, more than 1 race or unknown race.
† Visceral metastases included metastasis to digestive system, respiratory system, brain, retroperitoneum, adrenal glands, excretory system and/or reproductive system (based on NCCN Guidelines and National Cancer Institute definition) and were further refined based on clinical opinion.$^{15,27}$
‡ Latest test result prior to index date during 12-month baseline period was used.
REAL-WORLD MANAGEMENT OF MCSPC IN THE U.S.

Table 2. Therapy received in patients with mCSPC

|                           | COM/MA Database (6,517 pts) | Medicare-FFS Database (13,324 pts) |
|---------------------------|-----------------------------|-----------------------------------|
| Mean mos duration of mCSPC period±SD (median, IQR)* | 13.3±12.0 (9.6, 15.6) | 12.8±9.9 (10.5, 15.6) |
| No. pts with no mCSPC medication† or bilateral orchiectomy† (%) | 2,450 (37.6) | 6,967 (47.8) |
| No. pts with mCSPC therapy (%) | 4,067 (62.4) | 6,957 (52.2) |
| Mean mos time from index date to start of 1L therapy±SD (median, IQR)§ | 1.8±4.0 (0.5, 1.6) | 1.7±3.2 (0.7, 1.2) |
| Mean mos duration of 1L therapy±SD (median, IQR)¶ | 12.5±10.9 (9.4, 13.7) | 10.5±8.9 (8.1, 13.0) |

* mCSPC period was defined as period from index date until date of progression to castration resistance or end of followup.
† No medications used for mCSPC during entire mCSPC period.
‡ bilateral orchiectomy or 2 unilateral orchiectomies (including 1 in right side and 1 in left side). Was evaluated prior to index date (if available, data prior to January 1, 2014 were used) or during mCSPC period.
§ 1L therapy started on date of first claim for a bilateral orchiectomy or an appropriate medication for mCSPC patients after index date. If a patient received an orchiectomy prior to index date (if available, data prior to January 1, 2014 were used), date of start of 1L therapy was set to index date.
¶ Duration of 1L therapy was defined as number of months between start of the 1L therapy to earliest of (a) use of a new medication for mCSPC that was not part of the 1L therapy or (b) end of mCSPC period.
†† ADT monotherapy [ADT medications§ or bilateral orchiectomy¶] as 1L: 2,960 (45.4, 72.8) | 6,105 (45.8, 87.8)
ADT with at least one 90-day episode †‡ | 2,042 (31.3, 50.2) | 5,135 (38.5, 73.8)
ADT with no 90-day episode†‡ | 918 (14.1, 22.6) | 970 (7.3, 13.9)
First-generation androgen signaling inhibitors only§§ | 269 (4.1, 6.6) | 538 (4.0, 7.7)
Abiraterone acetate or docetaxel§§ | 838 (12.9, 20.6) | 316 (2.4, 4.5)
Abiraterone acetate: | 471 (7.2, 11.6) | 109 (0.6, 1.6)
Abiraterone acetate + Plus prednisone¶¶ | 470 (7.2, 11.6) | 92 (0.7, 1.3)
Docetaxel: | 364 (5.6, 9.0) | 207 (1.6, 3.0)
Abiraterone acetate + docetaxel | 3 (0.0, 0.1) | 0 (0.0, 0.0)
No. pts with ADT monotherapy only*** (bilateral orchiectomy¶ or ADT medications§ during entire mCSPC period (%) | 2,806 (43.1) | 5,121 (38.4)
ADT medications§ during entire mCSPC period (%): | | |
ADT only with no bilateral orchiectomy | 2,776 (42.6) | 4,948 (37.1)
ADT only with bilateral orchiectomy | 7 (0.1) | 0 (0.0)
Orchiectomy with no ADT medications | 23 (0.4) | 172 (1.3)

COM/MA and from $14,933 to $65,164 (Medicare-FFS), mainly driven by an increase in OP costs from $11,876 to $62,793 and from $6,302 to $22,785, respectively, as well as an increase in acute hospitalization costs from $2,422 to $16,074 and from $5,738 to $27,107, respectively (fig. 2). Mean health plan-paid pharmacy costs PPPY increased from $27,107 to $62,793 and from $6,422 to $16,074, respectively (fig. 2). Mean health plan-paid pharmacy costs PPPY increased from $27,107 to $62,793 and from $6,422 to $16,074, respectively (fig. 2).

Using the largest retrospective cohort of men with mCSPC studied to date, this analysis of current treatment patterns of commercially insured, Medicare Advantage, and Medicare-FFS patients in the U.S. demonstrates that 38%–48% of men with mCSPC remained untreated or deferred treatment, 45%–46% of them received only ADT monotherapy as their 1L treatment, and 38%–43% only received ADT monotherapy during the entire mCSPC period. These findings are noteworthy given demonstrated superior efficacy of abiraterone acetate and docetaxel compared to ADT monotherapy (hazard ratios for death of 0.61–0.78) and inclusion of ADT with abiraterone acetate plus prednisone or ADT with docetaxel as category 1 treatment options preferred over ADT monotherapy as a category 2A treatment for mCSPC in the NCCN Guidelines. This underutilization of abiraterone and docetaxel occurred during a time when evidence supporting their use was strong, albeit largely limited to high-volume or high-risk patients, with the exception of 1 trial outside of the U.S. Moreover, the studies supporting the use of abiraterone were not published until July near the end of the study period for the Medicare-FFS database. Nonetheless, the continued
underutilization of these agents even in the more recent time period in the COM/MA database highlights a mismatch between guideline recommendations and real-world practice. Although additional data (not shown here) revealed that 13%–16% of patients had only lymph node metastases at diagnosis (~15%–18% among those who received ADT monotherapy), and that mean age and Quan CCI were slightly higher among COM/MA patients with treatment deferral/ADT monotherapy (~1 year older than the overall population), potentially suggesting that they may be less fit for intensive treatment, these factors cannot completely explain the underutilization of abiraterone and docetaxel. In addition, similar findings were seen in a recent study of Medicare patients (2009–2018) with mCSPC, where 1L docetaxel was only used by 4.8%.

![Figure 1. 1L therapy in patients with mCSPC by year of index date, COM/MA database.](image)

**Table 3. All-cause HRU in patients with mCSPC**

|                      | COM/MA Database (6,517 pts) | Medicare-FFS Database (13,324 pts) |
|----------------------|-----------------------------|-----------------------------------|
|                      | Baseline Period | mCSPC Period  | Baseline Period | mCSPC Period  |
| **Acute hospitalizations:** |                |                |                |                |
| No. pts with ≥1 acute hospitalization episode (%) | 1,076 (16.5) | 2,902 (44.5) | 6,469 (34.9) | 7,250 (54.4) |
| Mean No. PPPY acute hospitalizations ± SD (median, IQR) | 0.2±0.6 | 1.6±3.2 | 0.5±1.0 | 2.3±4.7 |
| Mean total days of acute hospitalization± SD (median, IQR) | 1.1±4.2 | 12.0±32.2 | 3.0±8.7 | 15.8±38.8 |
| **Rehabilitation/SNF stays:** |                |                |                |                |
| No. pts with ≥1 rehabilitation/SNF stay (%) | 258 (4.0) | 935 (14.3) | 969 (7.3) | 2,588 (19.3) |
| Mean No. PPPY rehabilitation/SNF stays ± SD (median, IQR) | 0.6±0.3 | 0.4±1.5 | 0.2±0.8 | 1.0±3.2 |
| Mean total days of rehabilitation/SNF stay ± SD (median, IQR) | 1.5±8.9 | 8.8±33.2 | 2.6±12.8 | 13.8±44.2 |
| **ER visits:** |                |                |                |                |
| No. pts with ≥1 ER visit (%) | 2,661 (40.8) | 3,634 (55.8) | 6,250 (46.9) | 7,037 (52.8) |
| Mean No. PPPY ER visits ± SD (median, IQR) | 1.0±2.1 | 2.7±6.9 | 1.7±3.1 | 3.3±7.2 |
| **OP services:** |                |                |                |                |
| No. pts with ≥1 OP service (%) | 6,357 (97.5) | 6,394 (98.1) | 13,224 (99.2) | 13,270 (99.6) |
| Mean No. PPPY claims for OP services ± SD (median, IQR) | 4.7±63.3 | 134.7±159.6 | 37.7±313 | 97.6±105.1 |
| **Other services:** |                |                |                |                |
| No. pts with ≥1 other service (%) | 5,373 (82.4) | 5,368 (82.4) | 1,712 (12.8) | 4,683 (35.1) |
| Mean No. PPPY claims for other services ± SD (median, IQR) | 21.1±31.5 | 37.6±68.0 | 0.3±1.0 | 2.1±4.6 |
| **Pharmacy claims:** |                |                |                |                |
| No. pts with ≥1 claim (%) | 5,550 (85.2) | 5,459 (83.8) | 12,782 (95.9) | 12,826 (96.3) |
| Mean No. PPPY claims ± SD (median, IQR) | 30.2±34.5 | 38.7±42.8 | 21.9±17.8 | 27.2±20.1 |

* mCSPC period was defined as period from mCSPC index date until date of progression to castration resistance or end of followup.
† OP services included visits to a physician’s office or hospital outpatient visits.
‡ For COM/MA database, other services included home health, durable medical equipment and lab services not otherwise classified. For Medicare-FFS database, other services included home health and hospice.
of treated patients and novel agents (abiraterone acetate, apalutamide, enzalutamide) by 4.5%. A prior study also assessed real-world mCSPC treatment patterns using commercial claims (2000–2013; i.e., before the introduction of abiraterone acetate and docetaxel for mCSPC) and reported consistent findings: 51% received guideline-recommended medical or surgical castration, and 31% received no castration or drug therapy, including corticosteroids, over a mean followup of ∼3 years.

The current study revealed that a slight decrease in the use of 1L ADT monotherapy from 2015–2017 to 2018–2019 was offset by an increase in the use of abiraterone acetate. However, despite receiving U.S. Food and Drug Administration approval for mCSPC in February 2018, abiraterone acetate was used in only 10% of mCSPC patients in 2018–2019. In addition, while the use of docetaxel with ADT has been a standard of care for mCSPC since 2015, its use was observed in only 7% of patients in 2015–2017 and in even fewer patients (4%) in 2018–2019. Nevertheless, the overall use of abiraterone or docetaxel remained similar in the 2 periods. Whether the approval of the newer agents apalutamide and enzalutamide leads to changes in the management of mCSPC in the future remains to be determined.

In addition to treatment patterns, this study provides a comprehensive overview of the economic burden of mCSPC. All-cause HRU substantially increased with the onset of metastasis, leading to 4–5 times higher associated health plan-paid costs in the mCSPC period vs the baseline period. Further research is warranted to determine if the lack of exposure to more effective treatments contributed to the high HRU and medical costs observed. Although HRU and health care costs post-progression to mCRPC were not assessed in this study, 2 recent claims-based studies estimated a total cost of care ranging from $139,847–$182,156 PPPY among commercially insured (with Medicare Supplemental) patients with mCRPC. This is substantially higher than the $108,767 (COM/MA) and $69,639 (Medicare-FFS) of total health care costs observed in mCSPC patients in the current study. The impact of earlier treatment of mCSPC beyond ADT monotherapy on clinical and economic outcomes warrants further evaluation.

The results obtained in this study were consistent across the 2 databases and any differences observed may be due to variation in coverage policy, length of patient continuous enrollment, and study period.

As with all claims-based studies, coding inaccuracies may have led to case misidentification since analyses of claims data depend on correct diagnosis, procedure, and drug codes. For example, some patients may have been misclassified as untreated if orchiectomy was conducted before the beginning of the data stream; as orchiectomy is an uncommon form

Figure 2. Mean all-cause health plan-paid costs in 2019 U.S. dollars (USD) in patients with mCSPC (PPPY). a, mCSPC period was defined as period from index date until date of progression to castration resistance or end of followup. b, OP service was defined as either visit to physician’s office or hospital outpatient visit. c, for COM/MA database, other services included home health, durable medical equipment and lab services not otherwise classified. For Medicare-FFS database, other services included home health and hospice.
of ADT, the number of men affected by this is likely small. In addition, prescription claims do not necessarily indicate that the dispensed medication was taken as prescribed; therefore, reported treatment utilization may have been overestimated. Reasons for treatment discontinuation were also not available. The study period also predated the U.S. Food and Drug Administration approvals and inclusion of apalutamide and enzalutamide for mCSPC in the NCCN Guidelines.\(^{15,18}\) Lastly, the study included patients with Medicare-FFS, Medicare Advantage, and commercial insurance coverage, who may not be representative of the general U.S. population or patients without health insurance (with potentially worse outcomes and/or important unmet needs).\(^{26}\) Nonetheless, administrative claims data remain a valuable source of information, as they comprise a valid and large data pool and have the advantage of reflecting patient management in the real-world setting.

**CONCLUSION**

The findings of this retrospective U.S. real-world study highlight that the vast majority of mCSPC patients are not receiving agents that have recently shown superior treatment outcomes compared to ADT monotherapy. Despite level 1 evidence and updated NCCN recommendations,\(^{18}\) adoption of more efficacious therapies like abiraterone acetate and docetaxel remained low in this patient population. The substantial clinical and economic burden in patients with mCSPC highlights the importance of earlier and more effective treatment, although the impact of increased use of agents known to reduce progression on real-world clinical and economic outcomes has not been assessed. Given more recent data and an expanding pool of agents that improve outcomes relative to ADT monotherapy, whether treatment patterns change in the future requires further study.

**ACKNOWLEDGMENTS**

Medical writing support was provided by a professional medical writer, Christine Tam, an employee of Analysis Group, Inc.

**REFERENCES**

1. Cattrini C, Castro E, Lozano R et al: Current treatment options for metastatic hormone-sensitive prostate cancer. Cancers (Basel) 2019; 11: 1395.
2. Teo MY, Rathiopf DE and Kantoff P: Treatment of advanced prostate cancer. Ann Rev Med 2019; 70: 479.
3. Rajaram P, Rivera A, Muthima K et al: Second-generation androgen receptor antagonists as hormonal therapeutic approaches for three forms of prostate cancer. Molecules 2020; 25: 2448.
4. Armstrong AJ, Szmulewitz RZ, Petrylak DP et al: ARCHES: a randomized, phase III study of androgen deprivation therapy with enzalutamide or placebo in men with metastatic hormone-sensitive prostate cancer. J Clin Oncol 2019; 37: 2974.
5. Chi KN, Agarwal N, Bjartell A et al: Apalutamide for metastatic, castration-sensitive prostate cancer. N Engl J Med 2019; 381: 13.
6. Fizazi K, Tran N, Fein L et al: Abiraterone plus prednisone in metastatic, castration-sensitive prostate cancer. N Engl J Med 2017; 377: 352.
7. Fizazi K, Tran N, Fein L et al: Abiraterone acetate plus prednisone in patients with newly diagnosed high-risk metastatic castration-sensitive prostate cancer (LATITUDE): final overall survival analysis of a randomised, double-blind, phase 3 trial. Lancet Oncol 2019; 20: 686.
8. James ND, de Bono JS, Spears MR et al: Abiraterone for prostate cancer not previously treated with hormone therapy. N Engl J Med 2017; 377: 398.
9. James ND, Sydes MR, Clarke NW et al: Addition of docetaxel, zoledronic acid, or both to first-line long-term hormone therapy in prostate cancer (STAMPEDE): survival results from an adaptive, multarm, multistage, platform randomised controlled trial. Lancet 2016; 387: 1163.
10. Kyriakopoulus CE, Chen YH, Carducci MA et al: Chemohormonal therapy in metastatic hormone-sensitive prostate cancer: long-term survival analysis of the randomized phase III E3805 CHAARTED trial. J Clin Oncol 2018; 36: 1080.
11. Sweeney CJ, Chen YH, Carducci M et al: Chemo-hormonal therapy in metastatic hormone-sensitive prostate cancer. N Engl J Med 2015; 373: 737.
12. Wallis CJ, Klaassen Z, Bhindi B et al: Comparison of abiraterone acetate and docetaxel with androgen deprivation therapy in high-risk and metastatic hormone-naive prostate cancer: a systematic review and Network meta-analysis. Eur Urol 2018; 73: 834.
13. U.S. Food and Drug Administration (FDA): FDA approves enzalutamide for metastatic castration-sensitive prostate cancer. U.S. Food and Drug Administration 2019. Available at https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-enzalutamide-metastatic-castration-sensitive-prostate-cancer. Accessed July 31, 2020.
14. U.S. Food and Drug Administration (FDA): FDA approves apalutamide for metastatic castration-sensitive prostate cancer. U.S. Food and Drug Administration 2019. Available at https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-apalutamide-metastatic-castration-sensitive-prostate-cancer. Accessed November 23, 2020.
15. National Comprehensive Cancer Network® (NCCN®): NCCN Clinical Practice Guidelines in Oncology—Prostate Cancer. National Comprehensive Cancer Network 2020. Referenced with permission from the NCCN clinical practice guidelines in Oncology (NCCN Guidelines®) for prostate cancer V3.2020. © National comprehensive cancer Network, Inc. 2020. All rights reserved. Accessed November 23, 2020. To view the most recent and complete version of the guideline, go online to NCCN.org. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.
16. Freedland S, Ke X, Lafeuille M et al: Identification of patients with metastatic castration-sensitive or metastatic castration-resistant prostate cancer using administrative health claims and laboratory data. Curr Med Res Opin 2021; 37: 609.
17. Quan H, Sundararajan V, Halfon P et al: Coding algorithms for defining comorbidities in ICD-9-CM and ICD-10 administrative data. Med Care 2005; 43: 1130.
18. National Comprehensive Cancer Network® (NCCN®). NCCN Clinical Practice Guidelines in Oncology—Prostate Cancer. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for...
real life: analysis from a commercial claims database. Clin Genitourin Cancer 2017; 15:273.e271.
22. U.S. Food and Drug Administration (FDA). FDA approves abiraterone acetate in combination with prednisone for high-risk metastatic castration-sensitive prostate cancer. U.S. Food and Drug Administration 2018. Available at https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-abiraterone-acetate-combination-prednisone-high-risk-metastatic-castration-sensitive-prostate-cancer-(mCSPC). Accessed July 29, 2020.
23. Belderbos BPS, de Wit R, Lolkema MPJ et al: Novel treatment options in the management of metastatic castration-naive prostate cancer; which treatment modality to choose? Ann Oncol 2019; 30:1591.
24. Appukkuttan S, Tangirala K, Babajayan S et al: A retrospective claims analysis of advanced prostate cancer costs and resource use. Pharmacoecon Open 2020; 4: 439.
25. Wu B, Li SS, Song J et al: Total cost of care for castration-resistant prostate cancer in a commercially insured population and a Medicare supplemental insured population. J Med Econ 2020; 23:54.
26. Mahal BA, Aizer AA, Ziehr DR et al: The association between insurance status and prostate cancer outcomes: implications for the Affordable Care Act. Prostate Cancer Prostatic Dis 2014; 17:273.
27. National Cancer Institute (NCI): Visceral. National Cancer Institute 2020. Available at https://www.cancer.gov/publications/dictionaries/cancer-terms/def/visceral. Accessed August 27, 2020.

EDITORIAL COMMENT

Since 2014, multiple randomized clinical trials have established that up-front intensification of androgen deprivation therapy with a novel hormonal therapy (such as abiraterone, enzalutamide or apalutamide) or docetaxel significantly improve survival outcomes in men with mCSPC. However, these results have not yet impacted the treatment paradigm of men with mCSPC in the real world.

In a retrospective analysis from 2 large administrative health claim databases consisting of ~20,000 patients, Ryan and colleagues show that <10% patients with mCSPC received intensified ADT. When compared to 2015–2017, the use of intensified ADT in 2018–2019 did not change in this study. Along the same line, 3 additional real-world studies presented at the 2021 American Society of Clinical Oncology (ASCO) Virtual Annual Meeting (abstracts 5072, 5073, 5074) showed less than a third of men with mCSPC received intensified ADT in the United States each year over the past 4–5 years. These findings are quite alarming as intensified ADT regimens have not only shown remarkable improvement in overall survival but do so without adversely impacting the quality of life of these men.1,2

Investigations aimed at understanding the underlying reason(s) for such an enormous disconnect between the results of these large positive phase 3 registration trials and real-world practice should be highly prioritized. Possible causes for this disconnect may include a combination of 1 or more of the following: lack of awareness, communication barriers between physicians and patients, lack of access to these drugs, concern for financial and drug toxicities, or other barriers such as racial or social disparities, disease characteristics, or co-morbidities. In light of these findings, corrective action will need to be taken with the help of various stakeholders including physicians, professional societies, patient advocacy groups, pharmaceutical companies, and regulatory and governmental agencies. Until this happens, practice-changing trials are not changing practice in the real world.

Umang Swami,1 and Neeraj Agarwal1
1Division of Medical Oncology
Department of Internal Medicine
Huntsman Cancer Institute, University of Utah
Salt Lake City, Utah

REFERENCES
1. Swami U, McFarland TR, Nussenzveig R, et al: Advanced prostate cancer: treatment advances and future directions. Trends Cancer 2020; 6: 702.
2. Agarwal N, McQuarrie K, Bjartell A, et al: Health-related quality of life after apalutamide treatment in patients with metastatic castration-sensitive prostate cancer (TITAN): a randomised, placebo-controlled, phase 3 study. Lancet Oncol 2019; 20: 1518.