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Impact of Demographic and Socioeconomic Factors on Survival Associated With Androgen Receptor Pathway Inhibitor Use in Metastatic Prostate Cancer: An Analysis of the Surveillance, Epidemiology, and End Results (SEER)-Medicare Database

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Abstract

Purpose

Androgen receptor pathway inhibitors (ARPIs) are guideline-recommended standard therapy for metastatic prostate cancer. However, real-world utilization and survival differences across demographic and socioeconomic groups remain incompletely characterized. We assessed factors associated with overall survival (OS) among ARPI users and non-users in a population-based cohort.

Methods

We performed a retrospective cohort study using Surveillance, Epidemiology, and End Results (SEER)-Medicare data (2013-2017) of Medicare beneficiaries aged 65 or greater with metastatic prostate cancer (excluding secondary malignancies or <6 months of follow-up). ARPI exposure (abiraterone/enzalutamide) was identified via Medicare Part D claims. Patients were stratified by ARPI receipt, and Kaplan-Meier estimates and multivariable Cox proportional hazards models evaluated predictors of OS.

Results

A total of 5,889 patients were included; 2,298 (39%) patients received an ARPI. ARPI users were predominantly White (77.1%), resided in urban areas (98.1%), and more frequently belonged to higher socioeconomic groups (73.0%). Kaplan-Meier analyses demonstrated significant differences in OS by age and race among ARPI users, whereas among non-users, OS differed according to age, race, geographic location, socioeconomic status, and marital status. In multivariable analyses, among ARPI users, age $\geq$ 73 years was associated with an increased hazard of death (adjusted hazard ratio (aHR) 1.54, 95% confidence interval (CI) 1.39-1.71), whereas Black race was associated with a lower hazard of death than White race (aHR 0.83, 95% CI 0.71-0.97). Among non-users, age $\geq$ 73 years (aHR 2.25, 95% CI 2.01-2.51), low socioeconomic status (aHR 1.25, 95% CI 1.07-1.46), and never having married (aHR 1.53, 95% CI 1.33-1.77) were associated with worse OS.

Conclusion

In this SEER-Medicare cohort, 39% of patients with metastatic prostate cancer received an ARPI. Older age was associated with worse OS regardless of ARPI use, whereas socioeconomic disparities in survival were observed only among patients who did not receive ARPI therapy. This observed association suggests that improving access to ARPIs may be associated with reduced outcome disparities in metastatic prostate cancer, though prospective studies are needed to determine causality.

Categories: Public Health, Oncology

Keywords: androgen receptor pathway inhibitors, health care disparity, healthcare disparity, prostate cancer, real world

Introduction

Prostate cancer is the most commonly diagnosed cancer and one of the leading causes of cancer-related deaths in American men [1]. Most prostate cancers are diagnosed at an early stage with favorable outcomes. However, the incidence of metastatic prostate cancer has increased over the last decade [1,2]. For patients

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with metastatic disease, the five-year survival rate remains low at approximately 38% [3]. Androgen receptor pathway inhibitors (ARPIs) are a cornerstone of guideline-recommended treatment for metastatic prostate cancer [2,4]. Their use has improved survival outcomes in randomized clinical trial settings in both metastatic castration-sensitive prostate cancer (mCSPC) and metastatic castration-resistant prostate cancer (mCRPC) [5–9]. Abiraterone acetate, a CYP17A1 inhibitor, and enzalutamide, an androgen receptor blocker, were approved in 2011 and 2012, respectively, for the treatment of mCRPC. They are now routinely used in the management of castration-sensitive disease as well [7,9]. Despite their efficacy, access to ARPIs is limited by high costs, with studies reporting a significant financial burden, such as an annual incremental budget impact of \$510,641 for enzalutamide [10]. In addition, disparities in prostate cancer care based on race, geography, and socioeconomic status persist, with Black patients, rural residents, and those with lower socioeconomic status being less likely to receive guideline-concordant care [11–15]. Factors such as income, insurance status, education, and geographic access to care may further influence both treatment receipt and clinical outcomes among patients with metastatic prostate cancer [13,15]. Given the substantial survival benefits associated with ARPIs, unequal access to these therapies may contribute to persistent disparities in outcomes across demographic and socioeconomic groups. Although racial and socioeconomic differences in treatment outcomes have been explored in clinical trials and retrospective studies, population-based data evaluating survival among patients receiving contemporary ARPI therapy in routine clinical practice remain limited [16–18]. Furthermore, clinical trial populations may underrepresent racial minorities, older adults, rural residents, and socioeconomically disadvantaged patients, highlighting the need for real-world analyses that better reflect contemporary practice. As evidence-based guidelines define standards of care, understanding survival outcomes among patients treated with abiraterone acetate and enzalutamide in routine clinical practice is critical to identifying potential disparities in treatment benefit and informing equitable cancer care [19,20]. In this study, we sought to evaluate demographic and socioeconomic factors associated with survival outcomes among patients with metastatic prostate cancer receiving ARPI abiraterone acetate or enzalutamide and those who did not, using a population-based dataset. We hypothesized that lower socioeconomic status and racial minority background would be associated with worse overall survival (OS), but that receipt of ARPI therapy would attenuate these survival disparities. These findings may help inform strategies to address disparities and improve equitable outcomes in prostate cancer care.

Materials And Methods

Data source

We conducted a retrospective analysis using the Surveillance, Epidemiology, and End Results (SEER)-Medicare linked database, which combines National Cancer Institute (NCI) cancer registry data with Medicare administrative claims, capturing approximately 30% of US cancer diagnoses from demographically representative regions. This database links longitudinal Medicare Part D prescription claims, enabling precise tracking of oral therapies like ARPIs with census tract-level socioeconomic metrics (e.g., median income, poverty, and education). Additionally, it provides representation across diverse racial and ethnic subgroups, which provides robust population-level data needed for this study.

Study population

SEER-Medicare data capture patients who are 65 years and older enrolled in Medicare in SEER geographic areas. Eligible patients had a confirmed diagnosis of metastatic prostate cancer (International Classification of Diseases for Oncology, 3rd Edition (ICD-O-3) code C61.9, with metastatic disease indicated by American Joint Committee on Cancer (AJCC) stage IV or M1 status. The study period spanned a historical observation window from January 1, 2013, to December 31, 2017. Data were extracted from the database for all patients diagnosed within this timeframe. Patients were excluded if they had incomplete demographic or treatment data, secondary malignancies, initiated ARPI therapy and received fewer than two prescriptions, or had less than six months of follow-up data, which indicated insufficient response observation time.

Variables

The primary variable was the use of either abiraterone acetate or enzalutamide, identified through Medicare Part D claims using National Drug Codes (NDCs) [21]. Patients were categorized as ARPI users (received either ARPI alone or in combination with other therapies) if they received two or more dispensed Part D prescriptions for either agent. Covariates included age at diagnosis (continuous and categorized as <73 or ≥73 years), race/ethnicity (White, Black, and Other), geographic location (urban vs. rural, based on Rural-Urban Continuum Codes) [22], and marital status (married, divorced/separated/widowed, or never married). Socioeconomic status was assessed using the SEER census tract poverty indicator, an area-level measure based on the percentage of residents living below the federal poverty level within a patient's census tract, and was categorized into high (0%-5% poverty), middle (6%-20% poverty), and low (21%-100% poverty) socioeconomic groups. The primary outcome was OS, defined as the time from diagnosis to death from any cause or last follow-up (December 31, 2017).

Statistical analysis

Baseline demographic and socioeconomic characteristics were summarized using descriptive statistics.

Continuous variables (e.g., age) were reported as median and interquartile range, while categorical variables (e.g., race/ethnicity, marital status, geographic location, and socioeconomic status) were presented as frequencies and proportions. To evaluate survival outcomes and the impact of socioeconomic and demographic factors, Kaplan-Meier survival curves were generated to estimate OS, stratified by treatment groups (ARPI users vs. non-users). Log-rank tests compared OS distributions between groups. Separate simple and multivariable Cox proportional hazards regression models were fitted among ARPI users and non-users to evaluate associations of demographic and socioeconomic factors with the hazard of death. Variables that were statistically significant in univariable models and satisfied the proportional hazards assumption were included in the multivariable Cox regression model. All hypothesis tests were two-sided, with p < 0.05 considered statistically significant. Analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC, USA) and R version 4.2.3 [23].

Results

Patient characteristics and ARPI utilization

A total of 5,889 patients were included in the analysis. The majority of patients were White (4,515 (76.7%)), were married (3,464 (58.8%)), resided in urban areas (5,790 (98.3%)), and belonged to the middle socioeconomic status group (3,083 (52.4%)). The median age of the cohort was 73 years. Baseline demographic and clinical characteristics are summarized in Table 1. Among all patients, 2,298 (39.0%) received abiraterone acetate or enzalutamide, either alone or in combination with other therapies.

Demographic information: number (%)				
		All	ARPI	Non-ARPI
Number of patients		5,889 (100%)	2,298 (39%)	3,591 (61%)
Age	Age in years, median (IQR)	73 (13)	74 (13)	71 (12)
Race	White	4,515 (76.7)	1,771 (77.1)	2,744 (76.4)
	Black	903 (15.3)	343 (14.9)	560 (15.6)
	Other	449 (7.6)	179 (7.8)	270 (7.5)
	Missing	22 (0.4)	5 (0.2)	17 (0.5)
Marital status	Married	3,464 (58.8)	1,393 (60.6)	2,071 (57.7)
	Divorced, separated, or widowed	1,150 (19.5)	400 (17.4)	750 (20.9)
	Never married	862 (14.6)	340 (14.8)	522 (14.5)
	Missing	3,464 (58.8)	165 (7.2)	248 (6.9)
Location, n (%)	Urban	5,790 (98.3)	2,255 (98.1)	3,535 (98.4)
	Rural	99 (1.7)	43 (1.9)	56 (1.6)
Socioeconomic status	High	1,166 (19.8)	445 (19.3)	721 (20.1)
	Middle	3,083 (52.4)	1,233 (53.7)	1,850 (51.5)
	Low	1,377 (23.4)	521 (22.7)	856 (23.8)
	Missing	263 (4.4)	99 (4.3)	164 (4.6)

TABLE 1: Number of patients (n, %) who received an ARPI (ARPI group) and patients who did not receive ARPI (non-ARPI), stratified by demographic and socioeconomic characteristics.
Data are presented as count (percentage) (n (%)) for categorical variables or median (IQR) for continuous variables.
ARPI: androgen receptor pathway inhibitor; IQR: interquartile range; N: number of patients

Survival analysis

Table 2 summarizes the simple and multivariable Cox proportional hazards regression analyses stratified by ARPI use. Kaplan-Meier survival analyses demonstrated significant differences in OS across demographic and socioeconomic subgroups, with the pattern of associations differing between patients who received

ARPI therapy and those who did not.

	Variable	ARPI users unadjusted HR (95% CI)	p- value	ARPI users adjusted HR (95% CI)	p- value	Non-ARPI users unadjusted HR (95% CI)	p- value	Non-ARPI users adjusted HR (95% CI)	p- value
Age	Age ≥ 73 vs. <73 years	1.56 (1.41-1.73)	<0.001	1.54 (1.39-1.71)	<0.001	2.12 (1.91-2.35)	<0.001	2.25 (2.01-2.51)	<0.001
Race	Black vs. White	0.77 (0.66-0.90)	<0.001	0.83 (0.71-0.97)	0.016	1.29 (1.13-1.46)	<0.001	-	-
	Other vs. White	0.84 (0.68, 1.03)	0.090	0.82 (0.67-1.01)	0.061	0.75 (0.62-0.92)	0.007	-	-
Socioeconomic status	Middle vs. high	0.97 (0.85-1.12)	0.7	-	-	1.10 (0.97-1.26)	0.14	1.46 (1.29-1.65)	<0.001
	Low vs. high	1.02 (0.87-1.20)	0.8	-	-	1.27 (1.09-1.47)	0.002	1.25 (1.07-1.46)	<0.001
Marital status	Divorced/separated/widowed vs. married	1.07 (0.93-1.22)	0.4	-	-	1.60 (1.43-1.80)	<0.001	1.46 (1.29-1.65)	<0.001
	Never married vs. married	1.08 (0.94-1.25)	0.3	-	-	1.39 (1.21-1.59)	<0.001	1.53 (1.33-1.77)	<0.001
Location	Rural vs. urban	1.15 (0.81-1.64)	0.91	-	-	1.52 (1.08-2.14)	0.016	1.23 (0.78-1.94)	0.4

TABLE 2: Univariable and multivariable Cox proportional hazards regression analyses of OS stratified by ARPI use.

HR and 95% CI were estimated using univariate (unadjusted) and multivariate (adjusted) Cox proportional hazards models within the ARPI-treated and non-ARPI cohorts. Multivariate models were adjusted for baseline demographic and socioeconomic covariates (age, race, socioeconomic status, marital status, and geographic location). Dash (-) indicates variables that were excluded from the final adjusted model due to lack of statistical significance in unadjusted analysis or collinearity. All tests were two-sided, and a p-value < 0.05 was considered statistically significant.

ARPI: androgen receptor pathway inhibitor; CI: confidence interval; HR: hazard ratio; OS: overall survival

Patients Who Received ARPI

Among patients who received ARPI therapy, Kaplan-Meier curves and log-rank tests demonstrated significant differences in OS according to age and race (Figures 1, 2). Younger patients (<73 years) had significantly longer OS than older patients (≥73 years) (Figure 1). Black patients demonstrated improved OS compared with White patients (Figure 2).

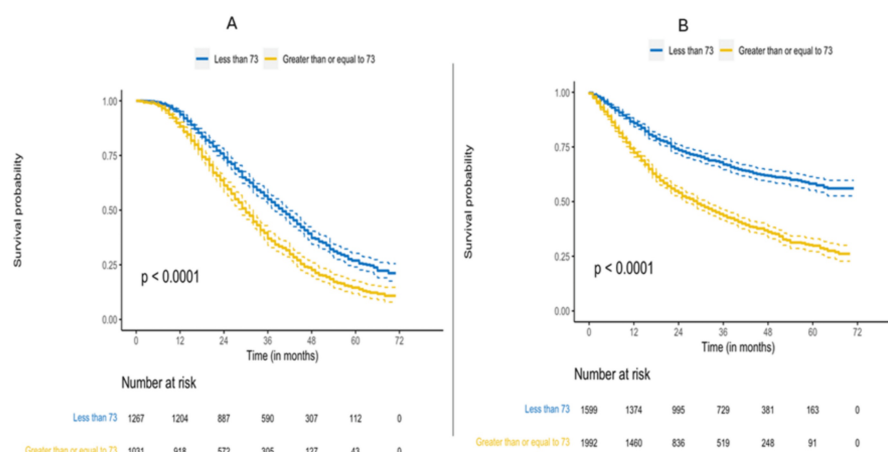


FIGURE 1: Kaplan-Meier estimates of OS showing significant differences in survival among different age groups in both ARPI (A) and non-ARPI (B) groups.

OS: overall survival; ARPI: androgen receptor pathway inhibitor

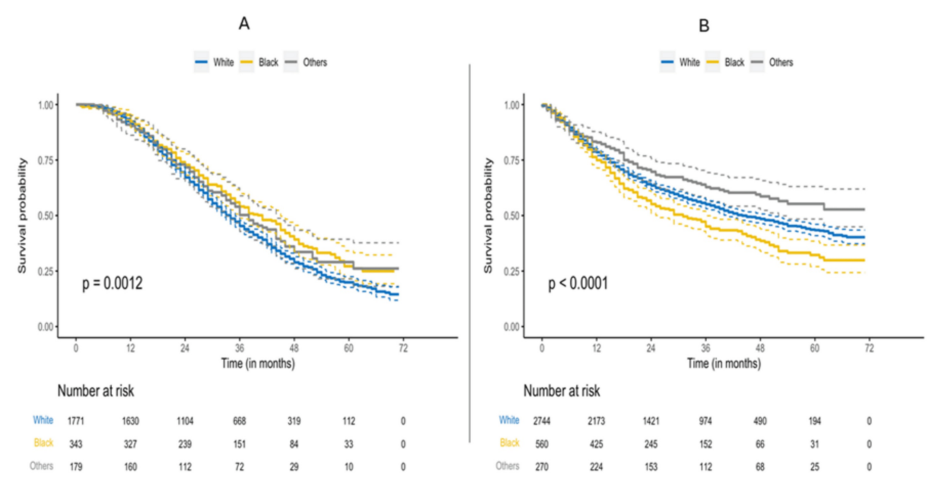


FIGURE 2: Kaplan-Meier estimates of OS showing significant differences in survival among different ethnic groups in both ARPI (A) and non-ARPI (B) groups.

OS: overall survival; ARPI: androgen receptor pathway inhibitor

No statistically significant differences in OS were observed according to geographic location, socioeconomic status, or marital status among ARPI users (Figures 3-5).

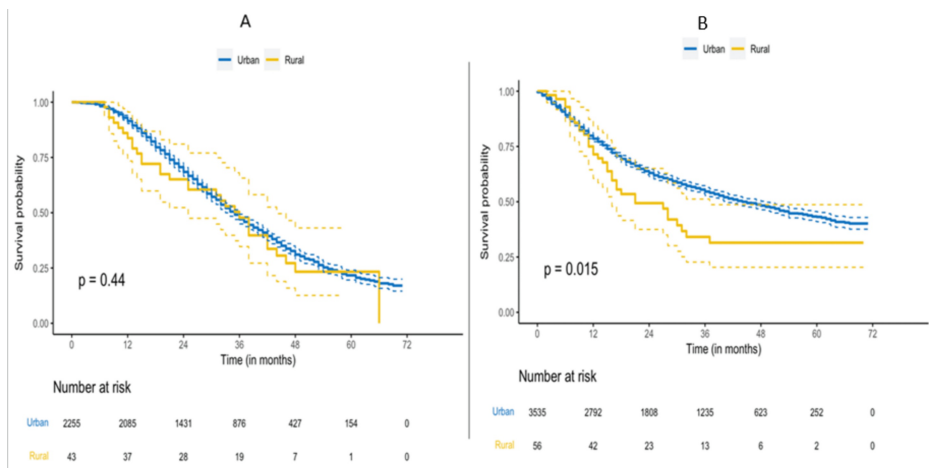


FIGURE 3: Kaplan-Meier estimates of OS showing no significant difference in survival among urban and rural locations in the ARPI group (A) and a significant difference in the non-ARPI group (B).

OS: overall survival; ARPI: androgen receptor pathway inhibitor

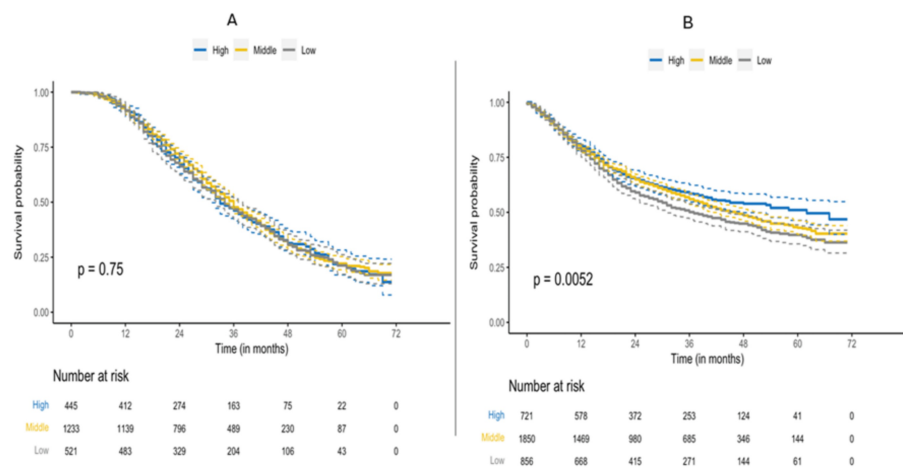


FIGURE 4: Kaplan-Meier estimates of OS showing no difference in survival among different socioeconomic groups in the ARPI group (A) but showing a significant difference in the non-ARPI group (B).

OS: overall survival; ARPI: androgen receptor pathway inhibitor

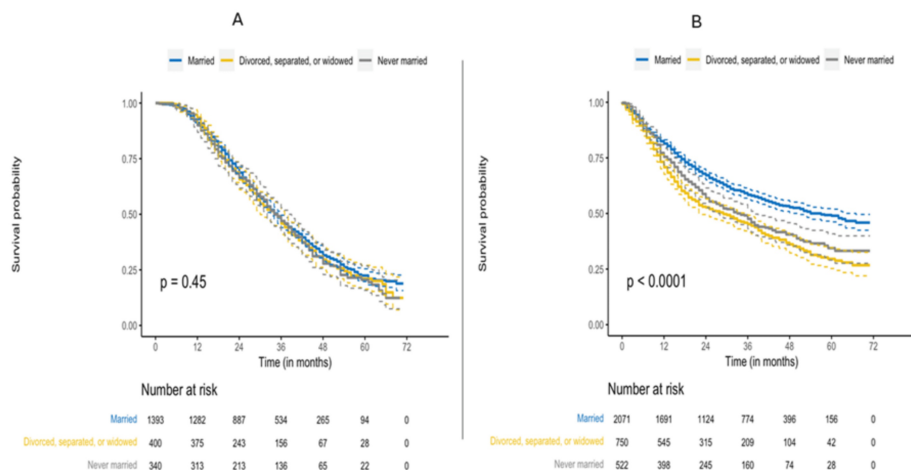


FIGURE 5: Kaplan-Meier estimates of OS showing no difference in survival among different marital statuses in the ARPI group (A) but showing a significant difference in the non-ARPI group (B).

OS: overall survival; ARPI: androgen receptor pathway inhibitor

In the multivariable Cox proportional hazards model, age and race remained significantly associated with the hazard of death after multivariable adjustment. Patients aged ≥ 73 years had a significantly higher hazard of death than those aged < 73 years (adjusted hazard ratio (aHR) 1.54; 95% confidence interval (CI) 1.39-1.71). Black patients had a significantly lower hazard of death than White patients (aHR 0.83; 95% CI 0.71-0.97). Geographic location, socioeconomic status, and marital status were not significantly associated with OS after adjustment.

Patients Who Did Not Receive ARPI

Among patients who did not receive ARPI therapy, Kaplan-Meier curves and log-rank tests demonstrated significant differences in OS according to age, race, geographic location, socioeconomic status, and marital status. Younger patients had significantly better OS than older patients, whereas Black patients had poorer OS than White patients (Figures 1, 2). Patients residing in urban areas had better OS than those in rural areas (Figure 3). Patients with higher socioeconomic status had improved OS compared with those with lower socioeconomic status (Figure 4), and married patients experienced better OS than unmarried patients (Figure 5).

In the multivariable Cox proportional hazards model, age, socioeconomic status, and marital status remained independently associated with OS. Patients aged ≥ 73 years had a significantly higher hazard of death than those aged < 73 years (aHR 2.25; 95% CI 2.01-2.51). Patients with low socioeconomic status had a significantly higher hazard of death than those with high socioeconomic status (aHR 1.25; 95% CI 1.07-1.46). Compared with married patients, divorced, separated, or widowed patients had a higher hazard of death (aHR 1.46; 95% CI 1.29-1.65), as did patients who had never married (aHR 1.53; 95% CI 1.33-1.77). Race was significantly associated with OS in the Kaplan-Meier and univariable analyses but was not included in the multivariable model because its inclusion violated the proportional hazards assumption.

Discussion

In this study, we assessed ARPI utilization and the association between socioeconomic factors and survival among patients with metastatic prostate cancer stratified by ARPI use. The study period (2013-2017) predated the approval of ARPIs for mCSPC cancer; therefore, patients who received ARPIs were likely to have had metastatic castration-resistant disease, whereas the non-ARPI cohort likely included a mixture of castration-sensitive and castration-resistant disease.

The observed ARPI utilization rate of 39% approximates published estimates of the proportion of patients with mCRPC in the Medicare population during this period. Claims-based data in the Medicare fee-for-service population analyses have reported a distribution of approximately 63% mCSPC and 37% mCRPC in similar cohorts [24]. Crucially, this utilization pattern must be interpreted within the regulatory context of the study window, during which ARPIs were FDA-approved exclusively for mCRPC. Prescribing ARPIs for mCSPC during this era would have constituted off-label practice, which was neither supported by standard clinical guidelines at the time nor routinely reimbursed under Medicare Part D. Furthermore, registry and administrative databases like SEER-Medicare lack the granular clinical data necessary to directly distinguish mCSPC from mCRPC without relying on secondary proxy definitions, meaning our broad denominator naturally included non-eligible mCSPC patients. More recent real-world studies demonstrate increasing utilization of ARPIs in Medicare populations, reflecting expanding adoption of this drug class following label expansions into mCSPC [20]. Contemporary global real-world data further confirm that ARPIs remain the predominant systemic therapy for mCRPC disease [25]. However, treatment patterns continue to evolve with earlier use of ARPIs in mCSPC and the incorporation of additional therapeutic classes, including poly(ADP-ribose) polymerase (PARP) inhibitors and radioligand therapies.

Our analysis demonstrated that associations between survival and demographic and socioeconomic factors differed between ARPI-treated and untreated cohorts. Older age was independently associated with worse survival in both groups. Although clinical trials have demonstrated the efficacy and tolerability of ARPIs in older patients, real-world studies suggest more conservative use in this population, likely reflecting concerns regarding comorbidity, frailty, and treatment tolerability [26-29].

Among patients receiving ARPIs, Black race was associated with a lower adjusted hazard of death compared with White race. This finding is consistent with prior literature demonstrating comparable or improved outcomes among Black patients receiving ARPI therapy. A large Veterans Affairs cohort study of 12,355 patients demonstrated longer OS (36.3 vs. 31 months) among Black patients compared with White patients despite higher disease burden [30]. A prospective randomized trial of abiraterone (Abi-Race study) demonstrated comparable survival between Black and White patients, with a trend toward improved prostate-specific antigen (PSA) response in Black patients [16]. In addition, a real-world cohort of approximately 3,800 patients treated with first-line abiraterone demonstrated significantly longer survival among Black patients compared with White patients (23 vs. 17 months) [17]. These findings suggest that Black patients derive at least comparable benefit from ARPI therapy.

The relationship between socioeconomic factors and outcomes in metastatic prostate cancer is complex and multifactorial. Prior studies suggest that socioeconomic disadvantage primarily influences access to and adherence to ARPI therapy rather than intrinsic treatment efficacy [31]. In our study, among patients receiving ARPIs, survival did not significantly differ by socioeconomic status or geographic location after multivariable adjustment. In contrast, among patients not receiving ARPIs, lower socioeconomic status and rural residence were associated with worse survival in unadjusted analyses. These findings suggest that equitable access to effective systemic therapy may help mitigate socioeconomic disparities in survival outcomes. However, causality cannot be inferred from this observational study.

This study has several limitations. The SEER-Medicare population is restricted to older patients and may not be generalizable to younger individuals < 65 years old. Disease classification limitations inherent to claims-based datasets may have resulted in the inclusion of a mixed population of metastatic castration-sensitive and castration-resistant disease. Additionally, important clinical variables such as performance status, metastatic burden, PSA levels, treatment sequencing, and comorbidity indices were not available, introducing the possibility of residual confounding. Moreover, treatment patterns have evolved substantially since the study period, particularly with earlier use of ARPIs and the approval of additional ARPIs, such as darolutamide and apalutamide, for advanced prostate cancer. This evolution of therapy may further confound the appreciation of the impact of ARPIs in the management of prostate cancer. Furthermore, because pharmacy claims were used to capture drug utilization without continuous tracking of monthly Part

D enrollment status, unobserved loss of prescription coverage during follow-up could result in misclassification of exposure duration. Finally, our multivariable models evaluated demographic and socioeconomic variables as independent main effects. We did not formally test for interaction effects or intersectional dynamics (such as the combined influence of race and marital status within specific strata), which limits our ability to determine whether factors like marital status differentially modify outcomes across racial or socioeconomic groups. Future studies with larger sample sizes specifically designed for subgroup interaction analyses are warranted to explore these complex intersecting relationships.

Conclusions

In conclusion, ARPI utilization in this real-world SEER-Medicare cohort reflected expected real-world practice patterns for metastatic disease during the study period. While older age was consistently associated with worse OS, Black race was associated with improved survival among ARPI recipients, and socioeconomic disparities in survival were attenuated in patients receiving ARPI therapy. These observational findings suggest that equitable access to potent systemic therapies may be associated with reduced racial and socioeconomic disparities in metastatic prostate cancer. To translate these insights into improved health equity, health policies and care delivery models should focus on removing financial and structural barriers to novel oral therapeutics, while future prospective studies are needed to confirm these observed associations and optimize equitable drug access.

Additional Information

Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

Concept and design: Samina Hirani, Asit Paul, Roy Sabo

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Critical review of the manuscript for important intellectual content: Asit Paul, Ashimiyu Durojaiye, Roy Sabo, Jian He, John Melson

Supervision: Asit Paul

Disclosures

Human subjects: Informed consent for treatment and open access publication was obtained or waived by all participants in this study. VCU issued approval HM20024560. **Animal subjects:** All authors have confirmed that this study did not involve animal subjects or tissue. **Conflicts of interest:** In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** A gift from the Hyde family to Asit Paul supported this project. Services and products in support of the research project (from RT Sabo) were generated by the VCU Massey Comprehensive Cancer Center Biostatistics Shared Resource, supported, in part, by funding from NIH-NCI Cancer Center Support Grant P30 CA016059. **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

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