Impact of Asian Race on Prognosis in De Novo Metastatic Prostate Cancer

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ABSTRACT

Background: Little is known about the impact of Asian race on the long-term survival outcomes of males with de novo metastatic prostate cancer (PCa). Understanding racial disparities in survival is critical for accurate prognostic risk stratification and for informing the design of multiregional clinical trials. **Methods:** This multiple-cohort study included individual patient-level data for males with de novo metastatic PCa from the following 3 cohorts: LATITUDE clinical trial data (n=1,199), the SEER program (n=15,476), and the National Cancer Database (NCDB; n=10,366). Primary outcomes were overall survival (OS) in LATITUDE and NCDB and OS and cancer-specific survival in SEER. **Results:** Across all 3 cohorts, Asian patients diagnosed with de novo metastatic PCa had better survival than white patients. In LATITUDE, median OS was significantly longer in Asian versus white patients in the androgen deprivation therapy (ADT) + abiraterone + prednisone group (not reached vs 43.8 months; hazard ratio [HR], 0.45; 95% CI, 0.28–0.73; P=.001) as well as in the ADT + placebo group (57.6 vs 32.7 months; HR, 0.51; 95% CI, 0.33–0.78; P=.002). In SEER, among all patients diagnosed with de novo metastatic PCa, median OS was significantly longer in Asian versus white males (49 vs 39 months; HR, 0.76; 95% CI, 0.68–0.84; P<.001). Among those who received chemotherapy, Asian patients again had longer OS (52 vs 42 months; HR, 0.71; 95% CI, 0.52–0.96; P=.025). Using data on cancer-specific survival in SEER resulted in similar conclusions. In NCDB, Asian patients also had longer OS than white patients in aggregate and in subgroups of males treated with ADT or chemotherapy (aggregate: 38 vs 26 months; HR, 0.72; 95% CI, 0.62–0.83; P<.001; ADT subgroup: 41 vs 26 months; HR, 0.71; 95% CI, 0.60–0.84; P<.001; chemotherapy subgroup: 34 vs 25 months; HR, 0.67; 95% CI, 0.57–0.78; P<.001). **Conclusions:** Asian males have better OS and cancer-specific survival than white males with metastatic PCa across different treatment regimens. This should be considered when assessing prognosis and in designing multinational clinical trials.

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Background

Racial and ethnic differences have been shown to affect prognosis and efficacy of prostate cancer (PCa) treatments.[1–3] However, among all 286 phase II/III randomized PCa clinical trials from 1989 to 2020, only 111 (39%) reported data on race or ethnicity.[4] In these clinical trials, races such as Black, Asian, and Hispanic are perennially underrepresented, and Asian males comprise only 1.5% of trial participants.[4,5] Although there has been a growing body of literature addressing disparities between white and Black patients,[6–8] less is known about disparities related to the Asian race.[9] According to our knowledge, few studies have focused on the survival differences between Asian and white males with de novo metastatic PCa.[10,11] Epidemiologic data suggest that Asian males may have lower incidence and cancer-specific mortality than other races. Between 2014 and 2019, the incidence of PCa in Asians was 55 per 100,000, which was lower than that in white (99.9), Black (172.6), Hispanic (85.3), and Native American (79.8) males. Furthermore, Asian males also have the lowest mortality rate (8.6) compared with white (17.8), Black (37.9), Hispanic (15.6), and Native American males (21.0).[12] In this study, we used 3 cohorts—the LATITUDE clinical trial, the SEER program, and the National Cancer Database (NCDB)—to further examine the association between race of and prognosis for patients diagnosed with de novo metastatic PCa. To adjust for known confounding variables such as age, prostate-specific antigen (PSA), Gleason score, ECOG status, and socioeconomic status, patient-level data were balanced by propensity score matching (PSM) before analyses.

Methods

We sampled physiologic males with de novo metastatic PCa from the LATITUDE clinical trial (ClinicalTrials.gov identifier: NCT01715285) from 2013 to 2014, the SEER database from 1975 to 2019, and the NCDB from 2004 to 2013. LATITUDE was an international, phase III, randomized, double-blind comparative study of abiraterone

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acetate + low-dose prednisone + androgen deprivation therapy (ADT) versus ADT alone in newly diagnosed patients with high-risk, metastatic hormone-naïve prostate cancer (mHNPC).

LATITUDE included males (aged ≥18 years) with newly diagnosed mHNPC, confirmed by histology or cytology as PCa, without neuroendocrine differentiation or small cell histology, and positive bone scan or metastatic bony or visceral lesions on CT or MRI. All patients were required to have an ECOG performance status of 0–2 and ≥2 of the 3 high-risk characteristics: Gleason score ≥8, bone scan with ≥3 lesions, and measurable visceral metastasis, but not including lymph node metastasis.[13]

The SEER program is sponsored by the NCI and collects cancer incidence data from population-based cancer registries covering approximately 47.9% of the US population.[14] Data in SEER are collected from both hospital and clinical settings. The registration sites were chosen based on the ability to maintain a high-quality cancer reporting system and for their epidemiologically significant subgroups of the population.

The NCDB is a hospital-based registry, sponsored by the American College of Surgeons and American Cancer Society, and collects patient-level data on approximately 70% of all new cancer cases across >1,500 Commission on Cancer (CoC)–accredited facilities.[15] CoC-accredited hospitals are larger and located more often in urban geographic areas.

Inclusion and exclusion criteria for patients from all 3 databases are shown in supplemental eTable 1 (available with this article at JNCCN.org). This study was deemed to be exempt from Institutional Board Review at the participating research institutions.

Study Participants

In LATITUDE, 1,199 patients with mHNPC were originally sampled, of whom 597 were treated with ADT + abiraterone + prednisone and 602 were treated with ADT + placebo. A total of 275 patients were from Asian countries: 137 from China, 70 from Japan, 32 from Korea, 30 from Israel, and 6 from Malaysia. We excluded patients of races other than white and Asian and those lacking data on age; PSA, hemoglobin (Hb), and lactate dehydrogenase (LDH) levels; ECOG performance status; Gleason score; and visceral and bone metastasis (supplemental eFigure 1). The final sample included 764 patients.

In SEER, 36,207 males with metastatic PCa from 2000 to 2019 were originally sampled. Data for those diagnosed with de novo metastatic PCa are available from 2004 onward, whereas the pathologic Gleason score was available only from 2010 onward. To capture those with data on both variables, our final sample included males with ICD-O-3/WHO 2008 = "Prostate" and combined summary stage = "distant" from 2010 to 2019. We excluded patients aged ≤18 years, those of races other than white or Asian, and those who lacked information on age, Gleason score, PSA level, median household income, or follow-up information (supplemental eFigure 1). The final sample included 15,476 patients.

In the NCDB, 52,331 males with metastatic PCa from 2004 to 2013 were originally sampled. We excluded patients aged ≤18 years, those of races other than white or Asian, and those who were missing survival outcome, follow-up information, median household income, or Gleason score (supplemental eFigure 1). The final sample included 10,366 patients.

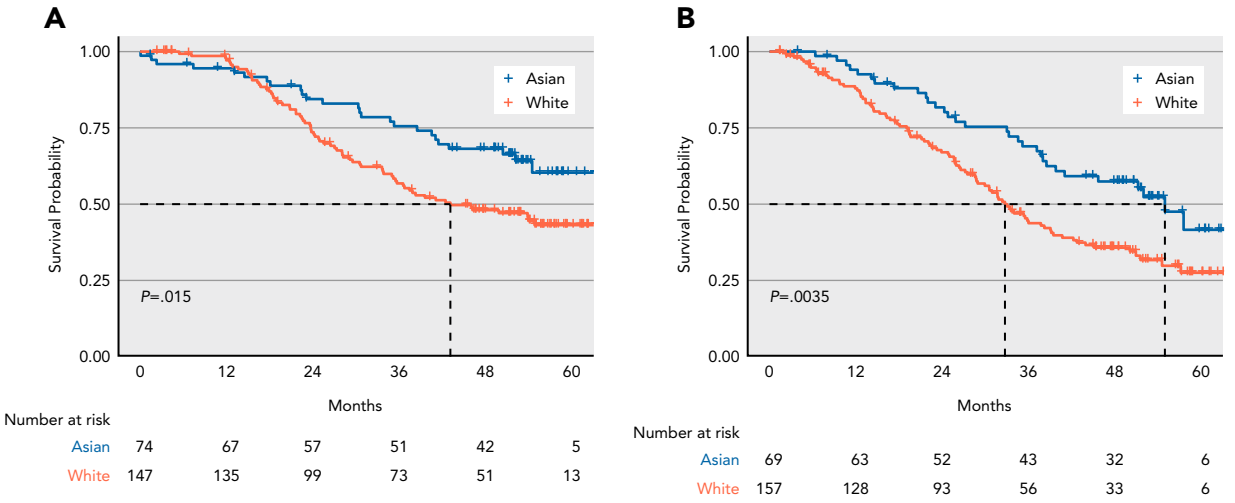

Figure 1. Kaplan-Meier analysis showing OS in men with de novo metastatic PCa treated with **(A)** abiraterone + ADT and **(B)** ADT alone in the LATITUDE cohort.
Abbreviations: ADT, androgen deprivation therapy; OS, overall survival; PCa, prostate cancer.

Table 1. Estimated HRs for the LATITUDE Cohort From a Multivariable Cox Model

	ADT + Abiraterone		ADT	
Variable	**HR (95% CI)**	***P* Value**	**HR (95% CI)**	***P* Value**
Race				
White	Ref		Ref	
Asian	0.45 (0.28–0.73)	.001	0.51 (0.33–0.78)	.002
Age				
≤65 y	Ref		Ref	
66–75 y	1.52 (1.00–2.3)	.052	1.01 (0.69–1.49)	.943
>75 y	3.69 (1.65–8.2)	.001	1.04 (0.37–2.98)	.935
Gleason score				
<8	Ref		Ref	
≥8	0.79 (0.10–6.1)	.825	0.77 (0.22–2.68)	.686
ECOG PS				
0	Ref		Ref	
1–2	1.22 (0.80–1.8)	.357	1.25 (0.85–1.83)	.264
Number of bone lesions				
≤10	Ref		Ref	
>10	1.57 (0.96–2.6)	.073	1.60 (1.03–2.48)	.036
Visceral metastasis				
No	Ref		Ref	
Yes	1.11 (0.72–1.7)	.632	1.58 (1.03–2.42)	.035
logPSA level	0.91 (0.837–1.0)	.043	0.94 (0.862–1.03)	.20
Hb level	0.98 (0.97–1.0)	.011	0.98 (0.97–0.99)	.002
LDH level	1.01 (1.00–1.0)	<.001	1.00 (1.00–1.01)	.11

Abbreviations: ADT, androgen deprivation therapy; Hb, hemoglobin; HR, hazard ratio; LDH, lactate dehydrogenase; PS, performance status; PSA, prostate-specific antigen.

Outcome, Exposure, and Covariates

In LATITUDE, the primary outcome was overall survival (OS), defined as the time from randomization to death. Covariates that were known risk factors for PCa survival were also included in models: age; PSA, Hb, and LDH levels; ECOG performance status; Gleason score; and visceral and bone metastasis at baseline. Consistent with previously reported thresholds,[13] we classified age into 3 groups: ≤65 years, 66–75, and >75 years; Gleason score into groups of <8 and ≥8; and the number of bone lesions into groups of ≤10 and >10.

In the SEER database, the primary outcomes were OS and cancer-specific survival (CSS). OS was defined as the time from diagnosis to death as a result of any cause, and CSS was defined as the time from diagnosis to death as a result of PCa. SEER identifies race according to the variable "Race record (W, B, AI, API)," which denotes white, Black, American Indian/Alaska Native, and Asian or Pacific Islander. SEER identifies use of chemotherapy according to the variable "Chemotherapy record," which was categorized as "Yes" or "No/Unknown." Covariates that were known risk factors for PCa survival (age, PSA level, and Gleason score) were also included in models.

In the NCDB, the primary outcome was OS, which was defined as the time from diagnosis to death as a result of any cause. CSS is not reported in the NCDB. The NCDB identifies race according to the variable "RACE," use of chemotherapy according to the variable "RX_SUMM_CHEMO," and use of ADT according to the variable "RX_SUMM_HORMONE." Covariates that were known risk factors for PCa survival were also included in the models.

Statistical Analysis

In LATITUDE, race and visceral metastasis were set as binary variables; age, logPSA level, Gleason score, Hb level, and LDH level were set as continuous variables; and ECOG performance status and number of bone lesions were set as ordinal variables. In the SEER database, race and chemotherapy record were set as binary variables, and age, logPSA level, Gleason score, and median household income were set as continuous variables. In the NCDB, age and logPSA level were set as continuous variables, and

race, Gleason score, and median household income were set as categorical variables. PSM was performed to reduce the effects of confounding (ratio = 1:3; clipper = 0.02).[16] PSM is a nonparametric technique aimed at balancing pretreatment covariates, which will make the causal effect inference from observational data as reliable as possible. This is accomplished by constructing propensity scores based on a multivariable logistic regression model for the conditional probability of being of Asian race, including age, PSA level, Gleason score, and median household income in the model. The nearest neighbor algorithm was used with a 1:3 ratio for matching white to Asian patients, with a caliper width of 0.02 standard deviations. Then, we performed Kaplan-Meier and multivariable Cox proportional hazards analyses based on the matched cohort. In the multivariable Cox proportional hazards model, to be consistent with the previous reported thresholds, we classified age into 3 groups: ≤65 years, 66–75 years, and >75 years; Gleason score into 2 groups: <8 and ≥8; and number of bone lesions into 2 groups: ≤10 and >10 (in LATITUDE). The proportional hazards assumption was assessed visually using the scaled Schoenfeld residual, and quantitatively using the goodness-of-fit test as proposed by Grambsch and Therneu.[17]

We used R studio version 4.0.2 for these analyses. PSM was performed using the MatchIt package, and Kaplan-Meier analysis and multivariate Cox proportional hazards model were performed using survival and survminer packages. We used a significance level of $P<.05$, and all tests were 2-tailed.

Results

Study Population

After PSM, among 447 patients in LATITUDE, 221 (74 Asian, 147 white) were in the abiraterone + ADT group,

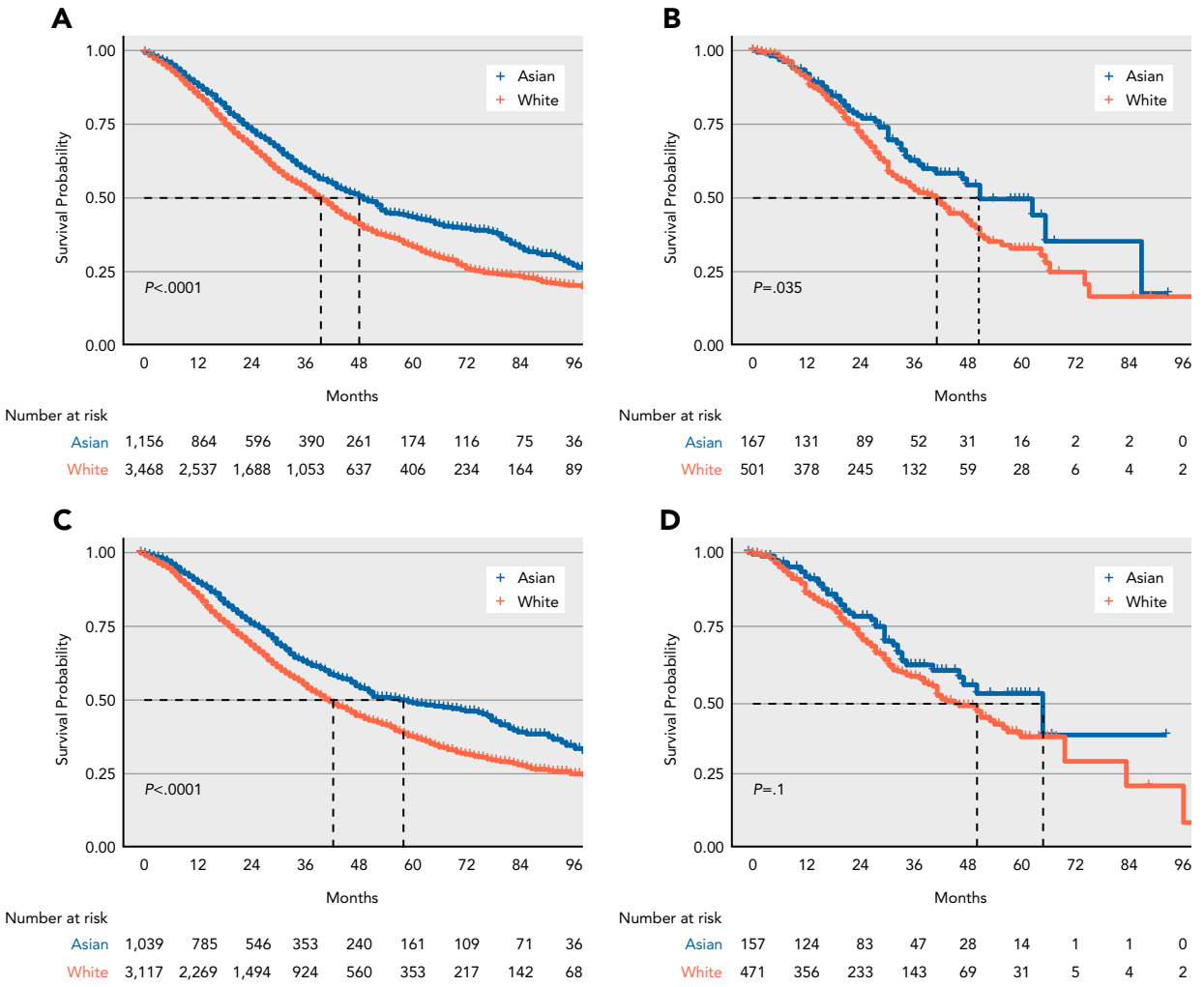

Figure 2. Kaplan-Meier analysis showing OS in **(A)** all men with de novo metastatic PCa and **(B)** those treated with chemotherapy in the SEER cohort, and CSS in **(C)** all men with de novo metastatic PCa and **(D)** those treated with chemotherapy in the SEER cohort.
Abbreviations: CSS, cancer-specific survival; OS, overall survival; PCa, prostate cancer.

and 226 (69 Asian, 157 white) were in the ADT alone group. In SEER, 4,624 patients diagnosed with de novo metastatic PCa remained after PSM (1,156 Asian, 3,468 white); 668 patients remained in the chemotherapy subgroup (167 Asian, 501 white). For CSS in SEER, 4,156 patients remained after PSM (1,039 Asian, 3,117 white); 628 patients remained in the chemotherapy subgroup (157 Asian, 471 white). The full cohort from NCDB had 1,284 patients after PSM (321 Asian, 963 white). The ADT cohort had 976 patients (244 Asian, 732 white), and the chemotherapy cohort had 1,196 patients (299 Asian, 897 white). Baseline characteristics of included patients from each cohort are reported in supplemental eTable 2.

Survival Outcomes From LATITUDE

In LATITUDE, Asian males had significantly longer median OS than white males in both the abiraterone + ADT group (not reached vs 43.8 months; Figure 1A) and ADT alone group (57.6 vs 32.7 months; Figure 1B). Multivariable Cox proportional hazards analysis indicated that Asian race was independently associated with OS in the abiraterone + ADT group (hazard ratio [HR], 0.45; 95% CI, 0.28–0.73; P=.001) and ADT alone group (HR, 0.51; 95% CI, 0.33–0.78; P=.002) (Table 1).

Survival Outcomes From SEER

In SEER, Asian males had better OS and CSS than white males in both the overall and chemotherapy cohorts. Median OS was significantly longer in Asian males than in white males in the overall cohort (53 vs 42 months; Figure 2A) and the chemotherapy cohort (median OS, 52 vs 38 months; Figure 2B). Multivariable Cox proportional hazards analysis indicated that Asian race was independently associated with OS in these cohorts (HR, 0.76; 95% CI, 0.68–0.84; P<.001, and HR, 0.71; 95% CI, 0.52–0.96; P=.025, respectively) (Table 2). Median CSS of Asian males was also longer compared with white males in the overall cohort (52 vs 42 months; Figure 2C) (HR, 0.71; 95% CI, 0.63–0.80; P<.001; Table 2). In the chemotherapy cohort, Asian race was also independently associated with CSS (median, 67 vs 52 months; Figure 2D) (HR, 0.75; 95% CI, 0.53–1.0; P=.089; Table 2). Although SEER and NCDB use a fundamentally distinct mechanism to collect patient data, we considered that some patients might be duplicated in both databases. Thus, we did a sensitivity analysis on SEER that was restricted to patients diagnosed from 2014 to 2019 to test for consistency, ensuring no overlap with NCDB (2004–2013). In time-restricted SEER, there was still a significant OS and CSS advantage for Asian males versus white males (median, 52 vs 40 months and 65 vs 49 months, respectively, for the whole cohort; and 64 vs 44 months and not reached vs 51 months, respectively, for the chemotherapy cohort) (supplemental eFigure 2).

Table 2. Estimated HRs for the SEER Cohort From a Multivariable Cox Model

	Whole Cohort		Chemotherapy Cohort		Whole Cohort CSS		Chemotherapy Cohort CSS	
Variable	**HR (95% CI)**	***P* Value**	**HR (95% CI)**	***P* Value**	**HR (95% CI)**	***P* Value**	**HR (95% CI)**	***P* Value**
Race								
White	Ref		Ref		Ref		Ref	
Asian	0.76 (0.68–0.84)	<.001	0.71 (0.52–0.96)	.025	0.71 (0.63–0.8)	<.001	0.75 (0.53–1.0)	.089
Age								
≤65 y	Ref		Ref		Ref		Ref	
66–75 y	1.08 (0.96–1.20)	.195	0.77 (0.58–1.03)	.079	1.06 (0.93–1.2)	.379	0.75 (0.54–1.0)	.049
>75 y	1.68 (1.51–1.87)	<.001	1.67 (1.18–2.36)	.004	1.62 (1.44–1.8)	<.001	1.39 (0.97–2.0)	.019
Gleason score								
<8	Ref		Ref		Ref		Ref	
≥8	1.51 (1.32–1.73)	<.001	0.75 (0.50–1.12)	.162	1.58 (1.34–1.9)	<.001	1.33 (0.81–2.2)	.049
logPSA level	1.18 (1.13–1.24)	<.001	0.91 (0.79–1.05)	.201	1.23 (1.17–1.3)	<.001	0.99 (0.84–1.2)	.856
Income								
≤$39,999	Ref		NA		Ref		NA	
$40,000–$54,999	0.49 (0.21–1.15)	.103	Ref		0.74 (0.18–3.1)	.681	Ref	
$55,000–$74,999	0.70 (0.31–1.57)	.39	1.07 (0.38–2.99)	.903	0.88 (0.22–3.5)	.859	0.93 (0.29–3.1)	.911
≥$75,000	0.64 (0.29–1.44)	.282	1.04 (0.38–2.85)	.942	0.76 (0.19–3.0)	.693	0.94 (0.30–3.0)	.914

Abbreviations: CSS, cancer-specific survival; HR, hazard ratio; NA, not applicable; PSA, prostate-specific antigen.

Survival Outcomes From NCDB

In the NCDB, Asian males also had better OS than white males in the overall, chemotherapy, and ADT cohorts, with the median OS being significantly longer in the overall cohort (38 vs 26 months, respectively; Figure 3A). Multivariable Cox proportional hazards analysis indicated that Asian race was independently associated with OS in the overall cohort (HR, 0.72; 95% CI, 0.62–0.83; $P<.001$), the chemotherapy cohort (34 vs 25 months; Figure 3B) (HR, 0.67; 95% CI, 0.57–0.78; $P<.001$), and the ADT cohort (41 vs 26 months; Figure 3C) (HR, 0.71; 95% CI, 0.60–0.84; $P<.001$) (Table 3).

Discussion

Our study shows that Asian males with de novo metastatic PCa have a better prognosis than white males with de novo metastatic PCa. This improvement in survival persists in subgroups receiving different kinds of systemic treatments including ADT, ADT + abiraterone, and ADT + chemotherapy. Our study is the most comprehensive analysis published to date on this topic and includes 3 of the largest extant datasets, with sufficient follow-up to analyze long-term outcomes across racial subgroups. These data build on the mounting evidence of better survivorship outcomes for Asian patients with de novo metastatic PCa[18,19] and will help to further refine the prognosis of Asian and white males with de novo metastatic PCa.[20–22] In addition, our data will help improve planning for international trials in this disease space.

Previous studies have clearly shown that PCa prognosis among all males with PCa differs by Black and white race, with PCa mortality in Black males almost double that of white males.[12] However, it is often overlooked that the PCa mortality rate among Asian males with PCa is only half that of white males.[12] However, unlike the differences in survival observed in our data between Asian and white patients with de novo metastatic PCa, survival disparities between Black and white patients seem to be related, in part, to access to and appropriateness of therapy.[2,23,24] A prospective, multicenter study that focused on the efficacy of abiraterone between Black and white patients (ClinicalTrials.gov identifier: NCT01940276) showed no difference in radiographic rogression-free survival among males with advanced disease.[25] Dess et al[6] showed that the worse outcomes among Black males were seen in SEER but were not seen in a randomized clinical trial cohort. In another retrospective cohort study, African American males had significantly longer median OS compared with non-Hispanic white males (23 vs 17 months) after first-line abiraterone therapy.[26] Marar et al[26] reported that among patients with metastatic castration-resistant prostate cancer (mCRPC) who were treated with docetaxel, the risk of death in Black patients was significantly lower than

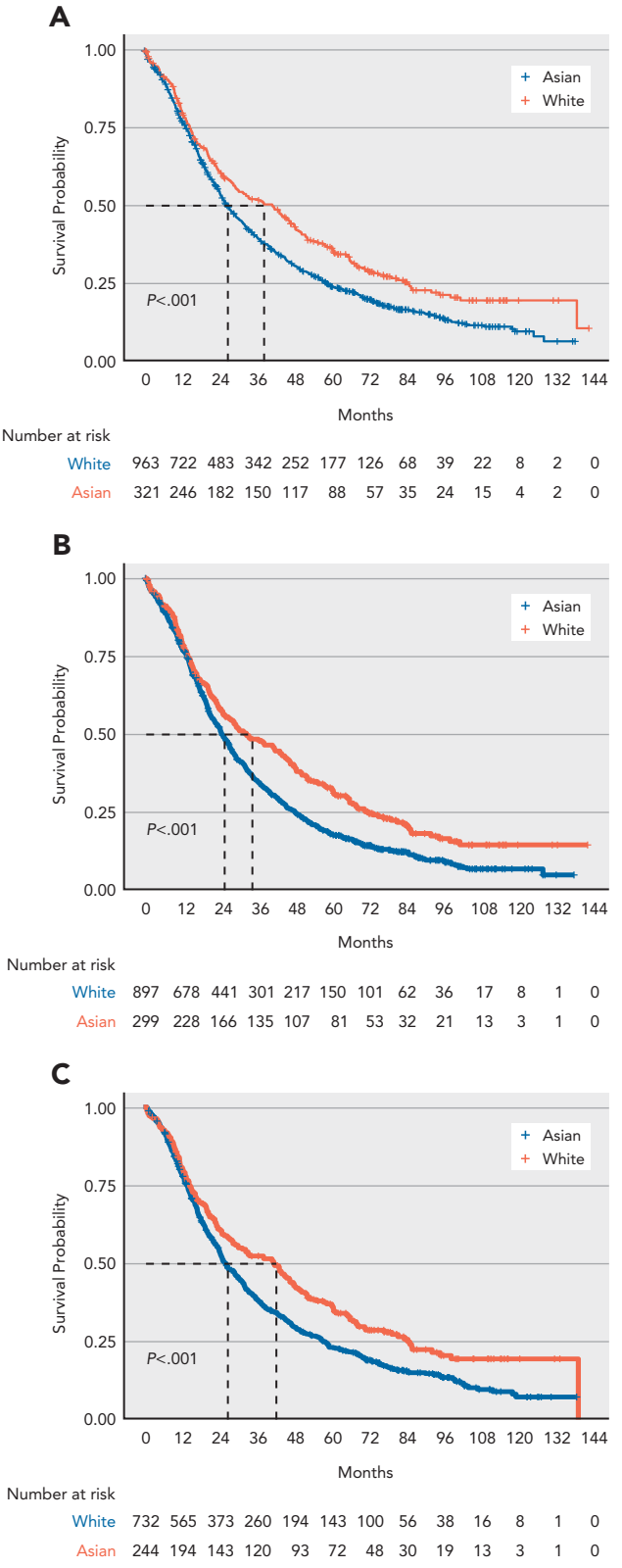

Figure 3. Kaplan-Meier analysis showing OS in **(A)** all men with de novo metastatic PCa, **(B)** those treated with chemotherapy, and **(C)** those treated with ADT in the NCDB.
Abbreviations: ADT, androgen deprivation therapy; NCDB, National Cancer Database; OS, overall survival; PCa, prostate cancer.

Table 3. Estimated HRs for the NCDB Cohort From a Multivariable Cox Model

	Whole Cohort		ADT Cohort		Chemotherapy Cohort	
Variable	HR (95% CI)	*P* Value	HR (95% CI)	*P* Value	HR (95% CI)	*P* Value
Race						
White	Ref		Ref		Ref	
Asian	0.72 (0.62–0.83)	<.001	0.71 (0.60–0.84)	<.001	0.67 (0.57–0.78)	<.001
Age						
≤65 y	Ref		Ref		Ref	
66–75 y	1.15 (0.99–1.33)	.076	1.12 (0.94–1.32)	.205	1.13 (0.97–1.32)	.121
>75 y	1.74 (1.49–2.03)	<.001	1.71 (1.43–2.05)	<.001	1.82 (1.55–2.14)	<.001
Gleason score						
<8	Ref		Ref		Ref	
≥8	1.61 (1.41–1.83)	<.001	1.65 (1.42–1.92)	<.001	1.72 (1.51–1.97)	<.001
logPSA level	1.24 (1.17–1.33)	<.001	1.24 (1.15–1.33)	<.001	1.28 (1.20–1.36)	<.001
Income						
<$40,277	Ref		Ref		Ref	
$40,277–$50,353	0.91 (0.72–1.14)	.399	0.90 (0.69–1.16)	.406	1.00 (0.79–1.26)	.997
$50,354–$63,332	1.03 (0.84–1.25)	.785	0.97 (0.77–1.22)	.722	0.99 (0.80–1.21)	.893
>$63,332	0.79 (0.66–0.96)	.017	0.74 (0.59–0.93)	.009	0.94 (0.77–1.14)	.507

Abbreviations: ADT, androgen deprivation therapy; HR, hazard ratio; NCDB, National Cancer Database; PSA, prostate-specific antigen.

that in white patients. These studies suggest that racial disparities in survival do exist, but they may be affected by multiple factors, including access to care and appropriateness of treatment.

In contrast, we found that Asian males had better survival than white males in all treatment subgroups, including ADT, ADT + abiraterone, and ADT + chemotherapy, across 3 large, diverse datasets. Asian males consistently had better OS than white males with metastatic PCa in all 3 datasets, and CSS was similarly better in Asian males in SEER, which includes data on cause-specific survival. Although these are retrospective analyses that are subject to selection bias, we attempted to reduce the impact of major confounding factors through PSM. Furthermore, we replicated our results in post hoc analyses of RCT data in LATITUDE, which also suggests that our findings are not purely mediated by selection factors. We also included both local Asian data (LATITUDE clinical trial) and Asian American data (SEER, NCDB), suggesting that these differences in survival are less likely to be mediated by environmental and geographical differences and more likely to be mediated by racial heritage and genetics.

It is possible that diversity in gene expression and mutation among hormone-metabolizing enzyme genes, oncogenes, and suppressor genes and the difference in copy number variation and microsatellite instability could explain at least some of the racial disparities observed in survival.[27,28] Liu et al[29] found that Black and white patients had more prominent drug metabolism, cytotoxic therapy resistance, and endocrine therapy resistance than Asians. Prizment et al[30] demonstrated that the critical androgen-regulating gene *HSD3B1* mutated differently among different races. Moreover, IPATential150, a multicenter phase III clinical trial for mCRPC, found that Asian patients had fewer instances of *PTEN* loss than white patients.[31] Other oncogenes, such as *TP53* and *TMPRSS2::ERG*, have also been found to be significantly less expressed in Asian individuals, whereas *FOXA1* and *SPOP* were expressed more.[32,33] *PTEN* loss is positively related to increasing Gleason score and poor prognosis[34] and the *TMPRSS2::ERG* gene fusion confers a worse prognosis and increasing biochemical recurrence,[35] whereas coding mutations in *FOXA1* promote epithelial-to-mesenchymal transition and metastasis.[36] Kwan et al[37] developed a prognostic whole-blood gene signature for patients with mCRPC. Further research is needed to establish associations between these genotypes and survival differences observed across males of various races.

Our results also have important implications for designing future global multicenter clinical trials. Understanding differences in survival across races may help project the numbers of patients needed to reach oncologic outcomes and the follow-up time needed to observe such events in different racial subgroups. Adequately powering

analyses to reach significance for racial subgroups will be important to achieving robust, generalizable results both in aggregate and in these racial minority subgroups. Genetic differences between races should also be considered when designing targeted molecular interventions. Our data certainly support a precision approach to prognostic assessment, and future trial data will determine whether genetic differences associated with race should be included in treatment decisions, recognizing that there is substantial genetic heterogeneity within males of the same race.

Our study has several limitations to consider. First, there are few cohorts of Asian males with metastatic PCa of sufficient size and follow-up to assess long-term survival outcomes, and only LATITUDE included prospectively collected, homogeneous data on Asian and white males. LATITUDE also included complete baseline data so that we can robustly use PSM to reduce the effects of measured confounders, unlike in SEER and NCDB. Second, some possible confounders such as ECOG performance status and visceral and bone metastasis were not included in SEER and NCDB. Third, only LATITUDE includes data on Asian males who reside in Asia, mainly from China, Japan, Korea, Israel, and Malaysia, whereas Asian Americans included in NCDB and SEER are a heterogeneous group that includes those with ancestors in central and south Asian countries. Future studies of disparities in survival outcomes would benefit from more local data on Asian males. Survival differences among patients with PCa from different regions of Asia also need to be explored. The retrospective nature of this study raises the possibility of residual confounding from unadjusted prognostic factors, such as bias introduced by Asian medical centers versus non-Asian medical centers in LATITUDE. A prospective design is needed to fully adjust the potential bias introduced by different medical sites in the future.

Conclusions

Our results show that Asian males have better OS than white males with metastatic PCa across different treatment regimens in all datasets examined, which is also consistent with CSS in SEER. These findings suggest that Asian race should be considered as an independent prognostic factor when evaluating prognosis for individual patients, and it also has important implications for the design of multiregional clinical trials. Further studies including biologic analyses are needed to understand the etiology of the apparent survival advantage for Asian males.

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Data availability statement: Data from LATITUDE clinical trials are available to researchers by directly contacting YODA at https://yoda.yale.edu/applications. Deidentified data, including data dictionaries, are available for request per the Yale University Open Data Access (YODA) Project. If the request is approved and if there are no restrictions to YODA sharing data, a data use agreement between the requestor's institution and Janssen Research & Development, LLC, must be in place before requested data can be released.

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Impact of Asian Race on Prognosis in De Novo Metastatic Prostate Cancer

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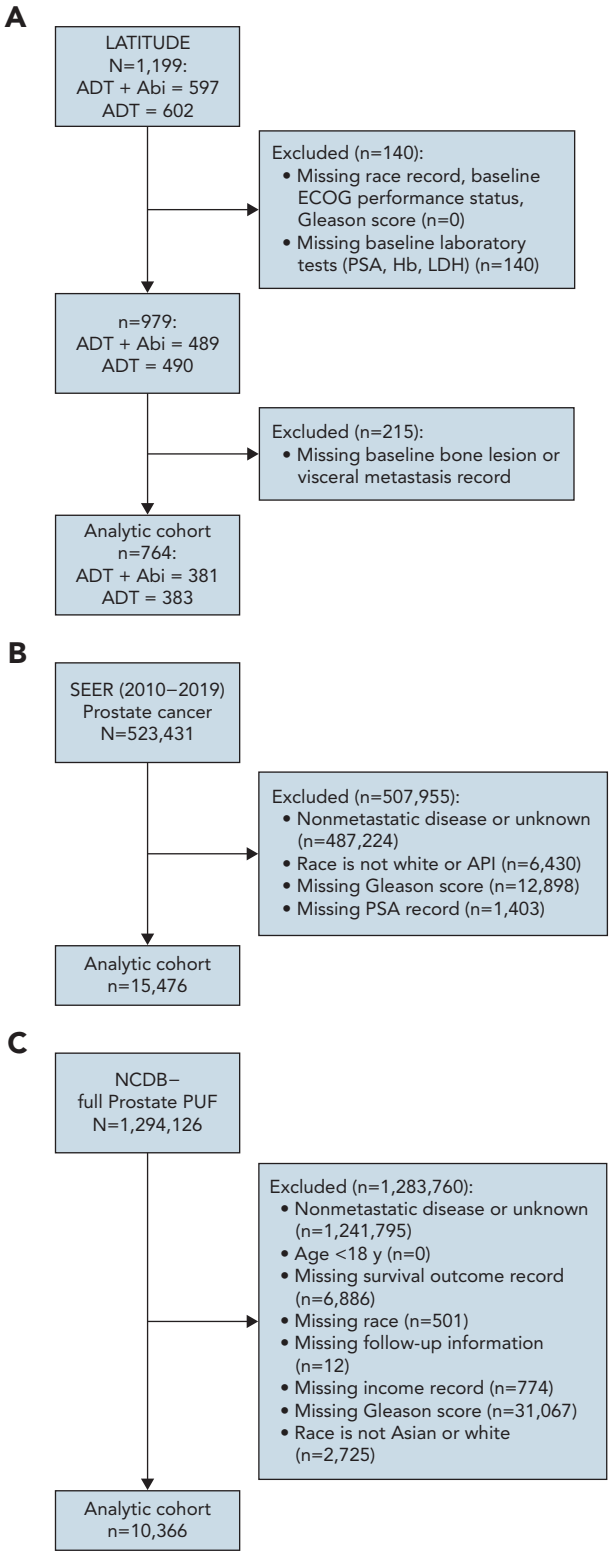
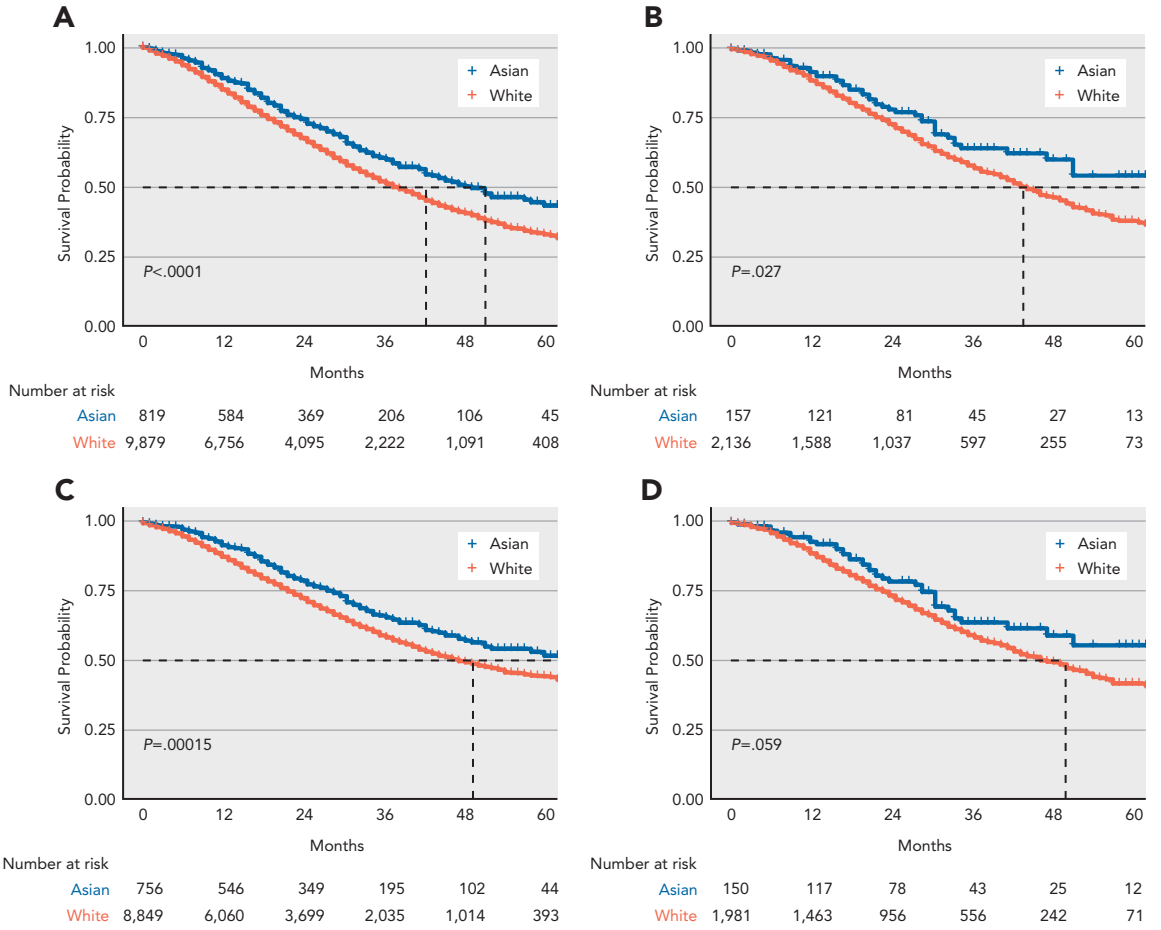


eFigure 1. Attrition in the **(A)** LATITUDE, **(B)** SEER, and **(C)** NCDB cohorts.
Abbreviations: Abi, abiraterone; ADT, androgen deprivation therapy; API, Asian/Pacific Islander; Hb, hemoglobin; LDH, lactate dehydrogenase; NCDB, National Cancer Database; PSA, prostate-specific antigen; PUF, participant use file.



eFigure 2. Kaplan-Meier analysis showing OS in **(A)** all men with de novo metastatic PCa and **(B)** those treated with chemotherapy in the time-restricted SEER cohort (2014–2019), and CSS in **(C)** all men with de novo metastatic PCa and **(D)** those treated with chemotherapy in the time-restricted SEER cohort (2014–2019).
Abbreviations: CSS, cancer-specific survival; OS, overall survival; PCa, prostate cancer.

eTable 1. Features of All 3 Databases

	LATITUDE	SEER	NCDB
Year of diagnosis	2013–2015	2010–2019	2004–2013
Disease		de novo metastatic prostate cancer	
Age		≥18 y	
ECOG PS	0–2	NA	NA
Risk factor[a]	High risk	NA	NA
Race	Asian or white	API or white	Asian or white
Therapy	ADT alone or ADT + abiraterone	ADT alone or ADT + chemotherapy	ADT alone or ADT + chemotherapy

Abbreviations: ADT, androgen deprivation therapy; API, Asian/Pacific Islander; NA, not applicable; NCDB, National Cancer Database; PS, performance status.
[a]Risk factor: Gleason score ≥8, at least 3 bone lesions, and presence of measurable visceral metastasis.

eTable 2. Descriptive Characteristics of Patients From Each Cohort

	LATITUDE Cohort		SEER Cohort		NCDB Cohort		
Characteristic	**ADT + Abi, n**	**ADT, n**	**Whole, n**	**Chemotherapy, n**	**Whole, n**	**ADT, n**	**Chemotherapy, n**
Total population	221	226	4,624	668	1,284	976	1,196
Race							
Asian	74	69	1,156	167	321	244	299
White	147	157	3,468	501	963	732	897
Age group							
≤65 y	116	141	1,289	298	488	365	476
66–75 y	94	78	1,664	261	441	358	406
>75 y	11	7	1,671	109	355	253	314
Gleason score							
<8	3	4	629	44	561	417	557
≥8	218	222	3,995	642	723	559	639
logPSA level	3.95 (1.87–5.30)	3.40 (1.69–5.05)	4.14 (2.92–4.58)	4.34 (3.10–4.58)	6.13 (5.15–6.89)	6.15 (5.20–6.89)	6.13 (5.23–6.89)
ECOG performance status							
0	128	117					
1–2	93	109					
Number of bone lesions							
≤10	73	87					
>10	148	139					
Visceral metastasis							
Yes	86	67					
No	135	159					
Median income							
≤$40,227 in NCDB ≤$39,999 in SEER			5	0	191	128	190
$40,227–$50,353 in NCDB $40,000–$54,999 in SEER			172	6	208	174	198
$50,353–$63,332 in NCDB $55,000–$74,999 in SEER			1,492	102	367	279	329
≥$63,333 in NCDB ≥$75,000 in SEER			2,591	506	518	395	479

Abbreviations: ADT, androgen deprivation therapy; Abi, abiraterone; NCDB, National Cancer Database; PSA, prostate-specific antigen.