

Efficacy and Safety of Darolutamide in Combination With Androgen-Deprivation Therapy and Docetaxel in Black Patients From the Randomized ARASENS Trial

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Abstract

Background: In the ARASENS trial (NCT02799602), darolutamide in combination with androgen-deprivation therapy (ADT) and docetaxel significantly reduced the risk of death by 32.5% (HR, 0.68; 95% CI, 0.57-0.80; $P < .0001$) compared with placebo plus ADT with docetaxel in patients with metastatic hormone-sensitive prostate cancer (mHSPC). We present efficacy and safety of darolutamide versus placebo in Black patients from ARASENS.

Patients and Methods: Patients with mHSPC were randomized 1:1 to darolutamide 600 mg or placebo twice daily in combination with ADT and docetaxel. The primary endpoint was overall survival. Key secondary endpoints included time to castration-resistant prostate cancer (CRPC) and safety.

Results: In ARASENS, 54 Black patients received darolutamide ($n = 26$) or placebo ($n = 28$) plus ADT and docetaxel. In Black patients, overall survival favored darolutamide versus placebo (median, not reached vs. 38.7 months; stratified HR, 0.41; 95% CI, 0.17-1.02), with 4-year survival rates of 62% versus 41%. The darolutamide group also had longer time to CRPC compared with the placebo group (median, not reached vs. 12.6 months; HR, 0.09; 95% CI, 0.02-0.30). The safety profile of darolutamide in Black patients was consistent with that observed for the overall ARASENS population (grade 3/4 treatment-emergent adverse events, TEAEs: 61.5% vs. 66.1%; serious TEAEs: 42.3% vs. 44.8%).

Conclusion: In this small population of Black patients with mHSPC from the ARASENS trial, darolutamide was associated with an improvement in survival and time to CRPC and was well tolerated. Efficacy and safety findings in Black patients were consistent with the overall ARASENS population.

Key words: androgen receptor inhibitor; darolutamide; metastatic hormone-sensitive prostate cancer; Black; survival analyses; safety.

Implications for Practice

Prostate cancer that has spread to other parts of the body and can be treated with hormonal therapy, including androgen-deprivation therapy (ADT), is called metastatic hormone-sensitive prostate cancer (mHSPC). Based on results of the phase III ARASENS study, darolutamide is an approved treatment for mHSPC when used in combination with ADT and docetaxel (chemotherapy). This report provides information on the effect of darolutamide, ADT, and docetaxel in the 54 Black patients in ARASENS. In these patients, darolutamide was well tolerated and lowered the risks of patients dying and their cancer progressing. These results are consistent with the overall ARASENS population.

Introduction

Globally, prostate cancer is the second most common malignancy behind lung cancer in men and ranks first in incidence among men in the United States.^{1,2} Black people are disproportionately affected by prostate cancer, with higher incidence and mortality rates versus other racial/ethnic groups. These higher rates have been attributed to multiple factors including longstanding inequalities in wealth leading to differences in risk factor exposure, access to healthcare, and equitable cancer prevention, screening, and treatment.² White participants are disproportionately represented in genomic databases, resulting in higher rates of genomically aggressive cancer observed among Black men with prostate cancer.^{2,3} Data from the Surveillance, Epidemiology, and End Results (SEER) database and the Veterans Affairs healthcare system, primarily in patients with non-metastatic disease, suggest that when disparities in access to care and known prognostic factors are controlled, outcomes are similar between Black patients and their White counterparts.⁴⁻⁶ However, data on outcomes in Black patients with metastatic prostate cancer are scarce.⁷

Metastatic prostate cancer has a 5-year survival rate of approximately 30% compared with >99% for localized and regional disease,² highlighting a need for treatments to prolong survival, and delay disease progression in patients with metastatic disease. For patients with metastatic hormone-sensitive prostate cancer (mHSPC), clinical outcomes have improved with the combination of androgen-deprivation therapy (ADT) plus an androgen receptor pathway inhibitor and/or docetaxel.⁸⁻¹³ However, limited data are available for Black participants from these clinical trials.⁷ Results of the CHAARTED trial comparing ADT alone or in combination with docetaxel in patients with mHSPC showed shorter median survival among Black patients ($n = 76$) versus White non-Hispanic patients ($n = 595$) receiving ADT alone (34.1 vs. 45.2 months) and similar survival between these racial groups receiving combination therapy (57.6 vs. 58.1 months).¹⁴ Pooled analyses of phase III trials evaluating docetaxel and prednisone regimens for metastatic castration-resistant prostate cancer (mCRPC) indicated approximately 6% of patients were Black and showed similar outcomes in this group compared with White patients.^{7,15}

Darolutamide, a structurally distinct and highly potent androgen receptor inhibitor, has demonstrated low blood-brain barrier penetration and a limited potential for clinically relevant drug-drug interactions.^{16,17} In the phase III ARASENS trial in patients with mHSPC, darolutamide in combination with ADT and docetaxel significantly reduced the risk of death by 32.5% (hazard ratio, HR, 0.68; 95% CI, 0.57-0.80; $P < .0001$) and significantly delayed onset of castration-resistant prostate cancer (CRPC) (HR, 0.36; 95% CI, 0.30-0.42; $P < .001$) versus ADT and docetaxel alone.¹³ Incidences of treatment-emergent adverse events (TEAEs) were similar in the 2 treatment groups and incidences of the most common TEAEs were highest during the overlapping docetaxel treatment period and progressively decreased thereafter. We present efficacy and safety results for the subgroup of Black patients from ARASENS.

Patients and Methods

Trial Design and Patients

ARASENS was a randomized, double-blind, placebo-controlled, phase III trial of darolutamide versus placebo

in combination with ADT and docetaxel in patients with mHSPC. Patients were randomized into the trial between 2016 and 2018 at 286 centers in 23 countries worldwide, and trial data readout occurred in 2021. Details of the trial design and methodology and CONSORT flow diagram of patient disposition have been published (Supplementary Fig. S1).¹³

The trial protocol was approved by the institutional review board at each participating center. The trial was conducted in accordance with the principles of the Declaration of Helsinki and the International Council for Harmonisation Good Clinical Practice guidelines. Written informed consent was provided by all patients.

Adult patients were required to have mHSPC with metastases beyond regional lymph nodes only detected on bone scanning, contrast-enhanced computed tomography, or magnetic resonance imaging. Patients had an Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1 and were considered candidates for treatment with ADT and docetaxel in the opinion of the investigator. Patients were excluded if they had received prior therapy with ADT more than 12 weeks before randomization, radiotherapy within 2 weeks of randomization, or second-generation androgen receptor pathway inhibitors, chemotherapy, or immunotherapy for prostate cancer before randomization.

All patients received standard ADT (or underwent orchiectomy) within 12 weeks of randomization and docetaxel within 6 weeks after randomization as previously described.¹³ Patients were equally randomized to darolutamide 600 mg twice daily or placebo, with stratification based on extent of metastasis (M1a: nonregional lymph nodes only, M1b: bone metastases with or without lymph node metastases, or M1c: visceral metastases with or without lymph node or bone metastases) and alkaline phosphatase level based on the upper level of normal ($<ULN$ vs. $\geq ULN$). Prespecified subgroup analyses included patients with de novo and recurrent disease. Treatment was continued until symptomatic disease progression, a change in chemotherapy, unacceptable toxicity, decision by patient or physician, death, or nonadherence.

Endpoints

Patients were assessed every 12 weeks for evidence of disease progression and treatment-emergent adverse events (TEAEs). Overall survival was the primary endpoint and time to CRPC was the first of several secondary endpoints analyzed hierarchically. Safety was assessed as TEAEs that occurred during treatment, including those commonly associated with androgen receptor pathway inhibitors (fatigue, vasodilation/flushing, hypertension, diabetes/hyperglycemia, cardiac disorders, fall, depressed mood disorders, rash, fracture, decreased weight, mental impairment, and breast disorders/gynecomastia).

Statistical Analyses

Patient demographics, baseline characteristics, and TEAEs are reported descriptively for the subgroup of Black patients. The exposure-adjusted incidence rate (EAIR) of TEAEs is defined as the number of patients with a given TEAE divided by the treatment duration (in years) of all patients in the respective subgroup, expressed in 100 patient-years (PY).

Overall survival and time to CRPC for this subgroup were analyzed post hoc using Kaplan-Meier estimates to compute medians and 95% CIs. A Cox regression model, stratified by

extent of disease and alkaline phosphatase (<ULN vs. ≥ULN), was used to calculate HRs and 95% CIs for comparison between treatment arms.

Results

Patients

Of 1305 patients in the overall ARASENS trial population, 54 were Black, of which 26 received darolutamide and 28 received placebo. Black patients represented 14.8% (36/244) of those enrolled in North America, 0.2% (1/473) from the Asia-Pacific region, and 2.9% (17/588) from the rest of the world. Demographics and baseline clinical characteristics of the Black subgroup were generally similar compared with the overall population, except that a greater proportion of Black patients were younger than 65 years of age (57.4% vs. 36.6%), had an ECOG performance status of 1 (37.0% vs. 28.7%), and had recurrent disease (24.1% vs. 12.9%; Table 1). Median prostate-specific antigen levels at baseline were similar in Black patients compared with all patients (35.9 vs. 27.6

μg/L), but alkaline phosphatase levels were lower in Black patients (109.5 vs. 143.0 U/L).

Median treatment duration was longer for darolutamide versus placebo among Black patients (29.6 vs. 12.4 months) and in the overall population (41.0 vs. 16.7 months), although treatment durations were longer in the overall population.¹³ Six cycles of docetaxel treatment were completed by similar proportions of patients in the darolutamide (77%) and placebo (75%) groups, which were slightly lower than rates observed in the overall population (87.6% and 85.5%, respectively).¹³

Efficacy

In Black patients, overall survival favored darolutamide in combination with ADT and docetaxel versus ADT and docetaxel alone, with a stratified hazard ratio of 0.41 (95% CI, 0.17-1.02; Fig. 1A). Median survival was not reached in the darolutamide group and was 38.7 months in the placebo group. Four-year survival rates were 62% for Black patients receiving darolutamide versus 41% for those receiving

Table 1. Patient demographics and clinical characteristics at baseline.

Characteristic at baseline	Black subgroup		Overall population ^a	
	Darolutamide + ADT + docetaxel (n = 26)	Placebo + ADT + docetaxel (n = 28)	Darolutamide + ADT + docetaxel (n = 651)	Placebo + ADT + docetaxel (n = 654 ^a)
Age, median (range), yr	63.5 (52-84)	63 (47-82)	67 (41-89)	67 (42-86)
Age group, n (%)				
<65 yr	15 (57.7)	16 (57.1)	243 (37.3)	234 (35.8)
65-74 yr	9 (34.6)	11 (39.3)	303 (46.5)	306 (46.8)
≥75 yr	2 (7.7)	1 (3.6)	105 (16.1)	114 (17.4)
ECOG performance status, n (%)				
0	15 (57.7)	19 (67.9)	466 (71.6)	462 (70.6)
1	11 (42.3)	9 (32.1)	185 (28.4)	190 (29.1)
Gleason score at initial diagnosis, n (%)				
<8	6 (23.1)	5 (17.9)	122 (18.7)	118 (18.0)
≥8	19 (73.1)	21 (75.0)	505 (77.6)	516 (78.9)
Missing	1 (3.8)	2 (7.1)	24 (3.7)	20 (3.1)
Metastatic stage at initial diagnosis, n (%)				
De novo	20 (76.9)	20 (71.4)	558 (85.7)	566 (86.5)
Recurrent	5 (19.2)	8 (28.6)	86 (13.2)	82 (12.5)
Distant metastasis not assessed	1 (3.8)	0	7 (1.1)	6 (0.9)
Metastasis stage at screening, n (%)				
M1a, nonregional LN only	1 (3.8)	1 (3.6)	23 (3.5)	16 (2.4)
M1b, bone ± LN	20 (76.9)	23 (82.1)	517 (79.4)	520 (79.5)
M1c, visceral ± LN or bone	5 (19.2)	4 (14.3)	111 (17.1)	118 (18.0)
PSA, median (range), ng/mL ^b	38.2 (0.0-949.0)	33.0 (0.2-5255.0)	30.3 (0.0-9219.0)	24.2 (0.0-11 947.0)
ALP, median (range), U/L ^b	113.5 (59-1031)	107.0 (55-2065)	148 (40-4885)	140 (36-7680)
ALP, n (%) ^b				
<ULN	14 (53.8)	17 (60.7)	209 (44.5)	291 (44.5)
≥ULN	12 (46.2)	11 (39.3)	361 (55.5)	363 (55.5)

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^aOne patient randomized to placebo but who received darolutamide was included in the placebo group for the full analysis set.

^bCentrally assessed; samples were collected while patients were receiving ADT.

Abbreviations: ADT: androgen-deprivation therapy; ALP: alkaline phosphatase; ECOG: Eastern Cooperative Oncology Group; LN: lymph node; PSA: prostate-specific antigen; ULN: upper limit of normal.

placebo. Survival results in the subgroup were consistent with those in the overall ARASENS population (Fig. 1B).

Time to CRPC was increased for Black patients receiving darolutamide compared with those receiving placebo (HR, 0.09; 95% CI, 0.02-0.30; Fig. 2A). The median time to CRPC was not reached in the darolutamide group and was 12.6

months in the placebo group. Results were consistent with the overall population (Fig. 2B).

Safety

The safety profile of darolutamide in Black patients was consistent with that observed for all patients (Table 2). In this

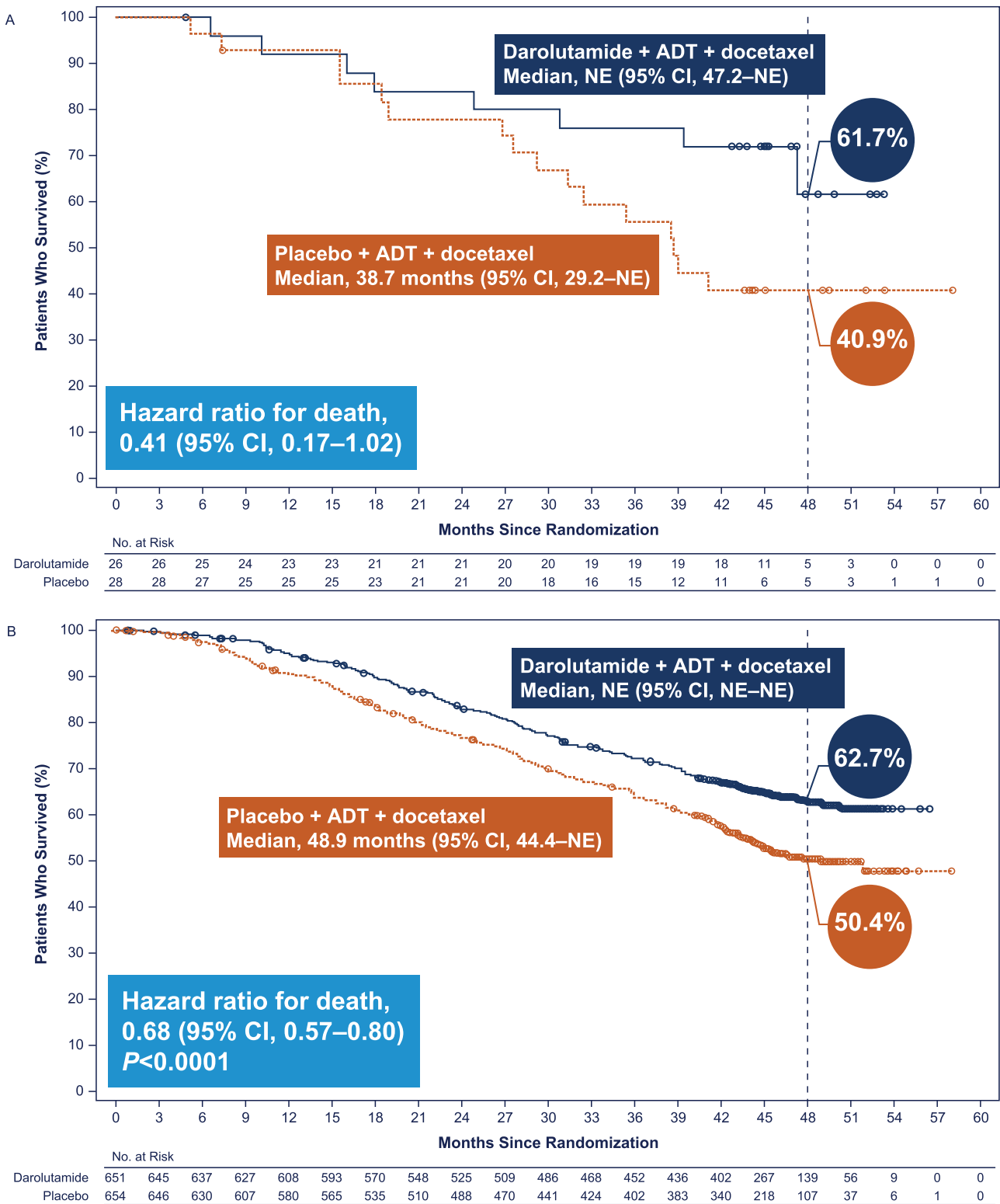
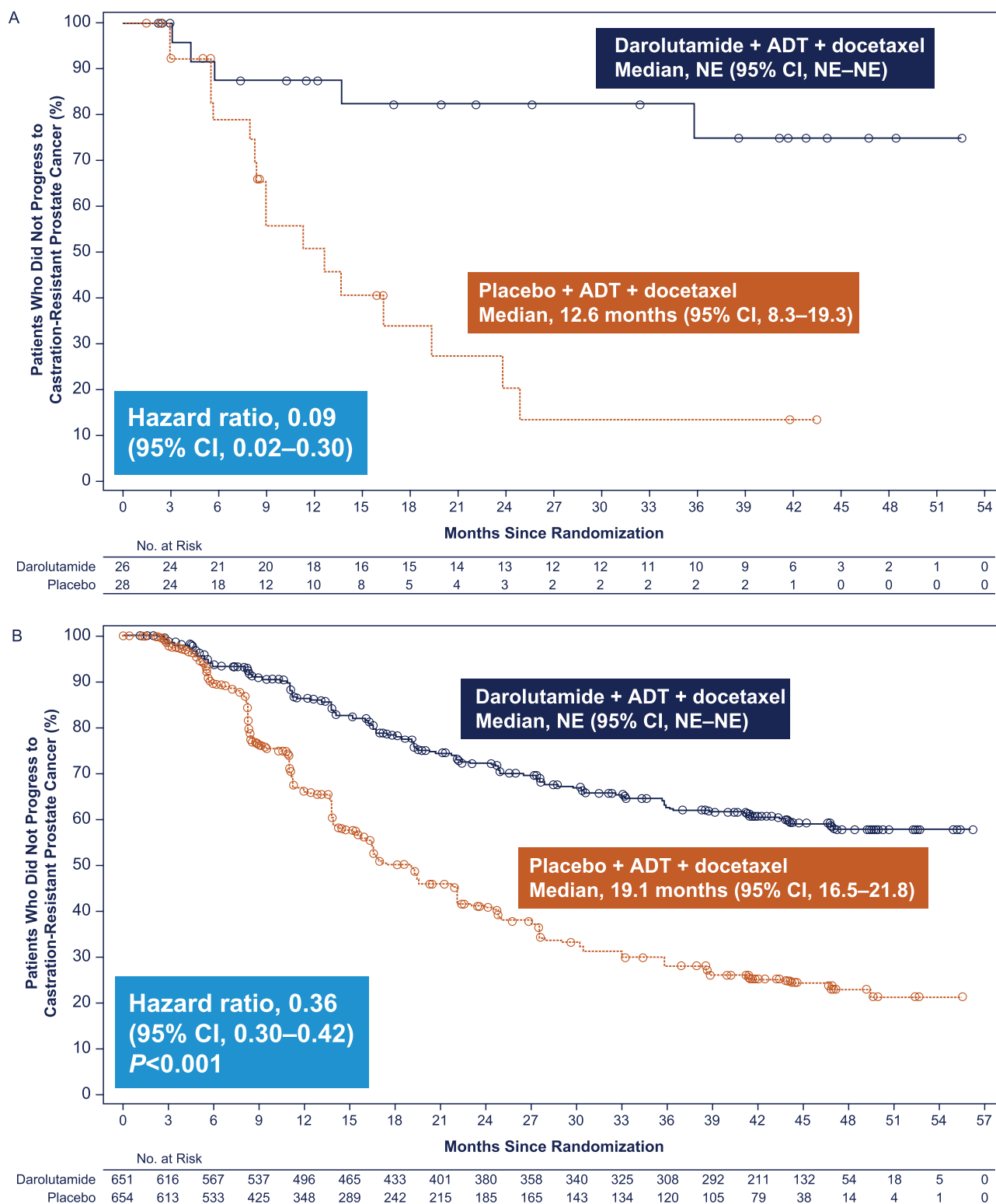


Figure 1. Overall survival in the (A) Black subgroup and (B) overall population. Analysis was conducted after 533 deaths (darolutamide, 229; placebo, 304) occurred in the overall population. Abbreviations: ADT: androgen-deprivation therapy; CI: confidence interval; NE: not estimable.



small subgroup of 54 patients, despite longer treatment duration with darolutamide versus placebo, numbers of patients with grade 3 or 4 adverse events (16 vs. 17), serious adverse events (11 vs. 7), and discontinuations of darolutamide or placebo due to adverse events (5 vs. 4) were similar between treatment groups.

Incidence rates of most TEAEs commonly associated with androgen receptor pathway inhibitors were similar between treatment groups and generally consistent with incidences observed in the overall population (Table 3). When they were adjusted for the longer duration of darolutamide treatment, the EAIRs between treatment groups for hypertension,

Table 2. Incidence of treatment-emergent adverse events.

TEAE, n (%)	Black subgroup		Overall population ^a	
	Darolutamide + ADT + docetaxel (n = 26)	Placebo + ADT + docetaxel (n = 28)	Darolutamide + ADT + docetaxel (n = 652)	Placebo + ADT + docetaxel (n = 650 ^a)
Any	26 (100.0)	27 (96.4)	649 (99.5)	643 (98.9)
Worst grade				
Grade 1 or 2	8 (30.8)	10 (35.7)	190 (29.1)	204 (31.4)
Grade 3 or 4	16 (61.5)	17 (60.7)	431 (66.1)	413 (63.5)
Grade 5	2 (7.7)	0	27 (4.1)	26 (4.0)
Serious	11 (42.3)	7 (25.0)	292 (44.8)	275 (42.3)
Leading to discontinuation of:				
Darolutamide/placebo	5 (19.2)	4 (14.3)	88 (13.5)	69 (10.6)
Exposure-adjusted incidence rate, per 100 patient years ^b	8.1	11.2	5.1	5.7

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^aThree randomized patients (all in the placebo group) were never treated and were excluded from the safety analysis set. One patient randomized to placebo but who received darolutamide was included in the darolutamide group for the safety analysis set.

^bExposure-adjusted incidence rate is defined as the number of patients with a given TEAE divided by the total darolutamide/placebo treatment duration for all patients in years.

Abbreviations: ADT: androgen-deprivation therapy; TEAE: treatment-emergent adverse event.

cardiac disorders, bone fracture, and depressed mood disorders were similar or decreased.

Discussion

In ARASENS, darolutamide significantly improved overall survival and key secondary endpoints compared with placebo and was well tolerated with no added toxicity when combined with ADT and docetaxel in patients with mHSPC.^{13,18} The results of this subgroup analysis of Black patients in ARASENS are consistent with results from the overall population showing a survival benefit with darolutamide. Four-year survival rates were 62% and 63% with darolutamide in the subgroup and overall populations, respectively, compared with 41% and 50% with placebo. Darolutamide also increased the time to castration-resistance versus placebo in Black patients. The favorable safety and tolerability profile of darolutamide was confirmed in Black patients with mHSPC. Most patients were able to receive 6 cycles of docetaxel therapy in both treatment groups. Incidence rates of grade 3 or 4 and serious TEAEs were similar across treatment groups, despite longer treatment with darolutamide versus placebo, and consistent with the overall population. No new safety findings were observed.

Clinical trials combining standard ADT with docetaxel and/or novel androgen receptor pathway inhibitors have enrolled small numbers of Black patients with mHSPC, providing limited efficacy and safety information for this population. The CHAARTED trial of ADT with or without docetaxel included 9.6% of patients who were Black,⁸ while TITAN and ARCHES trials of apalutamide and enzalutamide included 1.8% and 1.4%, respectively.^{19,20} Overall survival in CHAARTED was similar for Black patients and White patients who received ADT and docetaxel (57.6 vs. 58.1 months) but slightly lower for Black versus White patients who received ADT alone (34.1 v.s 45.2 months).¹⁴ Results

for TITAN and ARCHES by race subgroup have not been published. A real-world analysis of health record data identified 168 patients with mHSPC who received treatment with upfront docetaxel or abiraterone before any other systemic therapy, of which 92 (54.8%) patients were Black and 76 (45.2%) were non-Black, including 69 White patients and 7 Asian or Hispanic patients.²¹ Overall survival at 12 months among Black patients was 89.2% for docetaxel and 97.5% for abiraterone, with no significant difference versus the non-Black population (95.5% and 92.6%, respectively). A retrospective study across 7 academic institutions in the US reported favorable time to CRPC and overall survival for 107 Black patients with mHSPC who received ADT-based regimens, including first-generation anti-androgens, novel androgen receptor pathway inhibitors, and/or docetaxel.²² These findings from the literature suggest that Black patients can achieve similar benefits from treatments for mHSPC as observed for non-Black patients. Several larger studies provide further support in patients with metastatic prostate cancer not specifically defined as mHSPC. An analysis of the US National Cancer Database found similar survival outcomes for Black (n = 5932) and White (n = 24 659) patients with metastatic prostate cancer.²³ A meta-analysis of phase III trials of patients with metastatic CRPC showed similar median survival times for Black patients compared with White patients (21 months) with the pooled hazard ratio showing a survival benefit in Black patients (HR 0.81; 95% CI, 0.72-0.91).⁷ Further analyses of these pooled data indicated no differences between racial groups in progression-free survival (PFS) distributions, median PFS, prostate-specific antigen decline from baseline of 50% or more, and overall response rates.¹⁵

This analysis of Black patients in ARASENS was conducted post hoc in a small population. Our findings add valuable information to the growing body of work evaluating the treatment of advanced prostate cancer in this population. Current information suggests that equal access to care leads

Table 3. Incidence of treatment-emergent adverse events associated with androgen receptor pathway inhibitors.

TEAE, n (%)	Black subgroup				Overall population ^a			
	Darolutamide + ADT + docetaxel (n = 26)		Placebo + ADT + docetaxel (n = 28)		Darolutamide + ADT + docetaxel (n = 652)		Placebo + ADT + docetaxel (n = 650 ^a)	
	n (%)	EAIR/100 PY ^b	n (%)	EAIR/100 PY ^b	n (%)	EAIR/100 PY ^b	n (%)	EAIR/100 PY ^b
Fatigue	13 (50.0)	21.1	15 (53.6)	42.1	216 (33.1)	12.5	214 (32.9)	17.8
Vasodilation/flushing	8 (30.8)	13.0	15 (53.6)	42.1	133 (20.4)	7.7	141 (21.7)	11.7
Rash	2 (7.7)	3.2	2 (7.1)	5.6	108 (16.6)	6.2	88 (13.5)	7.3
Diabetes/hyperglycemia	4 (15.4)	6.5	7 (25.0)	19.6	99 (15.2)	5.7	93 (14.3)	7.7
Hypertension	8 (30.8)	13.0	6 (21.4)	16.8	89 (13.7)	5.1	60 (9.2)	5.0
Cardiac disorders	4 (15.4)	6.5	3 (10.7)	8.4	71 (10.9)	4.1	76 (11.7)	6.3
Bone fracture	2 (7.7)	3.2	1 (3.6)	2.8	49 (7.5)	2.8	33 (5.1)	2.7
Fall	4 (15.4)	6.5	0	0	43 (6.6)	2.5	30 (4.6)	2.5
Mental impairment disorders	1 (3.8)	1.6	0	0	23 (3.5)	1.3	15 (2.3)	1.2
Decreased weight	1 (3.8)	1.6	3 (10.7)	8.4	22 (3.4)	1.3	35 (5.4)	2.9
Depressed mood disorders	3 (11.5)	4.9	2 (7.1)	5.6	21 (3.2)	1.2	24 (3.7)	2.0
Breast disorders/gynecomastia	0	0	2 (7.1)	5.6	21 (3.2)	1.2	10 (1.5)	0.8

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^aThree randomized patients (all in the placebo group) were never treated and were excluded from the safety analysis set. One patient randomized to placebo but who received darolutamide was included in the darolutamide group for the safety analysis set.

^bExposure-adjusted incidence rate is defined as the number of patients with a given TEAE divided by the total darolutamide/placebo treatment duration for all patients in years.

Abbreviations: ADT: androgen-deprivation therapy; EAIR: exposure-adjusted incidence rate; PY: patient-years; TEAE: treatment-emergent adverse event.

to achievement of comparable outcomes for Black patients as achieved by White patients.^{4,6} However, racial disparities in prostate cancer incidence and mortality continue to exist and have been linked to social, economic, environmental, and genetic factors.²⁴ Patient numbers for Black participants remain small in clinical trials, and we strongly encourage all clinical research investigators to optimize racial and ethnic accrual for both existing and future trials. Findings from a pooled analysis of 7 phase III trials in CRPC underscore the importance of diverse participation in clinical trials to ensure equitable access to novel therapies and to accurately assess treatment efficacy in diverse populations. Out of a total of 7275 patients enrolled in the 7 trials from this analysis, only 3.3% were Black.²⁵ By mandating diversity in clinical trials, we can help address persistent racial disparities in prostate cancer outcomes and develop more tailored interventions that improve health outcomes for all individuals affected by this disease.

Conclusions

In Black patients with mHSPC, darolutamide in combination with ADT and docetaxel improved overall survival and time to CRPC compared with ADT and docetaxel alone and was well tolerated. Results in this subgroup of patients were consistent with those of the overall ARASENS population.

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Conflict of Interest

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Data Availability

Availability of the data underlying this publication will be determined according to Bayer's commitment to the EFPIA/PhRMA "Principles for responsible clinical trial data sharing." This pertains to scope, timepoint, and process of data access. As such, Bayer commits to sharing upon request from qualified scientific and medical researchers patient-level clinical trial data, study-level clinical trial data, and protocols from clinical trials in patients for medicines and indications approved in the United States (US) and European Union (EU) as necessary for conducting legitimate research. This applies to data on new medicines and indications that have been approved by the EU and US regulatory agencies on or after January 1, 2014. Interested researchers can use www.vivli.org to request access to anonymized patient-level data and supporting documents from clinical studies to conduct further research that can help advance medical science or improve patient care. Information on the Bayer criteria for listing studies and other relevant information is provided in the member section of the portal. Data access will be granted to anonymized patient-level data, protocols and clinical study reports after approval by an independent scientific review panel. Bayer is not involved in the decisions made by the independent review panel. Bayer will take all necessary measures to ensure that patient privacy is safeguarded.

Supplementary Material

Supplementary material is available at *The Oncologist* online.

References

1. Sung H, Ferlay J, Siegel RL, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin.* 2021;71(3):209-249. <https://doi.org/10.3322/caac.21660>
2. Siegel RL, Miller KD, Wagle NS, Jemal A. Cancer statistics, 2023. *CA Cancer J Clin.* 2023;73(1):17-48. <https://doi.org/10.3322/caac.21763>
3. Awasthi S, Grass GD, Torres-Roca J, et al. Genomic testing in localized prostate cancer can identify subsets of African Americans with

- aggressive disease. *J Natl Cancer Inst.* 2022;114(12):1656-1664. <https://doi.org/10.1093/jnci/djac162>
4. Dess RT, Hartman HE, Mahal BA, et al. Association of black race with prostate cancer-specific and other-cause mortality. *JAMA Oncol.* 2019;5(7):975-983. <https://doi.org/10.1001/jamaoncol.2019.0826>
 5. Riviere P, Luterstein E, Kumar A, et al. Survival of African American and non-Hispanic white men with prostate cancer in an equal-access health care system. *Cancer.* 2020;126(8):1683-1690. <https://doi.org/10.1002/cncr.32666>
 6. Rasmussen KM, Patil V, Li C, et al. Care in an equal access system delays prostate cancer progression in minorities [poster]. 2023.
 7. Halabi S, Dutta S, Tangen CM, et al. Overall survival of black and white men with metastatic castration-resistant prostate cancer treated with docetaxel. *J Clin Oncol.* 2019;37(5):403-410. <https://doi.org/10.1200/JCO.18.01279>
 8. Sweeney CJ, Chen YH, Carducci M, et al. Chemohormonal therapy in metastatic hormone-sensitive prostate cancer. *N Engl J Med.* 2015;373(8):737-746. <https://doi.org/10.1056/NEJMoa1503747>
 9. 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(5):686-700. [https://doi.org/10.1016/S1470-2045\(19\)30082-8](https://doi.org/10.1016/S1470-2045(19)30082-8)
 10. Chi KN, Chowdhury S, Bjartell A, et al. Apalutamide in patients with metastatic castration-sensitive prostate cancer: final survival analysis of the randomized, double-blind, phase III TITAN study. *J Clin Oncol.* 2021;39(20):2294-2303. <https://doi.org/10.1200/JCO.20.03488>
 11. Armstrong AJ, Azad AA, Iguchi T, et al. Improved survival with enzalutamide in patients with metastatic hormone-sensitive prostate cancer. *J Clin Oncol.* 2022;40(15):1616-1622. <https://doi.org/10.1200/JCO.22.00193>
 12. Fizazi K, Foulon S, Carles J, et al. Abiraterone plus prednisone added to androgen deprivation therapy and docetaxel in de novo metastatic castration-sensitive prostate cancer (PEACE-1): a multicentre, open-label, randomised, phase 3 study with a 2x2 factorial design. *Lancet.* 2022;399(10336):1695-1707. [https://doi.org/10.1016/s0140-6736\(22\)00367-1](https://doi.org/10.1016/s0140-6736(22)00367-1)
 13. Smith MR, Hussain M, Saad F, et al. Darolutamide and survival in metastatic, hormone-sensitive prostate cancer. *N Engl J Med.* 2022;386(12):1132-1142. <https://doi.org/10.1056/nejmoa2119115>
 14. Bernard B, Muralidhar V, Chen YH, et al. Impact of ethnicity on the outcome of men with metastatic, hormone-sensitive prostate cancer. *Cancer.* 2017;123(9):1536-1544. <https://doi.org/10.1002/cncr.30503>
 15. Halabi S, Dutta S, Tangen CM, et al. Clinical outcomes in men of diverse ethnic backgrounds with metastatic castration-resistant prostate cancer. *Ann Oncol.* 2020;31(7):930-941. <https://doi.org/10.1016/j.annonc.2020.03.309>
 16. Moilanen AM, Riikonen R, Oksala R, et al. Discovery of ODM-201, a new-generation androgen receptor inhibitor targeting resistance mechanisms to androgen signaling-directed prostate cancer therapies. *Sci Rep.* 2015;5(1):12007. <https://doi.org/10.1038/srep12007>
 17. Shore N, Zurth C, Fricke R, et al. Evaluation of clinically relevant drug-drug interactions and population pharmacokinetics of darolutamide in patients with nonmetastatic castration-resistant prostate cancer: results of pre-specified and post hoc analyses of the phase III ARAMIS trial. *Target Oncol.* 2019;14(5):527-539. <https://doi.org/10.1007/s11523-019-00674-0>
 18. Hussain M, Tombal B, Saad F, et al. Darolutamide plus androgen-deprivation therapy and docetaxel in metastatic hormone-sensitive prostate cancer by disease volume and risk subgroups in the phase III ARASENS trial. *J Clin Oncol.* 2023;16. <https://doi.org/10.1200/jco.23.00041>
 19. Chi KN, Agarwal N, Bjartell A, et al. Apalutamide for metastatic, castration-sensitive prostate cancer. *N Engl J Med.* 2019;381(1):13-24. <https://doi.org/10.1056/NEJMoa1903307>
 20. 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(32):2974-2986. <https://doi.org/10.1200/JCO.19.00799>
 21. Smith KER, Brown JT, Wan L, et al. Clinical outcomes and racial disparities in metastatic hormone-sensitive prostate cancer in the era of novel treatment options. *Oncologist.* 2021;26(11):956-964. <https://doi.org/10.1002/onco.13848>
 22. Freeman MN, Jang A, Zhu J, et al. Multi-institutional analysis of the clinical and genomic characteristics of black patients with metastatic hormone-sensitive prostate cancer. *Oncologist.* 2022;27(3):220-227. <https://doi.org/10.1093/oncolo/oyab057>
 23. Vengaloor Thomas T, Gordy XZ, Lirette ST, et al. Lack of racial survival differences in metastatic prostate cancer in national cancer data base (NCDB): a different finding compared to non-metastatic disease. *Front Oncol.* 2020;10(5):533070. <https://doi.org/10.3389/fonc.2020.533070>
 24. Chowdhury-Paulino IM, Ericsson C, Vince R Jr, et al. Racial disparities in prostate cancer among black men: epidemiology and outcomes. *Prostate Cancer Prostatic Dis.* 2022;25(3):397-402. <https://doi.org/10.1038/s41391-021-00451-z>
 25. Spratt DE, Osborne JR. Disparities in castration-resistant prostate cancer trials. *J Clin Oncol.* 2015;33(10):1101-1103. <https://doi.org/10.1200/JCO.2014.58.1751>