clinical trial updates

Improved Survival With Enzalutamide in Patients With Metastatic Hormone-Sensitive Prostate Cancer

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abstract

Clinical trials frequently include multiple end points that mature at different times. The initial report, typically based on the primary end point, may be published when key planned co-primary or secondary analyses are not yet available. Clinical Trial Updates provide an opportunity to disseminate additional results from studies, published in JCO or elsewhere, for which the primary end point has already been reported.

In primary analysis, enzalutamide plus androgen deprivation therapy (ADT) improved radiographic progression-free survival (rPFS) in patients with metastatic hormone-sensitive prostate cancer (mHSPC); however, overall survival data were immature. In the phase III, double-blind, global ARCHES trial (ClinicalTrials.gov identifier: NCT02677896), 1,150 patients with mHSPC were randomly assigned 1:1 to enzalutamide (160 mg once daily) plus ADT or placebo plus ADT, stratified by disease volume and prior docetaxel use. Here, we report the final prespecified analysis of overall survival (key secondary end point) and an update on rPFS, other secondary end points, and safety. After unblinding, 180 (31.3%) progression-free patients randomly assigned to placebo plus ADT crossed over to open-label enzalutamide plus ADT. As of May 28, 2021 (median follow-up, 44.6 months), 154 of 574 patients randomly assigned to enzalutamide plus ADT and 202 of 576 patients randomly assigned to placebo plus ADT had died. Enzalutamide plus ADT reduced risk of death by 34% versus placebo plus ADT (median not reached in either group; hazard ratio, 0.66; 95% CI, 0.53 to 0.81; $P < .001$). Enzalutamide plus ADT continued to improve rPFS and other secondary end points. Adverse events were generally consistent with previous reports of long-term enzalutamide use. In conclusion, enzalutamide plus ADT significantly prolongs survival versus placebo plus ADT in patients with mHSPC.

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ASSOCIATED CONTENT

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Data Supplement

Protocol

Author affiliations and support information (if applicable) appear at the end of this article.

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INTRODUCTION

Enzalutamide in combination with androgen deprivation therapy (ADT) is approved for the treatment of metastatic hormone-sensitive prostate cancer (mHSPC [also referred to as metastatic castration-sensitive prostate cancer])[1,2] on the basis of proven clinical benefits in the phase III ARCHES trial (ClinicalTrials.gov identifier: NCT02677896). At the time of the primary analysis, enzalutamide plus ADT significantly reduced the risk of radiographic disease progression or death in men with mHSPC; however, overall survival (OS) data were considered immature.[3]

Herein, we report the final prespecified OS analysis and an update on radiographic progression-free survival (rPFS), other secondary end points, and safety.

METHODS

Study Design

Details of the study design of ARCHES have been published previously.[3]

Enrolled patients were randomly assigned 1:1 to receive enzalutamide (160 mg once daily) plus ADT or placebo plus ADT, stratified by disease volume and prior docetaxel use. After the primary analysis, ARCHES was unblinded to allow patients randomly assigned to placebo plus ADT to cross over to enzalutamide plus ADT in an open-label extension.

End Points

OS (key secondary end point) was defined as the time from random assignment to death from any cause. We also report an update on rPFS and other

TABLE 1. Patient Demographics and Disease Characteristics (intent-to-treat population)

Characteristic	ENZA + ADT (n = 574)	PBO + ADT (n = 576)	PBO Crossover (n = 184)
Median age, years (range)	70.0 (46-92)	70.0 (42-92)	69.0 (51-89)
Age, years, No. (%)			
< 65	148 (25.8)	152 (26.4)	39 (21.2)
65-74	256 (44.6)	255 (44.3)	96 (52.2)
≥ 75	170 (29.6)	169 (29.3)	49 (26.6)
Race, No. (%)[a]			
White	466 (81.2)	460 (79.9)	140 (76.1)
Asian	75 (13.1)	80 (13.9)	38 (20.7)
Black or African American	8 (1.4)	8 (1.4)	4 (2.2)
Other	2 (0.3)	3 (0.5)	1 (0.5)
Missing	23 (4.0)	25 (4.3)	1 (0.5)
Geographic region, No. (%)			
Europe	341 (59.4)	344 (59.7)	102 (55.4)
Asia-Pacific	104 (18.1)	113 (19.6)	49 (26.6)
North America	86 (15.0)	77 (13.4)	18 (9.8)
South America	32 (5.6)	30 (5.2)	11 (6.0)
Other	11 (1.9)	12 (2.1)	4 (2.2)
ECOG status, No. (%)			
0	448 (78.0)	443 (76.9)	155 (84.2)
1	125 (21.8)	133 (23.1)	29 (15.8)
Disease volume, No. (%)			
High[b]	354 (61.7)	373 (64.8)	92 (50.0)
Low	220 (38.3)	203 (35.2)	92 (50.0)
Total Gleason score at initial diagnosis, No. (%)			
< 8	171 (29.8)	187 (32.5)	70 (38.0)
≥ 8	386 (67.2)	373 (64.8)	108 (58.7)
Confirmed metastases at screening, No. (%)[c]			
Yes	536 (93.4)	531 (92.2)	157 (85.3)
No	34 (5.9)	45 (7.8)	27 (14.7)
Unknown	4 (0.7)	0	0
Localization of confirmed metastases at screening, No. (%)[c]			
Lymph node only[d]	74 (12.9)	80 (13.9)	41 (22.8)
Bone disease, with or without lymph node	432 (75.3)	432 (75.0)	122 (67.8)
Visceral disease, with or without bone or lymph node	64 (11.1)	64 (11.1)	17 (9.4)
Distant metastasis at initial diagnosis, No. (%)			
M1	402 (70.0)	365 (63.4)	107 (58.2)
M0	83 (14.5)	86 (14.9)	32 (17.4)
MX/unknown	88 (15.3)	125 (21.7)	45 (24.5)
Prior local therapy, No. (%)			
Radical prostatectomy	72 (12.5)	89 (15.5)	32 (17.4)
Radiation therapy	73 (12.7)	72 (12.5)	36 (19.6)
No. of cycles of prior docetaxel chemotherapy, No. (%)			
0	471 (82.1)	474 (82.3)	155 (84.2)
1-5	14 (2.4)	11 (1.9)	6 (3.3)
6	89 (15.5)	91 (15.8)	23 (12.5)
Previous use of ADT, No. (%)			
None	39 (6.8)	61 (10.6)	21 (11.4)
≤ 3 months	414 (72.1)	394 (68.4)	125 (67.9)
> 3 months	121 (21.1)	120 (20.8)	37 (20.1)
Unknown[e]	0	1 (0.2)	1 (0.5)
Median PSA, ng/mL (range)	5.4 (0-4,823.5)	5.1 (0-19,000.0)	4.05 (0-3,192.0)

Abbreviations: ADT, androgen deprivation therapy; ECOG, Eastern Cooperative Oncology Group; ENZA, enzalutamide; M0, no distant metastasis; M1, distant metastasis; MX, distant metastasis cannot be assessed (not evaluated by any modality); PBO, placebo; PSA, prostate-specific antigen.

[a]By country regulations, race is not collected in France.

[b]Defined by CHAARTED criteria as the presence of metastases involving the viscera or, in the absence of visceral lesions, four or more bone lesions, one or more of which must be in a bony structure beyond the vertebral column and pelvic bone; some study sites incorrectly reported disease volume information for some patients at the time of random assignment, which was corrected during medical review on study entry, resulting in a difference of approximately 20 patients with either high or low disease volume between the treatment arms.

[c]Assessed by independent central review after investigator assessment at study entry.

[d]Lymph node metastases or unconfirmed metastatic disease.

[e]The patient had prior ADT; however, the duration of ADT use was unknown.

[f]Safety analysis set patients (ENZA plus ADT, n = 572; PBO plus ADT, n = 574; PBO plus ADT crossover, n = 180).

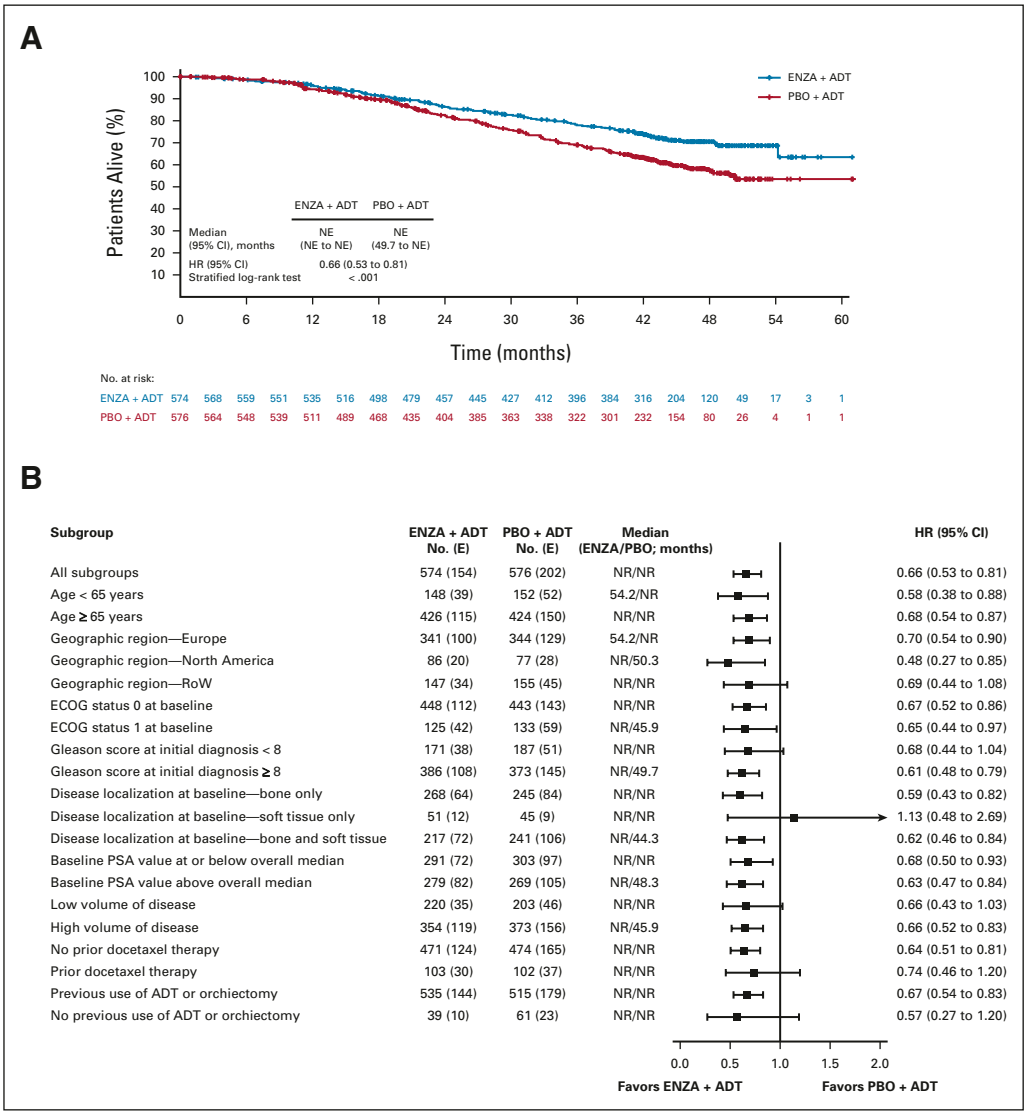

FIG 1. Efficacy analyses (intent-to-treat population) showing (A) Kaplan-Meier estimate of final OS analysis, (B) forest plot of OS subgroup analyses, (C) Kaplan-Meier estimates of time to first subsequent antineoplastic therapy, and (D) Kaplan-Meier estimates of rPFS (investigator assessed). ADT, androgen deprivation therapy; E, events; ECOG, Eastern Cooperative Oncology Group; ENZA, enzalutamide; HR, hazard ratio; NE, not evaluable; NR, not reached; OS, overall survival; PBO, placebo; PSA, prostate-specific antigen; RoW, rest of world; rPFS, radiographic progression-free survival. (continued on following page)

key secondary end points. The data cutoff for this report was May 28, 2021.

Statistical analysis methodology is reported in the Data Supplement (online only).

RESULTS

Baseline Demographics and Patient History

From March 21, 2016, to January 12, 2018, 1,150 patients were randomly assigned. Baseline demographics are presented in Table 1. Patient disposition is summarized in the Data Supplement.

After study unblinding, 184 patients (31.9%) randomly assigned to placebo plus ADT remained progression-free and consented to cross over, 180 (31.3%) of whom received treatment with enzalutamide plus ADT (median time to crossover, 21.5 months). After a total of 356 deaths (enzalutamide plus ADT, n = 154; placebo plus ADT, n = 202), the data cutoff for the final OS analysis was May 28, 2021; the median follow-up time was 44.6 months.

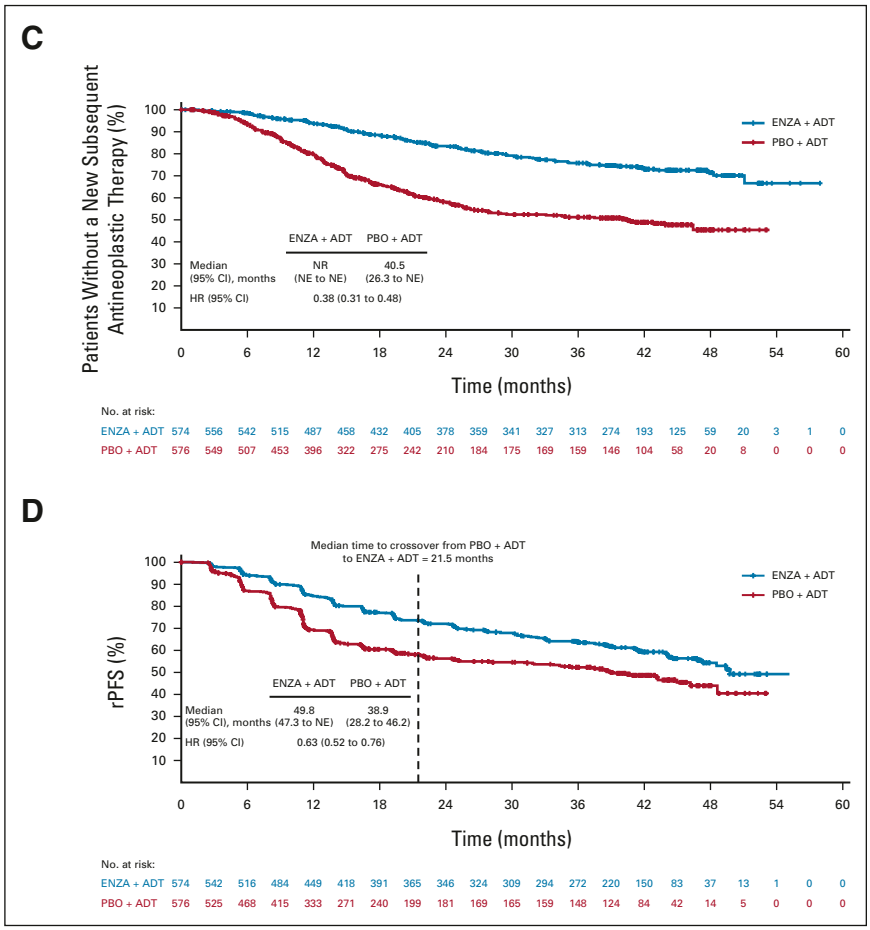

FIG 1. (Continued).

After treatment discontinuation, 131 patients (23%) randomly assigned to enzalutamide plus ADT and 221 patients (38%) randomly assigned to placebo plus ADT received subsequent life-prolonging therapy; an additional 15 patients (8%) in the crossover group received subsequent life-prolonging therapy after discontinuing enzalutamide plus ADT (Data Supplement). Inclusive of crossover, 401 patients (70%) randomly assigned to placebo plus ADT received subsequent life-prolonging therapy, with 241 (42%) receiving enzalutamide as the first subsequent life-prolonging therapy.

OS

Patients randomly assigned to enzalutamide plus ADT had a 34% reduction in the risk of death versus placebo plus ADT (hazard ratio [HR], 0.66; 95% CI, 0.53 to 0.81; $P < .001$; Fig 1A); the median OS was not reached in either group. At 24, 36, and 48 months, 86%, 78%, and 71% of patients randomly assigned to enzalutamide plus ADT were estimated to be alive, respectively, compared with 82%, 69%, and 57% of patients randomly assigned to placebo plus ADT.

A prespecified rank-preserving structural failure time sensitivity analysis to adjust for a possible crossover effect demonstrated a 43% reduction in risk of death with enzalutamide plus ADT versus placebo plus ADT (HR, 0.57; 95% CI, 0.45 to 0.70; $P < .001$; Data Supplement). Median OS was not reached for enzalutamide plus ADT, but was 47.7 months (95% CI, 43.3 to not evaluable) for placebo plus ADT.

The clinical benefit of enzalutamide plus ADT was generally consistent across prespecified subgroups, except in patients with only soft tissue disease at baseline (n = 96; Fig 1B). Further exploratory post hoc subgroup analyses confirmed a survival benefit after enzalutamide plus ADT in all subgroups except for patients with lymph node metastases only and visceral metastases, most likely because of small patient numbers (Data Supplement).

rPFS and Secondary Efficacy End Points

Enzalutamide plus ADT delayed time to first subsequent antineoplastic therapy; median was not reached for enzalutamide plus ADT versus 40.5 months for placebo

TABLE 2. Summary of TEAEs and Exposure-Adjusted TEAEs of Special Interest (safety analysis set)

TEAEs	ENZA + ADT (n = 572)	PBO + ADT[a] (n = 574)
Median treatment duration, months (range)	40.2 (0.2-58.1)	13.8 (0.2-27.6)
Total exposure, PY	1,521.5	733.2
Any TEAE, No. (%)	520 (90.9)	504 (87.8)
Any grade 3-4 TEAE, No. (%)	224 (39.2)	160 (27.9)
Any TEAE leading to death, No. (%)	30 (5.2)	12 (2.1)
Any study drug-related TEAE, No. (%)	339 (59.3)	273 (47.6)
Any study drug-related TEAE leading to death, No. (%)	0	1 (0.2)
Any TEAE of special interest, No. (%)	416 (72.7)	327 (57.0)

	All Grades		Grade 3-4		All Grades		Grade 3-4	
TEAE of Special Interest by Group Term[b]	No. (%)	Events (rate)[c]	No. (%)	Events (rate)[c]	No. (%)	Events (rate)[c]	No. (%)	Events (rate)[c]
Convulsions	3 (0.5)	3 (0.2)	3 (0.5)	3 (0.2)	3 (0.5)	3 (0.4)	2 (0.3)	2 (0.3)
Hypertension	82 (14.3)	88 (5.8)	29 (5.1)	30 (2.0)	39 (6.8)	40 (5.5)	13 (2.3)	13 (1.8)
Decreased neutrophil count	8 (1.4)	10 (0.7)	4 (0.7)	5 (0.3)	4 (0.7)	6 (0.8)	2 (0.3)	4 (0.5)
Cognitive/memory impairment	38 (6.6)	46 (3.0)	4 (0.7)	5 (0.3)	15 (2.6)	15 (2.0)	0	0
Ischemic heart disease	26 (4.5)	31 (2.0)	7 (1.2)	8 (0.5)	11 (1.9)	14 (1.9)	8 (1.4)	9 (1.2)
Other selected cardiovascular events	25 (4.4)	33 (2.2)	10 (1.7)	11 (0.7)	10 (1.7)	11 (1.5)	4 (0.7)	5 (0.7)
Posterior reversible encephalopathy syndrome	0	0	0	0	0	0	0	0
Fatigue	184 (32.2)	216 (14.2)	16 (2.8)	26 (1.7)	118 (20.6)	126 (17.2)	11 (1.9)	12 (1.6)
Renal disorders	11 (1.9)	13 (0.9)	2 (0.3)	2 (0.1)	4 (0.7)	5 (0.7)	0	0
Second primary malignancies	22 (3.8)	23 (1.5)	15 (2.6)	16 (1.1)	11 (1.9)	14 (1.9)	7 (1.2)	7 (1.0)
Falls	58 (10.1)	86 (5.7)	7 (1.2)	10 (0.7)	19 (3.3)	20 (2.7)	3 (0.5)	4 (0.5)
Fractures	77 (13.5)	106 (7.0)	20 (3.5)	23 (1.5)	31 (5.4)	36 (4.9)	9 (1.6)	12 (1.6)
Loss of consciousness	15 (2.6)	16 (1.1)	9 (1.6)	10 (0.7)	2 (0.3)	2 (0.3)	1 (0.2)	1 (0.1)
Thrombocytopenia	3 (0.5)	7 (0.5)	0	16 (1.1)	3 (0.5)	3 (0.4)	0	0
Musculoskeletal events	223 (39.0)	395 (26.0)	14 (2.4)	1 (0.1)	170 (29.6)	257 (35.1)	17 (3.0)	20 (2.7)
Severe cutaneous adverse reactions	1 (0.2)	1 (0.1)	0	0	1 (0.2)	1 (0.1)	0	0
Angioedema	10 (1.7)	11 (0.7)	1 (0.2)	1 (0.1)	1 (0.2)	1 (0.1)	0	0
Rash	22 (3.8)	26 (1.7)	0	0	10 (1.7)	12 (1.6)	0	0
Hepatic disorder	34 (5.9)	43 (2.8)	8 (1.4)	11 (0.7)	34 (5.9)	55 (7.5)	4 (0.7)	9 (1.2)

Abbreviations: ADT, androgen deprivation therapy; ENZA, enzalutamide; PBO, placebo; PY, patient-year; TEAE, treatment-emergent adverse event.

[a]TEAEs were reported for events that occurred during the period that patients were treated with placebo plus ADT and up to 30 days after the last dose or up to the day before the start of open-label enzalutamide plus ADT, whichever was sooner.

[b]TEAEs of special interest were based on prespecified combinations of preferred terms (Medical Dictionary for Regulatory Activities v23.0) and were graded on the basis of the National Cancer Institute Common Terminology Criteria for Adverse Events v4.03 by the investigator.

[c]Per 100 PYs of exposure.

plus ADT (HR, 0.38; 95% CI, 0.31 to 0.48; Data Supplement; Fig 1C).

Compared with placebo plus ADT, enzalutamide plus ADT reduced the risk of radiographic progression or death by 37%, extending the median rPFS by approximately 11 months (Data Supplement; Fig 1D). A total of 117 patients (20%) randomly assigned to enzalutamide plus ADT had prostate-specific antigen (PSA) progression compared with 259 (45%) randomly assigned to placebo plus ADT, equating to a risk reduction of 72% (Data Supplement). After median time to crossover (21.5 months) was reached, the rate of radiographic and PSA progression slowed over time with placebo plus ADT (Fig 1D; Data Supplement).The reduced risk of radiographic progression or death and PSA progression observed with enzalutamide plus ADT, as compared with placebo plus ADT, was sustained after adjustment for crossover (Data Supplement). Enzalutamide plus ADT also delayed time to

first symptomatic skeletal event (Data Supplement) and castration resistance (Data Supplement). Results of other secondary end point analyses are reported in the Data Supplement.

Safety

The median treatment duration was 40.2, 13.8, and 23.9 months in the enzalutamide plus ADT, placebo plus ADT, and crossover groups, respectively. Incidence of treatment-emergent adverse events was consistent with the primary analysis[3] (Table 2; Data Supplement), and no new safety signals were identified.

DISCUSSION

In ARCHES, enzalutamide plus ADT significantly reduced the risk of death in patients with mHSPC by 34% versus placebo plus ADT. The survival benefit of enzalutamide plus ADT became more apparent with additional follow-up. Enzalutamide plus ADT also delayed time to initiation of the first subsequent antineoplastic therapy. In total, 70% of patients who initially received placebo plus ADT went on to receive a life-prolonging treatment and, inclusive of those who crossed over, 42% went on to treatment with enzalutamide. Despite this, a statistically significant survival benefit was observed with enzalutamide plus ADT, highlighting the importance of early enzalutamide use in patients with mHSPC, rather than delaying initiation until the development of castration resistance. Importantly, improvement in OS with enzalutamide is unlikely to be the result of patients in the placebo plus ADT group receiving inadequate postprotocol therapy.

The survival benefit with early use of enzalutamide plus ADT was generally consistent across subgroups, with the exception of patients with lymph node metastases only and visceral metastases; however, both subgroups had relatively low patient numbers and statistical analyses were underpowered, as also reported in other large trials of mHSPC.[4-6] Nevertheless, clinicians assessing and prescribing therapy for patients with mHSPC should feel reassured regarding survival benefit with enzalutamide for the majority of patients.

The superiority of enzalutamide plus ADT over placebo plus ADT for other efficacy end points was previously reported[3] and maintained with additional follow-up. No new safety signals emerged. Taken together, these data indicate that longer-term use of enzalutamide was well tolerated and not associated with any new toxicity concerns, a key consideration for clinicians when choosing a systemic treatment for patients with advanced prostate cancer.

In conclusion, enzalutamide plus ADT significantly prolongs survival versus placebo plus ADT in patients with mHSPC, including across clinically important subgroups, and thus represents an effective and well-tolerated therapeutic option for patients with mHSPC.

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DATA SHARING STATEMENT

Researchers may request access to anonymized participant-level data, trial-level data, and protocols from Astellas-sponsored clinical trials at www.clinicalstudydatarequest.com. For the Astellas criteria on data sharing, see https://clinicalstudydatarequest.com/Study-Sponsors/Study-Sponsors-Astellas.aspx.

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AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

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Travel, Accommodations, Expenses: Astellas Pharma, Sanofi, Merck Serono, Amgen, Janssen, Tolmar, Pfizer

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Consulting or Advisory Role: Astellas Pharma, Bayer
Speakers' Bureau: Astellas Pharma, Bayer Yakuhin, Janssen, Sanofi, AstraZeneca, Takeda
Research Funding: Astellas Pharma, Bayer Yakuhin

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Consulting or Advisory Role: AstraZeneca, AbbVie, Exelixis, Merck, Amgen, Janssen Oncology, Sanofi, Astellas Pharma, Pfizer
Research Funding: AbbVie (Inst), Astellas Pharma (Inst), MacroGenics (Inst), Janssen Oncology (Inst), Plexxikon (Inst), Harpoon Therapeutics (Inst), Merck (Inst), Novartis (Inst)
Patents, Royalties, Other Intellectual Property: Patent licensed by The University of Chicago, of which I am a coinventor to Corcept Therapeutics for combination AR/GR inhibition in prostate cancer
Travel, Accommodations, Expenses: Corcept Therapeutics

Daniel P. Petrylak
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Consulting or Advisory Role: Bayer, Exelixis, Pfizer, Roche, Astellas Pharma, AstraZeneca, Lilly, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Clovis Oncology, Incyte, Janssen, Pharmacyclics, Seattle Genetics, UroGen Pharma, Advanced Accelerator Applications, Ipsen, Bicycle Therapeutics, Mirati Therapeutics, Monopteros Therapeutics, Regeneron, Gilead Sciences
Research Funding: Progenics (Inst), Sanofi (Inst), Endocyte (Inst), Genentech (Inst), Merck (Inst), Astellas Medivation (Inst), Novartis (Inst), AstraZeneca (Inst), Bayer (Inst), Lilly (Inst), Innocrin Pharma (Inst), MedImmune (Inst), Pfizer (Inst), Roche (Inst), Seattle Genetics (Inst), Clovis Oncology (Inst), Bristol Myers Squibb (Inst), Advanced Accelerator Applications (Inst), Agensys (Inst), BioXcel Therapeutics (Inst), Eisai (Inst), Mirati Therapeutics (Inst), Replimune (Inst), Medivation (Inst), Gilead Sciences (Inst)
Expert Testimony: Celgene, Sanofi

Jeffrey Holzbeierlein
Consulting or Advisory Role: Basilea, KDx Diagnostics
Research Funding: MDxHealth (Inst)
Uncompensated Relationships: Astellas Medivation

Arnauld Villers
Research Funding: Astellas Pharma (Inst), Janssen Oncology (Inst), Ipsen (Inst)

Antonio Alcaraz
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Travel, Accommodations, Expenses: Olympus, Ipsen, Janssen, Bayer

Boris Alexeev
Honoraria: AstraZeneca, Astellas Pharma, Ferring, Eisai, Janssen, Bayer, MSD, Merck, Pfizer, Roche, Sanofi, Bristol Myers Squibb
Consulting or Advisory Role: AstraZeneca, Astellas Pharma, Bayer, Bristol Myers Squibb, Ferring, Janssen, Merck, Sanofi, Pfizer, MSD, Roche, Eisai
Speakers' Bureau: Janssen, Sanofi, Ferring, Astellas Pharma, Pfizer, AstraZeneca, Bayer, Merck, Bristol Myers Squibb, MSD, Eisai, Roche
Research Funding: AstraZeneca, Merck, Sanofi, Bayer, Astellas Pharma, Janssen, Bristol Myers Squibb, Bavarian Nordic, Pfizer, ICON Clinical Research, Eisai, MSD, Roche
Travel, Accommodations, Expenses: AstraZeneca, Astellas Pharma, Bayer, Bristol Myers Squibb, Janssen, MSD, Pfizer, Sanofi

Neal D. Shore
Consulting or Advisory Role: Bayer, Janssen Scientific Affairs, Dendreon, Tolmar, Ferring, Medivation/Astellas, Amgen, Pfizer, AstraZeneca, Myovant Sciences, Astellas Pharma, AbbVie, Merck, Bristol Myers Squibb/Sanofi, Boston Scientific, Clovis Oncology, Exact Imaging, FerGene, Foundation Medicine, CG Oncology, Invitae, MDxHealth, Myriad Genetics, Nymox, Propella Therapeutics, Genzyme, Sanofi, Sesen Bio, CG Oncology, Exact Sciences, Genesis Cancer Care, Pacific Edge Biotechnology, Phosphorus, UroGen Pharma, Speciality Networks, PreView
Speakers' Bureau: Janssen, Bayer, Dendreon, Astellas Pharma, AstraZeneca, Clovis Oncology, Pfizer, Guardant Health, Merck, Foundation Medicine
Research Funding: AbbVie, Amgen, Astellas Pharma, AstraZeneca, Bayer, Bristol Myers Squibb/Pfizer, Boston Scientific, Clovis Oncology, Dendreon, Exact Imaging, Ferring, Foundation Medicine, Invitae, Janssen, MDxHealth, Merck, Myovant Sciences, Myriad Genetics, Nymox, Pfizer, Sanofi, Sesen Bio, Tolmar

Francisco Gomez-Veiga
Honoraria: AbbVie, Astellas, AstraZeneca, Bayer, Ferring, GE, GlaxoSmithKline, Ipsen, Janssen, Sanofi
Consulting or Advisory Role: AbbVie, Astellas, AstraZeneca, Bayer, Ferring, GE, GlaxoSmithKline, Ipsen, Janssen, Sanofi
Speakers' Bureau: AbbVie, Astellas, AstraZeneca, Bayer, GE, Janssen, Orion
Research Funding: AbbVie, Astellas, AstraZeneca, Ipsen, Janssen
Travel, Accommodations, Expenses: AbbVie, Astellas, Bayer, Janssen, Orion

Brad Rosbrook
Employment: Pfizer
Stock and Other Ownership Interests: Pfizer

Fabian Zohren
Employment: Pfizer
Stock and Other Ownership Interests: Pfizer, AlloVir Inc (I)
Patents, Royalties, Other Intellectual Property: AlloVir Inc (I)

Shunsuke Yamada
Employment: Astellas Pharma
Stock and Other Ownership Interests: Astellas Pharma

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Employment: Astellas Pharma

Arnulf Stenzl
Consulting or Advisory Role: Ipsen, Roche, Janssen, Alere, Bristol Myers Squibb, Steba Biotech, Synergo, Ferring, Bayer, Astellas Pharma
Research Funding: Karl Storz (Inst), Astellas Pharma, AstraZeneca, Medivation, Janssen, Johnson & Johnson (Inst), Roche (Inst), Cepheid (Inst), Immatics (Inst), Bayer (Inst), Novartis (Inst), Amgen (Inst), GenomeDx (Inst)
Patents, Royalties, Other Intellectual Property: Patent A290/99 Implantable incontinence device, AT00/0001:C-Trap, implantable device to treat urinary incontinence, 2018/6579 Gene expression signature for subtype and prognostic prediction of renal cell carcinoma
Expert Testimony: GBA Pharma
Travel, Accommodations, Expenses: Janssen, Ipsen, Sanofi/Aventis, CureVac, Ferring, Astellas Pharma, Amgen, AstraZeneca

No other potential conflicts of interest were reported.