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Radiographic Progression-Free Survival as a Clinically Meaningful End Point in Metastatic Castration-Resistant Prostate Cancer

The PREVAIL Randomized Clinical Trial

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Key Points

Question

What is the clinical relevance of the Prostate Cancer Clinical Trials Working Group 2 (PCWG2) definition of radiographic progression-free survival (rPFS)?

Findings

In a series of prespecified sensitivity analyses of rPFS in the PREVAIL randomized clinical trial of 1717 men with chemotherapy-naive metastatic castration-resistant prostate cancer, enzalutamide significantly reduced the risk of radiographic progression or death. Using 2 different statistical methods, rPFS and overall survival were found to be positively correlated.

Meaning

The PCWG2 definition of rPFS is a robust end point that is clinically meaningful and associated with overall survival.

This phase 3 randomized clinical trial uses prespecified sensitivity analyses from 1717 men with chemotherapy-naive metastatic castration-resistant prostate cancer to assess the clinical relevance of the Prostate Cancer Working Group 2 definition of radiographic progression-free survival.

Abstract

Importance

Drug development for metastatic castration-resistant prostate cancer has been limited by a lack of clinically relevant trial end points short of overall survival (OS). Radiographic progression-free survival (rPFS) as defined by the Prostate Cancer Clinical Trials Working Group 2 (PCWG2) is a candidate end point that represents a clinically meaningful benefit to patients.

Objective

To demonstrate the robustness of the PCWG2 definition and to examine the relationship between rPFS and OS.

Design, Setting, and Participants

PREVAIL was a phase 3, randomized, double-blind, placebo-controlled multinational study that enrolled 1717 chemotherapy-naive men with metastatic castration-resistant prostate cancer from September 2010 through September 2012. The data were analyzed in November 2016.

Interventions

Patients were randomized 1:1 to enzalutamide 160 mg or placebo until confirmed radiographic disease progression or a skeletal-related event and initiation of either cytotoxic chemotherapy or an investigational agent for prostate cancer treatment.

Main Outcomes and Measures

Sensitivity analyses (SAs) of investigator-assessed rPFS were performed using the final rPFS data cutoff (May 6, 2012; 439 events; SA1) and the interim OS data cutoff (September 16, 2013; 540 events; SA2). Additional SAs using investigator-assessed rPFS from the final rPFS data cutoff assessed the impact of skeletal-related events (SA3), clinical progression (SA4), a confirmatory scan for soft-tissue disease progression (SA5), and all deaths regardless of time after study drug discontinuation (SA6). Correlations between investigator-assessed rPFS (SA2) and OS were calculated using Spearman ρ and Kendall τ via Clayton copula.

Results

In the 1717 men (mean age, 72.0 [range, 43.0-93.0] years in enzalutamide arm and 71.0 [range, 42.0-93.0] years in placebo arm), enzalutamide significantly reduced risk of radiographic progression or death in all SAs, with hazard ratios of 0.22 (SA1; 95% CI, 0.18-0.27), 0.31 (SA2; 95% CI, 0.27-0.35), 0.21 (SA3; 95% CI, 0.18-0.26), 0.21 (SA4; 95% CI, 0.17-0.26), 0.23 (SA5; 95% CI, 0.19-0.30), and 0.23 (SA6; 95% CI, 0.19-0.30) ($P < .001$ for all). Correlations of rPFS and OS in enzalutamide-treated patients were 0.89 (95% CI, 0.86-0.92) by Spearman ρ and 0.72 (95% CI, 0.68-0.77) by Kendall τ.

Conclusions and Relevance

Sensitivity analyses in PREVAIL demonstrated the robustness of the PCWG2 rPFS definition using additional measures of progression. There was concordance between central and investigator review and a positive correlation between rPFS and OS among enzalutamide-treated patients.

Trial Registration

clinicaltrials.gov Identifier: NCT01212991

Introduction

Overall survival (OS) is the benchmark for regulatory drug approval for patients with advanced cancer. Since 2010, 5 agents have achieved the milestone of prolonging OS for men with metastatic castration-resistant prostate cancer (mCRPC), and these agents have transformed the management of the disease.[1,2,3,4,5,6,7,8] The availability of these effective therapies, although clinically beneficial to patients, can have a secondary effect of blunting the impact of an investigational agent on OS by virtue of postprotocol exposures. Consequently, development efforts focusing on OS are likely to shift to more advanced and heavily pretreated clinical settings. End points short of survival that represent clinical benefit and can independently support regulatory approval will be necessary to ensure that effective drugs are available to improve outcomes for patients across all stages of disease.

To address this, the Prostate Cancer Clinical Trials Working Group 2 (PCWG2) developed a set of consensus criteria in 2008 regarding clinical trial conduct for contemporary studies in men with mCRPC.[9] The PCWG2 stressed the importance of time-to-event measures that are not affected by posttreatment therapies and that could be strongly linked to clinical outcomes that were indicative of a worsening disease status, including deteriorations in quality of life, a need for a change in anticancer therapy, and, ultimately, death from disease. One such end point, radiographic progression-free survival (rPFS), is not affected by postprotocol treatments, but it has been difficult to quantify because of the lack of standardization of the outcome measure itself.

The PCWG2 sought to establish a definition for rPFS that would ensure that a drug was not working before therapy was discontinued. One definition proposed by PCWG2 was a “2 + 2” rule, which stated that progression not be declared early in a patient’s treatment course unless at least 2 new lesions were seen on the first on-treatment scan, followed by at least 2 additional lesions on the second posttreatment scan. The rule was designed to control for tumor flare, a paradoxical worsening of the bone scan attributed to bone healing as a result of a favorable antitumor effect.[9,10] The central hypothesis was that the continuous development of new lesions on sequential scans was an indication that the cancer was continuing to grow and spread as opposed to healing.

To enable the clinical validation of the PCWG2-proposed bone scan progression measure, a quantitative and reproducible bone scan assay was developed, analytically validated, and subsequently used as an integral part of the case report forms of serial, prospectively conducted,

large phase 3 studies using androgen receptor (AR)–directed therapy.[7,11,12] The progression biomarker was used first in the COU-AA-302 study of abiraterone acetate plus prednisone in chemotherapy-naive patients with mCRPC as a component of the definition of rPFS, which was a co–primary end point of the study.[12] PREVAIL, a phase 3, randomized, double-blind, placebo-controlled study evaluating the efficacy and safety of enzalutamide in chemotherapy-naive patients with mCRPC,[7] was another trial that used rPFS as a co–primary end point with OS, allowing for further validation of the bone scan assay based on the PCWG2 criteria. As previously reported, PREVAIL demonstrated that enzalutamide therapy decreased the risk of death by 29% (hazard ratio [HR], 0.71; 95% CI, 0.60-0.84; $P < .001$) and the risk of radiographic progression by 81% (HR, 0.19; 95% CI, 0.15-0.23; $P < .001$).[7]

A series of sensitivity analyses (SAs) were included in the trial design of PREVAIL to evaluate how robust and clinically meaningful the rPFS result signified.[7,13] These prespecified analyses examined the impact of additional measures of progression, including skeletal-related events (SREs), initiation of radiotherapy and or new antineoplastic therapy, and unequivocal clinical progression, on the primary rPFS analysis. The goals of these SAs were to confirm the clinical relevance of the PCWG2 rPFS definition, to further examine concordance between central and investigator assessment using the bone capture data assay form, and to examine the correlation between rPFS and OS.

Methods

The PREVAIL study design has previously been described,[7] and the trial protocol is available in Supplement 1. This study was conducted in accordance with the Declaration of Helsinki and was approved by the ethics committee at each participating center. All patients provided written informed consent before enrollment.

Randomization and Masking

Patients were assigned 1:1 to receive enzalutamide 160 mg or placebo using a centrally administered, randomized permuted-block method and stratified by study site. All patients, investigators, site personnel, and sponsor personnel involved in the conduct of the study were blinded to treatment assignment.

Primary Assessment of rPFS

The co–primary end points of PREVAIL were OS and rPFS, in which rPFS was defined as the time from randomization to first objective evidence of radiographic disease progression assessed by blinded independent central review or death from any cause within 168 days after treatment discontinuation, whichever occurred first. Radiographic disease progression was evaluated using a modified form of the PCWG2 guidelines for bone disease[9] and Response Evaluation Criteria in Solid Tumors, version 1.1, for soft-tissue disease.[14]

A separate investigator assessment of imaging was performed at each site using a bone scan worksheet adapted from the Prostate Cancer Clinical Trials Consortium.[11] As specified, progression in bone (≥2 new lesions on radionuclide bone scan) observed at week 9 necessitated 2 or more additional new lesions on a confirmatory scan at least 6 weeks later; radiographic

disease progression in bone observed after week 9 necessitated 2 or more new lesions relative to the week 9 scan, confirmed on a subsequent scan at least 6 weeks later. Radiographic disease progression in soft tissue did not require a confirmatory scan.[14]

Sensitivity Analysis of rPFS

Six SAs (SA1-SA6) based on investigator assessments were performed (eTable 1 in Supplement 2).

Statistical Analysis and Censoring Procedures

The final intention-to-treat analysis of rPFS was performed by the independent central review facility after 439 events (data cutoff, May 6, 2012), and the interim intention-to-treat OS analysis was performed after 540 events (data cutoff, September 16, 2013).

In all analyses, patients who were not known to have had an rPFS event at the time of data cutoff were censored at the date of last assessment. In the primary analysis, SA1, and SA2, patients were censored for rPFS if, prior to objective evidence of disease progression, there was a change in tumor scan modality, initiation of a new antineoplastic treatment and/or radiation therapy for prostate cancer, SRE, treatment discontinuation, 2 or more consecutive missed tumor assessments, or death after 168 days following treatment discontinuation without progression. In SA4, patients who discontinued study drug primarily because of clinical progression before objective evidence of radiographic disease progression were considered to have clinical progression on the date of the last dose of study drug. In SA5, patients with soft-tissue disease progression through week 13 without a confirmatory scan were censored at the date of earliest soft-tissue disease progression prior to week 13. In SA3 and SA6, the same censoring rules for the primary analysis applied, except that new SREs, any radiation therapy for prostate cancer, or new antineoplastic therapy (SA3) and all deaths (SA6) were considered rPFS events.

All data analyses were performed using SAS, version 9.1.3 (SAS Institute), as previously described.[7] Estimates of medians and 95% CIs were determined using the Kaplan-Meier method. Hazard ratio relative to placebo (with less than 1.00 favoring enzalutamide) was determined using an unstratified Cox regression model with treatment as the only covariate. The analysis of rPFS was conducted using a 2-sided unstratified log-rank test with a type 1 error rate of .001.

Overall concordance between independent central review and investigator assessments (using SA1) of the intention-to-treat population was calculated as (concordance for progressive disease) + (concordance for nonprogressive disease). In addition, correlations between rPFS (using SA2) and OS were calculated using 2 methods: Spearman ρ and Kendall τ via Clayton copula.[15,16,17,18]

Results

Patient Disposition and Demographic and Clinical Characteristics

The primary results of PREVAIL have been published previously and showed that patient demographic and disease characteristics were similar between treatment arms at baseline.[7] The mean age at baseline was 72.0 (range, 43.0-93.0) years in the enzalutamide arm and 71.0 (range, 42.0-93.0) years in the placebo arm.[7] Patient disposition is presented in Figure 1. In all SAs presented here (except SA2), analyses were based on data from 832 patients in the enzalutamide arm and 801 patients in the placebo arm. In SA2, data from all randomized patients were used in the analysis (enzalutamide arm, n = 872; placebo arm, n = 845). Results from all analyses are presented in Table 1.

Primary Analysis of rPFS

At the final cutoff date for primary rPFS analysis, 118 of 832 patients (14.2%) in the enzalutamide arm had an rPFS event, compared with 321 of 801 patients (40.1%) in the placebo arm. The majority of rPFS events resulted from radiographic progression (105 of 118 and 295 of 321 patients, respectively). Thirteen of 832 patients (1.6%) in the enzalutamide arm and 26 of 801 patients (3.2%) in the placebo arm died without radiographic progression. Enzalutamide reduced the risk of radiographic progression or death by 81% compared with placebo (HR, 0.19; 95% CI, 0.15-0.23; $P < .001$).[7] Median time to an rPFS event was not reached (95% CI, 13.8 to not reached [NR]) in the enzalutamide arm and was 3.9 months (95% CI, 3.7-5.4 months) in the placebo arm (Figure 2A).[7]

Concordance Between Independent and Investigator Assessments of rPFS

Using the same censoring rules and final rPFS data cutoff date, there was a high level of agreement between investigator assessments of radiographic progression (SA1) and those obtained by independent central assessment (eTable 2 in Supplement 2). Agreement at the final rPFS analysis between independent and investigator assessments for progressive and nonprogressive disease was 87.6% (90.9% with enzalutamide and 84.0% with placebo). Results from the remaining SAs were consistent between investigator assessment and central review (eTable 3 in Supplement 2). The main difference in investigator and central assessment for the subset analyses was the identification of soft-tissue progression, which did not use a standardized data capture form and was consistently higher when assessed by central review (eTable 4 in Supplement 2).

Sensitivity Analyses of rPFS

To remove the confounding factor of investigator assessment vs independent central review, and because SA1 differed from the primary analysis only in the use of investigator assessment, we used SA1 as the comparator. In SA1, enzalutamide treatment reduced the risk of radiographic progression or death by 78% compared with placebo (HR, 0.22; 95% CI, 0.18-0.27; $P < .001$) (Table 1). Median time to an rPFS event was 16.4 months (95% CI, 13.8 months to NR) in the enzalutamide arm and 5.5 months (95% CI, 5.2-5.6 months) in the placebo arm (Figure 2A).

SA2 included all randomized patients with an additional 16 months of data collection. As expected, the number of qualifying events increased substantially (Table 1). Enzalutamide therapy reduced the risk of radiographic progression or death by 69% (HR, 0.31; 95% CI, 0.27-

0.35; $P < .001$). Median time to an rPFS event was 19.7 months (95% CI, 18.1-22.3 months) in the enzalutamide arm and 5.4 months (95% CI, 4.2-5.6 months) in the placebo arm (Figure 2 B).

In SA3, in which SREs or any use of radiation or antineoplastic therapy were counted as rPFS events, there was an increase in the number of events, particularly in the placebo arm (Table 1). In both treatment arms, rPFS resulting from death decreased, whereas the bulk of the additional rPFS events were associated with new SREs and/or initiation of new antineoplastic therapies. Enzalutamide reduced the risk of radiographic progression or death by 79% (HR, 0.21; 95% CI, 0.18-0.26; $P < .001$). Median time to an rPFS event was 13.3 months (95% CI, 11.2-16.4 months) in the enzalutamide arm and 3.7 months (95% CI, 3.6-4.4 months) in the placebo arm (Figure 3A).

In SA4, in which rPFS events included discontinuation of treatment resulting from clinical progression prior to objective evidence of radiographic disease progression, there was a modest increase in the number of qualifying events in both treatment arms (Table 1). Enzalutamide therapy reduced the risk of radiographic progression or death by 79% (HR, 0.21; 95% CI, 0.17-0.26; $P < .001$). Median time to an rPFS event was 14.2 months (95% CI, 13.8 months to NR) in the enzalutamide arm and 5.4 months (95% CI, 4.6-5.6 months) in the placebo arm (Figure 3B).

In SA5, in which progression related to soft-tissue disease required a confirmatory scan, there was a decrease in the number of qualifying events in both treatment arms. Although the number of radiographic progression events decreased in both treatment arms, the number of deaths remained the same in the enzalutamide arm and increased in the placebo arm (Table 1). Enzalutamide treatment reduced the risk of radiographic progression or death by 77% (HR, 0.23; 95% CI, 0.19-0.30; $P < .001$). The median time to an rPFS event was 16.4 months (95% CI, 13.8 months to NR) in the enzalutamide arm and 5.7 months (95% CI, 5.5-8.2 months) in the placebo arm (Figure 3C).

The definition of rPFS in the primary analysis included death from any cause within 168 days of treatment discontinuation. In SA6, any death was considered an rPFS event, regardless of length of time after study drug discontinuation, which resulted in a modest decrease in the number of qualifying events in both treatment arms (Table 1). The number of radiographic progression events decreased in both treatment arms. As expected, the number of deaths increased in both treatment arms, although the increase was modest in the enzalutamide arm. Enzalutamide therapy reduced the risk of radiographic progression or death by 77% (HR, 0.23; 95% CI, 0.19-0.30; $P < .001$). Median time to an rPFS event was 15.0 months (95% CI, 13.8 months to NR) in the enzalutamide arm and 6.0 months (95% CI, 5.5-8.2 months) in the placebo arm (Figure 3D).

Correlation of rPFS and OS

At the planned interim analysis for OS, there were 540 deaths and 889 investigator-assessed rPFS events. Treatment with enzalutamide resulted in a 29% decrease in the risk of death compared with placebo (HR, 0.71; 95% CI, 0.60-0.84; $P < .001$).[7] Using SA2, rPFS was positively associated with OS among all patients and patients in each treatment arm using 2 different methods (Table 2). Spearman ρ was 0.72 (95% CI, 0.67-0.76) among all patients, 0.89 (95% CI, 0.86-

0.92) among enzalutamide-treated patients, and 0.53 (95% CI, 0.43-0.61) among placebo-treated patients. Kendall τ was 0.53 (95% CI, 0.49-0.57) among all patients, 0.72 (95% CI, 0.68-0.77) among enzalutamide-treated patients, and 0.37 (95% CI, 0.30-0.44) among placebo-treated patients.

Discussion

As more life-prolonging drugs are approved for the treatment of mCRPC, addressing the need for outcome measures that strongly correlate with survival or reflect clinical benefit in their own right is essential to ensure the timely development of drugs needed to further improve patient outcomes. Toward this objective, PREVAIL included in its design the co–primary end points of OS and rPFS.

The results of PREVAIL further confirmed the rigor of the PCWG2 definition of rPFS using a standardized bone scan data capture assay in patients with mCRPC. There was a high degree of concordance between the central and investigator reviews in both treatment arms. Notably, individual investigators were trained at each site using the bone scan data capture forms and the end result was a high level of reproducibility between readers, which highlights the clinical utility of this end point. The prespecified SAs in the PREVAIL study showed the impact of different clinical factors on rPFS, including SREs, initiation of radiotherapy and/or new antineoplastic therapy, and unequivocal clinical progression, which all confirmed the superiority of enzalutamide over placebo.

The PREVAIL analysis is the second to demonstrate a positive correlation between rPFS using the PCWG2 criteria and OS (Spearman ρ of 0.72 and Kendall τ of 0.53 for all patients). The COU-AA-302 trial also demonstrated a correlation between rPFS and OS[12]; both studies used the PCWG2 definition of radiographic progression, involved patients with mCRPC who had not received chemotherapy, and involved treatment that targeted the AR axis. Both studies also found a high concordance between the central and investigator reads, validating the reproducibility of the analytically validated bone scan progression biomarker to document rPFS disease progression. Notably, there were only 188 progression events in the PREVAIL enzalutamide arm vs 542 in the COU-AA-302 abiraterone acetate plus prednisone arm. As a result, although the HR was high for the enzalutamide arm (0.19), the event rate was relatively low, a fact that may bias the analyses accordingly.

Because the distribution of data was not known up front, 2 different statistical methods were used that measured correlation in slightly different ways. Spearman ρ and Kendall τ rank correlations are both nonparametric tests, with no assumption about the distribution of data and often used for nonlinear monotonic relationships.[19] Spearman ρ measures how the magnitude and direction of change of one end point corresponds to the magnitude and direction of change of the other end point, whereas Kendall τ only considers the direction of change. Consequently, Kendall τ generally results in a value closer to 0 (no correlation) than Spearman ρ does.[20] Results from both analyses in this study were consistent, with a positive correlation.

In our analysis, the lower correlation between rPFS and OS seen with placebo-treated patients than seen with enzalutamide-treated patients could be partly related to postprotocol exposure to life-prolonging therapy. Patients in the placebo arm received more postprotocol therapies

than those in the enzalutamide arm (76% vs 44%), including docetaxel (57% vs 33%), abiraterone acetate (46% vs 21%), and enzalutamide (4% vs 1%).[7]

Limitations

PREVAIL and COU-AA-302 both studied drugs that target the AR signaling pathway and enrolled chemotherapy-naive patients with mCRPC. The use of a co–primary end point using both OS and rPFS in both studies was designed to clearly demonstrate clinical benefit; however, the studies were not designed to address rPFS as a surrogate for survival. In addition, the results based on end points from these AR-directed trials may not be applicable to biologic agents, bone microenvironment-directed approaches, and non-AR-targeted therapies, whose impact on the tumor, and consequently on radiographic progression, has not yet been fully defined. It is anticipated that a one-size-fits-all end point that is general enough to encompass all therapies in all clinical scenarios will not be sufficient to enable regulatory approvals. As a result, the definition of rPFS as a clinically relevant end point may need to be adapted and, if so, revalidated accordingly to fit the disease, population, imaging modality, and treatment involved.

Conclusions

In this series of prespecified SAs of data from the PREVAIL trial of men with chemotherapy-naive mCRPC, the PCWG2 definition of rPFS was found to be a robust and clinically meaningful end point associated with OS in enzalutamide-treated patients.

Notes

Supplement 1.

Trial Protocol

Supplement 2.

eTable 1. PFS Criteria for the Primary Analysis and Sensitivity Analyses

eTable 2. Concordance Between Independent Central Review and Investigator Assessments (ITT Population)

eTable 3. Summary of rPFS Sensitivity Analyses (ITT Population) by Central Review

eTable 4. Summary of Radiographic Progression Analyses (ITT Population) by Central Review and Investigator Assessment

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Figures and Tables

Figure 1.

CONSORT Diagram

Table 1.

Summary of Radiographic Progression-Free Survival (rPFS) Sensitivity Analyses (SAs) (Intention-to-Treat Population)

Sensitivity Analysis[a]	No. (%)		HR (95% CI)
	Enzalutamide (n = 832)	Placebo (n = 801)	
Primary			
Total events[b]	118 (14.2)	321 (40.1)	
Radiographic progression	105 (12.6)	295 (36.8)	0.19 (0.15-0.23)
Death[c]	13 (1.6)	26 (3.2)	
SA1			
Total events[b]	117 (14.1)	296 (37.0)	
Radiographic progression	102 (12.3)	271 (33.8)	0.22 (0.18-0.27)
Death[c]	15 (1.8)	25 (3.1)	
SA2			
Total events[b,d]	387 (44.4)	502 (59.4)	
Radiographic progression	343 (39.3)	459 (54.3)	0.31 (0.27-0.35)
Death[c]	44 (5.0)	43 (5.1)	
SA3			
Total events[b]	161 (19.4)	409 (51.1)	
Radiographic progression	94 (11.3)	219 (27.3)	
Death[c]	9 (1.1)	24 (3.0)	
Initiated antineoplastic therapy	13 (1.6)	87 (10.9)	0.21 (0.18-0.26)
Initiated radiation therapy	2 (0.2)	5 (0.6)	
SRE	15 (1.8)	21 (2.6)	
SRE, initiated antineoplastic therapy	2 (0.2)	6 (0.7)	
SRE, initiated radiation therapy	26 (3.1)	47 (5.9)	
SA4			
Total events[b]	120 (14.4)	299 (37.3)	
Clinical progression	17 (2.0)	67 (8.4)	0.21 (0.17-0.26)
Radiographic progression	92 (11.1)	205 (25.6)	
Death[c]	11 (1.3)	27 (3.4)	
SA5			
Total events[b]	108 (13.0)	245 (30.6)	
Radiographic progression	92 (11.1)	205 (25.6)	0.23 (0.19-0.30)

Abbreviations: HR, hazard ratio; SRE, skeletal-related event.

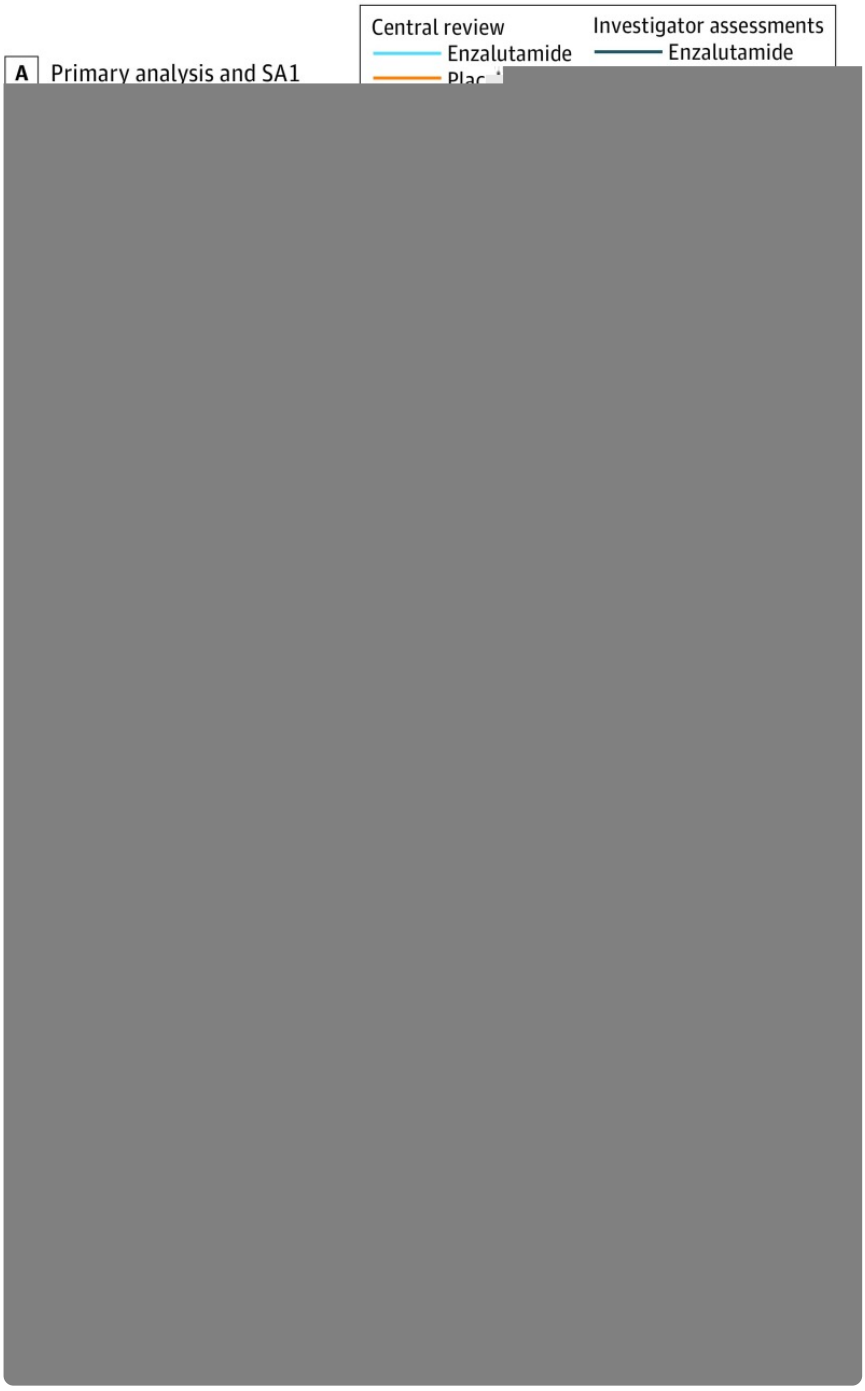
[a]SA1 was based on investigator's assessments using final rPFS cutoff; SA2, investigator's assessments using interim overall survival cutoff; SA3, SRE, initiation of radiation therapy, and new antineoplastic therapy; SA4, clinical progression; SA5, confirmatory scan requirement for progressive disease related to soft-tissue disease; and SA6, all deaths.

[b]Based on the earliest contributing event (eTable 1 in the Supplement).

[c]Deaths only counted as rPFS events if they occurred within 168 d of treatment discontinuation and in the absence of radiographic progression.

[d]Includes all randomized patients (n = 872 for enzalutamide; n = 845 for placebo).

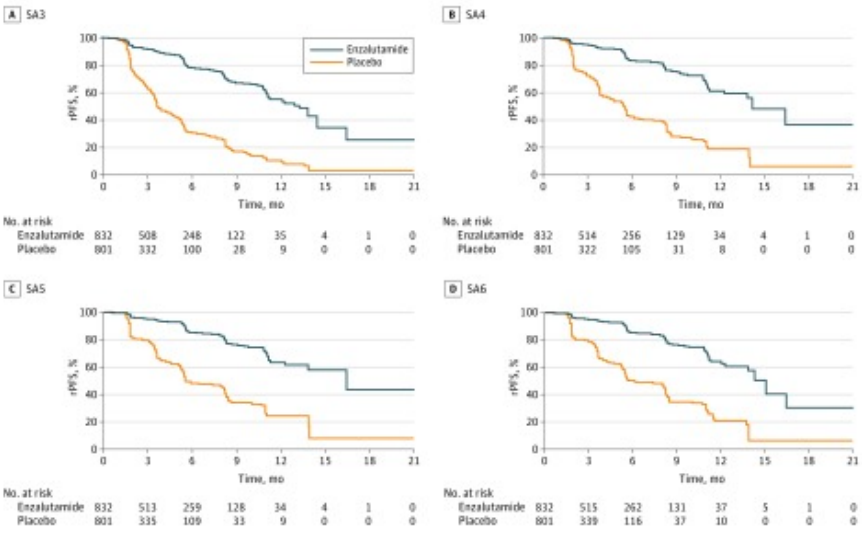
Figure 2.



Duration of Radiographic Progression-Free Survival (rPFS) in Primary Analysis, Sensitivity Analysis 1 (SA1), and SA2

A, Primary analysis and SA1 (intention-to-treat population, data cutoff May 6, 2012). B, SA2 (intention-to-treat population, data cutoff September 16, 2013).

Figure 3.



Duration of Radiographic Progression-Free Survival (rPFS) in Sensitivity Analysis 3 (SA3), SA4, SA5, and SA6

All intention-to-treat population; data cutoff, May 6, 2012.

Table 2.

Correlation of Radiographic Progression-Free Survival With Overall Survival[a]

Method	Correlation (95% CI)		
	Total (N = 1717)	Enzalutamide (n = 872)	Placebo (n = 845)
Spearman ρ	0.72 (0.67-0.76)	0.89 (0.86-0.92)	0.53 (0.43-0.61)
Kendall τ	0.53 (0.49-0.57)	0.72 (0.68-0.77)	0.37 (0.30-0.44)

[a]The analysis data cutoff was September 16, 2013.