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ORIGINAL ARTICLE

Apalutamide and overall survival in non-metastatic castration-resistant prostate cancer

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Background: In the SPARTAN study, compared with placebo, apalutamide added to ongoing androgen deprivation therapy significantly prolonged metastasis-free survival (MFS) and time to symptomatic progression in patients with high-risk non-metastatic castration-resistant prostate cancer (nmCRPC). Overall survival (OS) results at the first interim analysis (IA1) were immature, with 104 of 427 (24%) events required for planned final OS analysis. Here, we report the results of a second pre-specified interim analysis (IA2).

Methods: One thousand two hundred and seven patients with nmCRPC were randomized 2 : 1 to apalutamide (240 mg daily) or placebo. The primary end point of the study was MFS. Subsequent therapy for metastatic CRPC was permitted. When the primary end point was met, the study was unblinded. Patients receiving placebo who had not yet developed metastases were offered open-label apalutamide. At IA2, pre-specified analysis of OS was undertaken, using a group-sequential testing procedure with O'Brien–Fleming-type alpha spending function. Safety and second progression-free survival (PFS2) were assessed.

Results: Median follow-up was 41 months. With 285 (67% of required) OS events, apalutamide was associated with an improved OS compared with placebo (HR 0.75; 95% CI 0.59–0.96; $P = 0.0197$), although the P-value did not cross the pre-specified O'Brien–Fleming boundary of 0.0121. Apalutamide improved PFS2 (HR 0.55; 95% CI 0.45–0.68). At IA2, 69% of placebo-treated and 40% of apalutamide-treated patients had received subsequent life-prolonging therapy for metastatic CRPC. No new safety signals were observed.

Conclusion: In patients with nmCRPC, apalutamide was associated with a 25% reduction in risk of death compared with placebo. This OS benefit was observed despite crossover of placebo-treated patients and higher rates of subsequent life-prolonging therapy for the placebo group.

Key words: apalutamide, non-metastatic castration-resistant prostate cancer, overall survival, subsequent therapy

Introduction

Androgen deprivation therapy (ADT), a backbone of therapy for patients with metastatic prostate cancer, is increasingly used in patients with prostate-specific antigen (PSA) progression in the absence of visible metastases on conventional imaging [1–3]. Although ADT is initially effective, the emergence of castration-resistant prostate cancer (CRPC) is near universal [1, 3]. Non-metastatic CRPC (nmCRPC) is characterized by an increasing PSA in the setting of castrate testosterone levels with no metastases visible on conventional imaging [4]. nmCRPC is clinically heterogeneous, ranging from indolent inconsequential disease to aggressive disease that rapidly metastasizes with subsequent morbidity and mortality [5–7]. A shorter PSA doubling time (PSADT) identifies nmCRPC patients with a shorter time to metastasis or death [6].

Apalutamide, an androgen receptor inhibitor, is approved for treatment of nmCRPC [8, 9]. In SPARTAN, a placebo-controlled phase III study in patients with nmCRPC, PSADT <10 months and PSA serum concentration above 2 ng/ml, the addition of apalutamide to ongoing ADT improved median metastasis-free survival (MFS) by 2 years, with a hazard ratio (HR) for metastasis or death of 0.28 ($P<0.001$) [10]. Apalutamide also significantly improved time to symptomatic progression. At the time final MFS data were reported, the median follow-up for all patients was 20.3 months, and only 24% of overall survival (OS) events required for the pre-specified OS final analysis had occurred; this was considered the first OS interim analysis (IA1). At IA1, the OS HR was 0.70, favoring apalutamide, but did not reach statistical significance ($P=0.07$) [10]. To better characterize the effect of apalutamide on survival, we undertook a second pre-specified IA (IA2), after approximately two-thirds of the OS events required for the final survival analysis were observed.

Materials and methods

Study design

Study design details for SPARTAN (ClinicalTrials.gov, NCT01946204) have been reported [10]. Briefly, patients with nmCRPC were randomized 2 : 1 to receive apalutamide or placebo. Patients who reached the primary end point (MFS) by developing metastases identified on blinded central review remained blinded to their study-assigned treatment but were permitted subsequent therapy per treating physician, including open-label abiraterone acetate plus prednisone, provided by the study sponsor. Institutional review boards at all institutions approved the study, which was conducted in accordance with International Conference on Harmonization Guidelines for Good Clinical Practice, and according to the principles of the Declaration of Helsinki. All patients provided written informed consent. The sponsor, Janssen Research & Development, commissioned an independent data and safety monitoring committee (IDMC) to monitor safety data on an ongoing basis, and to serve as the primary reviewer of the efficacy analysis to make recommendations regarding study conduct.

End points

The primary end point of SPARTAN was MFS, defined as time from randomization to first evidence of distant metastases on conventional imaging, assessed by blinded independent central review, or death, whichever came first. Secondary end points, in hierarchical testing order, were time to metastasis, PFS, time to symptomatic progression, OS and time to initiation of cytotoxic chemotherapy (TTChemo). Second PFS (PFS2) was an exploratory end point and was defined as the time from randomization to investigator-assessed disease progression (by PSA, on imaging or symptomatic) during the first subsequent treatment of metastatic CRPC, or death from any cause, whichever occurred first.

MFS, time to metastasis, PFS and time to symptomatic progression met statistical significance and, consistent with the study design, IA1 (clinical cutoff date, 19 May 2017) served as the first and final analysis for these end points. Based on these data, the IDMC unanimously recommended unblinding the study and allowing placebo-treated patients to cross over to receive open-label apalutamide. After unblinding, all patients were still followed for survival, with crossover patients analyzed as part of the placebo group intention-to-treat population. No additional interim analyses were planned for the two secondary end points for which statistical significance could not be claimed (OS, TTChemo). The study protocol was subsequently amended to allow addition of a pre-specified IA2 of OS and TTChemo, as well as safety. The clinical cutoff date for IA2 was 1 February 2019.

Statistical analysis

The study was designed with an approximate 80% power to detect a 25% reduction (HR 0.75) in the risk of death for patients receiving apalutamide with ongoing ADT, based on an assumed median OS of 49 months in the placebo group. IA2 was scheduled to occur after ~65% of the 427 death events required for the final OS analysis. Testing of OS at IA2 was based on the original pre-specified O'Brien–Fleming-type alpha spending function to ensure control of overall type I error. A significance level of 0.0121 for IA2 was allocated to the OS end point. If the hierarchical testing of OS was statistically significant, the planned hierarchical testing of TTChemo would occur at an overall alpha level of .05 (two-sided) with the appropriate alpha adjustment made based on O'Brien–Fleming-type alpha spending function. Kaplan–Meier methods were used to estimate median OS for each treatment group. A log-rank test stratified by pre-specified factors [PSADT ($\leq$6 versus $>$6 months), bone-sparing agent use (yes versus no), and loco-regional disease (N0 versus N1)] was used to determine *P*-value. HRs and respective 95% confidence intervals (CIs) were determined from a stratified proportional hazards model with a single factor of treatment group. Unstratified analyses of OS HRs and respective 95% CIs were evaluated for pre-specified subgroups and illustrated as a forest plot. In addition, a post-hoc analysis was undertaken to evaluate the OS HR for patients who had and had not undergone definitive local therapy before study enrollment. Data regarding prior local therapy were prospectively collected from each patient at study enrollment, but these subgroups were not pre-specified in the analysis plan.

Exploratory sensitivity analyses of OS accounted for patients who crossed over from placebo to apalutamide after unblinding. In a naive censoring approach, patients who received placebo and crossed over to apalutamide were censored at crossover. Patients assigned to placebo who subsequently received an androgen-signaling inhibitor such as abiraterone acetate plus prednisone or enzalutamide after metastasis/progression were not censored. An inverse probability of censoring weighted (IPCW) analysis was also conducted to estimate the treatment effect of apalutamide on OS by re-weighting the patients receiving placebo based on the three stratification factors (PSADT, bone-sparing agent use, loco-regional disease).

Descriptive safety results and exposure-adjusted event rates per 100 patient-years of exposure were calculated. Adverse events (AEs) experienced by placebo patients while taking apalutamide following crossover were counted independently from AEs while taking placebo.

Results

Patient disposition

Patient disposition is summarized in supplementary Figure S1, available at *Annals of Oncology* online. One thousand two hundred and seven nmCRPC patients were randomized between 14 October 2013 and 15 December 2016—806 to the apalutamide group and 401 to the placebo group. Patient demographic and disease characteristics were well balanced between treatment groups [10]. Three patients in each group were randomized but never received study treatment. At unblinding, of 398 patients in the placebo treatment group, 322 had already discontinued therapy, 238 (74%) for progressive disease. The remaining 76 placebo patients received open-label apalutamide (crossover group). At the IA2 data cut, 325 of 803 patients (41%) randomized to apalutamide and 58 of 76 (76%) crossover patients continued treatment with apalutamide. Progressive disease was the most frequent reason for treatment discontinuation (supplementary Table S1, available at *Annals of Oncology* online). Median follow-up for all patients was 41.0 months and median treatment duration was 31.4, 11.5, and 15.0 months in the apalutamide, placebo, and crossover groups, respectively (Table 1).

Overall survival

Median OS was not reached in the apalutamide or the placebo group. However, compared with placebo, the addition of apalutamide to ongoing ADT was associated with a 25% reduction in the risk of death (HR for apalutamide versus placebo, 0.75; 95% CI 0.59–0.96; $P = 0.0197$), as shown in Figure 1A. Of the 285 deaths at IA2, 178 of 806 (22%) occurred in the apalutamide group and 107 of 401 (27%) in the placebo group. Because the *P*-value for OS at IA2 did not cross the pre-specified O'Brien–Fleming boundary of 0.0121, the final OS analysis is planned when 427 deaths have been observed. OS analyses undertaken to account for patients who crossed over from the placebo group to the apalutamide group using two independent methods, naive censoring and IPCW, revealed similar results (Figure 1B). The HR for apalutamide versus placebo was 0.68 (95% CI 0.54–0.87), with a nominal *P*-value of 0.0021 using naive censoring, and 0.68 (0.53–0.87), with a nominal *P*-value of 0.0024 with IPCW. The 4-year survival rate was 72% (95% CI 68%–76%) in the apalutamide group and 65% (58%–71%) in the placebo group. When adjusted to account for patients who crossed over from placebo to apalutamide, the 4-year survival rate was 72% (68%–76%) in the apalutamide group and 61% (54%–68%) in the placebo group.

The treatment effect of apalutamide was consistent across pre-specified subgroups analyzed (Figure 1C), with point estimates for the HR for OS favoring apalutamide, although in some subgroups with smaller sample sizes, the 95% CI included 1.0. Overall, 500 patients had undergone first prior definitive local therapy with curative intent [radical prostatectomy ($n = 406$) or primary radiation therapy ($n = 94$)]. The median time from primary local therapy to randomization on SPARTAN was 8.6 years [range 0.4–27] for patients in the apalutamide group, and 7.7 years [0.3–26] for patients in the placebo group. Baseline patient characteristics of those who had and had not undergone prior local therapy were generally comparable (supplementary Table S2, available at *Annals of Oncology* online), with a similar baseline PSADT, although patients with no prior local therapy had a shorter time from diagnosis to randomization (6.84 versus 9.98 years), and a slightly higher median PSA level (9.34 versus 6.36 ng/dl); also a smaller proportion had an Eastern Cooperative Oncology Group performance status of 0. In patients who had undergone prior definitive local therapy, the HR for OS favored apalutamide versus placebo (HR 0.67; 95% CI 0.45–0.98). In patients who had not undergone definitive local therapy, while the HR still favored apalutamide (HR 0.82), the 95% CI overlapped 1.0 (0.60–1.11) (Figure 1D and E).

Time to initiation of cytotoxic chemotherapy

At IA2, 197 patients had initiated cytotoxic chemotherapy—115 of 806 (14%) in the apalutamide group and 82 of 401 (20%) in the placebo group. Compared with placebo, apalutamide extended TTChemo, although the median was not reached in either group (HR for apalutamide versus placebo 0.60; 95% CI 0.45–0.80) (Figure 2A). TTChemo was not formally tested for significance, as the *P*-value for OS did not cross the pre-specified boundary in hierarchical testing. Without stratification factors considered, the 4-year event-free rate for chemotherapy initiation was 80% (95% CI 76%–84%) in the apalutamide group and 73% (67%–78%) in the placebo group.

Subsequent therapy

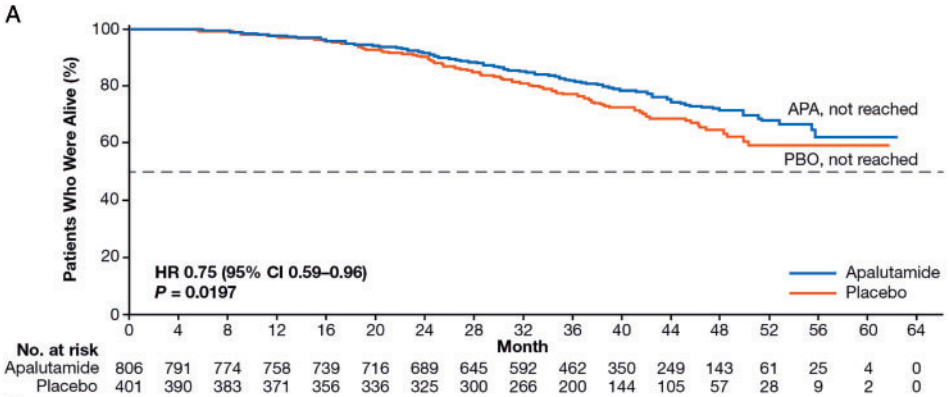
Progressive disease was the most frequent reason for treatment discontinuation (supplementary Table S1, available at *Annals of Oncology* online). In the intent-to-treat population, 276 patients in the placebo group (69%) and 322 in the apalutamide group (40%) received subsequent life-prolonging therapy (supplementary Table S3, available at *Annals of Oncology* online). Abiraterone acetate plus prednisone was the most common post-progression treatment and, together with enzalutamide, accounted for post-progression therapy in 84% of patients in each treatment group (266/322 apalutamide patients, 237/276 placebo patients).

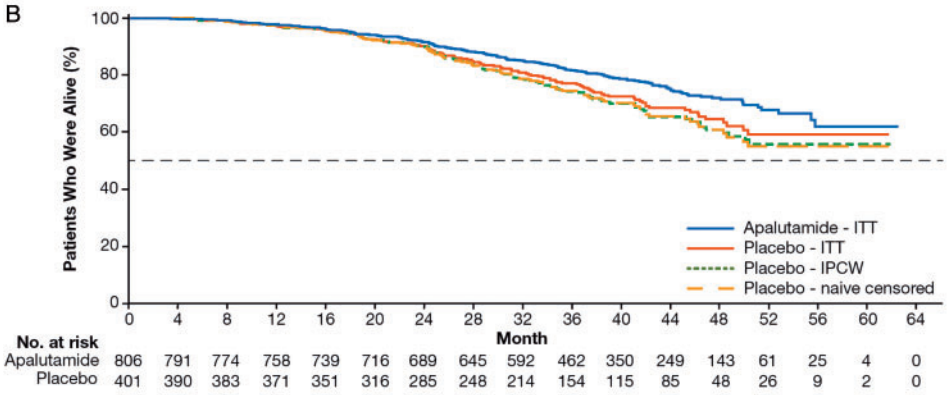
Second progression-free survival

At IA2, 228 of 806 (28%) apalutamide-treated patients and 149 of 401 (37%) placebo-treated patients experienced disease progression following second-line therapy. Apalutamide extended PFS2 by 11.8 months versus placebo (apalutamide, 55.6 versus placebo, 43.8 months; HR 0.55; 95% CI 0.45–0.68; $P < 0.0001$) (Figure 2B). The 4-year PFS2 event-free rate was 64% (59%–68%) in the apalutamide group and 45% (38%–52%) for placebo.

Safety

At IA2, with 20.7 months' additional data, the difference in median treatment duration between apalutamide and placebo groups was 19.9 months (apalutamide, 31.4 months; placebo, 11.5 months). AEs (all grades, without regard to attribution) were observed in 97% of patients receiving apalutamide and 94%





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Subgroup	Median overall survival (mo) Apalutamide	Placebo	HR (95% CI)	Events/N Apalutamide	Placebo
All patients	NR	NR	0.76 (0.60–0.96)	178/806	107/401
Age					
< 65 years	NR	NR	0.33 (0.14–0.74)	12/106	11/43
≥ 65 years	NR	NR	0.83 (0.65–1.07)	166/700	96/358
Race					
White	NR	NR	0.74 (0.56–0.98)	124/524	80/276
Black	NR	NR	0.94 (0.29–3.06)	9/48	4/20
Asian	NR	NR	0.82 (0.36–1.86)	15/93	9/47
Others	NR	NR	0.81 (0.43–1.53)	30/141	14/58
Region					
North America	NR	NR	0.84 (0.58–1.22)	78/285	43/134
Europe	NR	NR	0.73 (0.51–1.04)	79/395	50/204
Rest of the world	NR	NR	0.66 (0.34–1.31)	21/126	14/63
Prior hormonal therapy, no.					
1	NR	NR	0.70 (0.40–1.23)	29/155	21/84
≥ 2	NR	NR	0.78 (0.60–1.01)	149/646	86/316
Baseline ECOG PS					
0	NR	NR	0.69 (0.51–0.93)	110/623	72/311
1	NR	45.7	0.87 (0.58–1.31)	68/183	35/89
Baseline PSA value					
At or below median	NR	NR	0.68 (0.46–1.01)	60/406	42/198
Above median	NR	NR	0.81 (0.60–1.09)	118/400	65/203
PSA doubling time					
≤ 6 months	NR	NR	0.81 (0.62–1.06)	145/576	81/284
> 6 months	NR	NR	0.57 (0.34–0.95)	33/230	26/117
Bone-sparing agent					
Yes	NR	NR	0.55 (0.27–1.11)	18/82	13/39
No	NR	NR	0.79 (0.61–1.02)	160/724	94/362
Loco-regional disease					
N0	NR	NR	0.81 (0.62–1.06)	153/673	87/336
N1	NR	NR	0.52 (0.29–0.94)	25/133	20/65

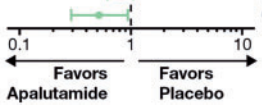

Figure 1. Overall survival (A) Kaplan–Meier estimates, (B) adjusted for patient crossover from placebo to apalutamide, and (C) forest plot subgroup analysis by baseline patient characteristics. Analyses for the Kaplan–Meier plot (Figure 1A) were stratified, and those for the forest plot were unstratified. Kaplan–Meier estimates of OS for patients (D) with prior radical prostatectomy or radiation therapy and (E) without prior radical prostatectomy or radiation therapy. For Figure 1B, inverse probability of censoring weighted (IPCW) and naive-censored Kaplan–Meier estimates of overall survival for placebo arm are presented along with the standard Kaplan–Meier estimates of overall survival for apalutamide arm and placebo arm. Patients at risk are presented for the naive-censored curve. Patients at risk for the IPCW curve are not included due to lack of clear clinical interpretation on the number of patients at risk associated with the weighted methodology.

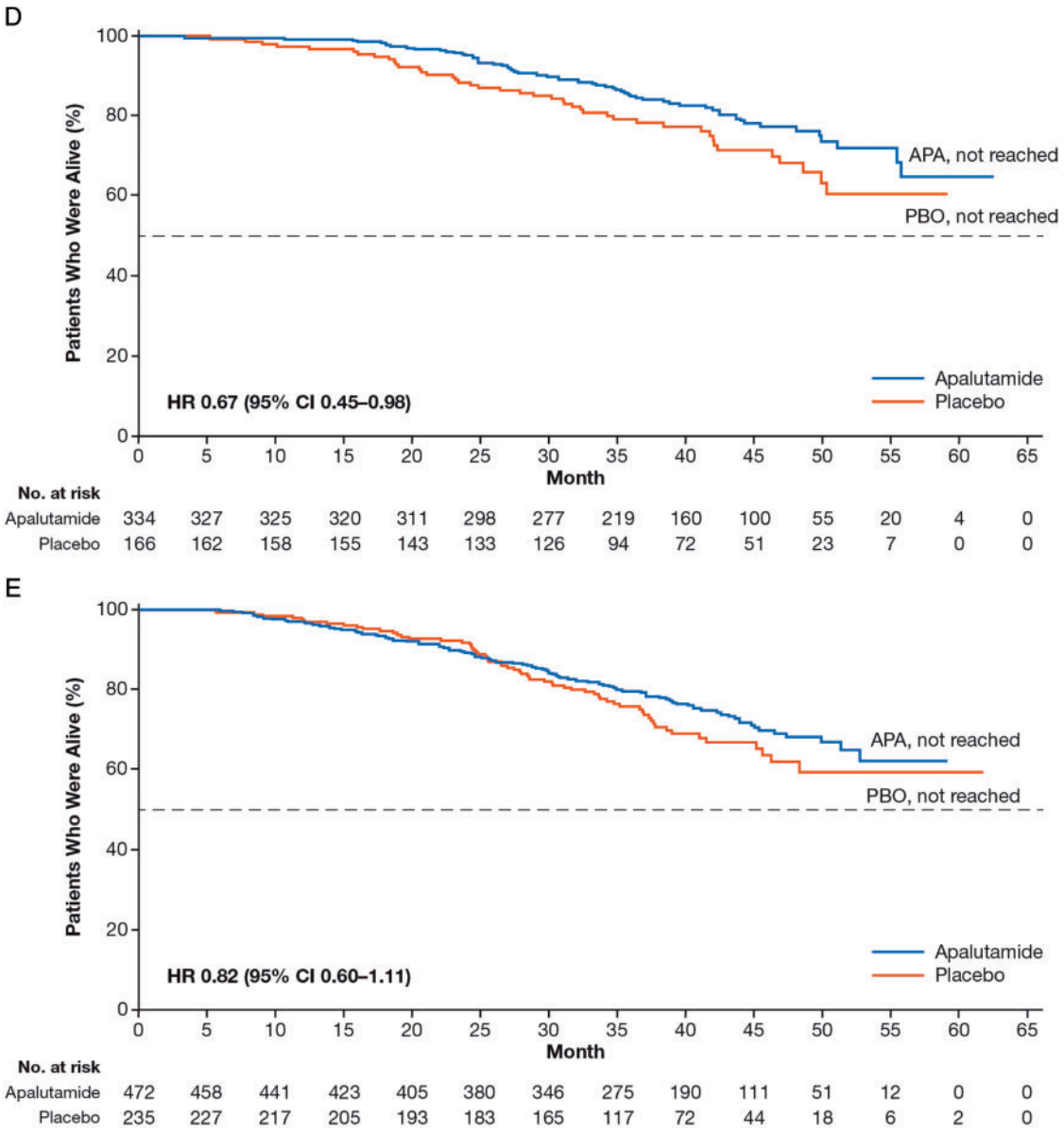

Figure 1. Continued.

of patients receiving placebo (Table 1). The most frequent AEs occurring in patients who received apalutamide were fatigue, hypertension, diarrhea, and fall. Grades 3–4 AEs, without regard to attribution, were observed in 53% of patients in the apalutamide group and 37% of patients in the placebo group. After adjusting for the difference in time of exposure, rates of grades 3–4 events were 54% and 68% for the apalutamide and placebo groups, respectively. At IA2, exposure-adjusted grades 3–4 AEs (apalutamide versus placebo) included skin rash (2.7% versus 0.2%), falls (1.2% versus 0.7%), and fractures (2.0% versus 0.9%) (supplementary Table S4, available at *Annals of Oncology* online). After adjusting for the exposure difference, incidence of rash, falls, and fractures in the apalutamide group (event rates/100 patient-years) did not change substantially after IA1 [IA1 versus IA2: grade 3–4 rash (4.2 versus 2.7), falls (1.2 versus 1.2), fractures (2.1 versus 2.0)]. Cumulative incidence plots demonstrated no increasing trend in incidence of grades 3–4 falls, fractures, or skin rash with continued apalutamide treatment of 60 months (supplementary Figure S2, available at *Annals of Oncology* online). Incidences of grades 3–4 AEs and serious AEs (SAEs) plateaued by 32 months (supplementary Figure S3, available at *Annals of Oncology* online).

Discussion

In this planned IA2 of SPARTAN, compared with placebo, the addition of apalutamide to ongoing ADT in nmCRPC patients was associated with a 25% reduction in risk of death (HR 0.75; 95% CI 0.59–0.96; $P = 0.0197$). Because the difference in OS between groups did not cross the pre-specified O'Brien–Fleming boundary for statistical significance, the final OS analysis will occur when 427 deaths are observed. The OS difference favoring

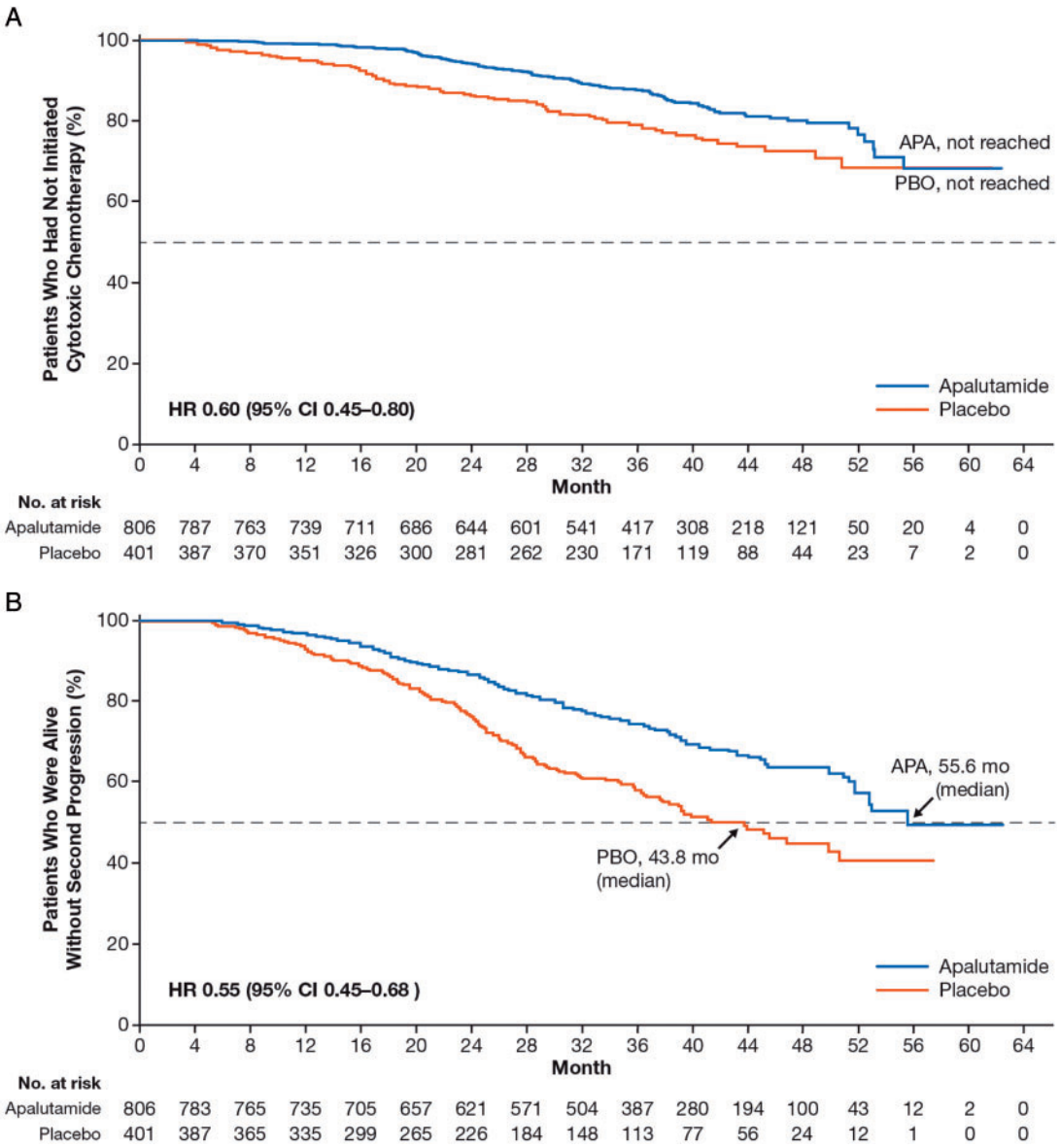

Figure 2. Kaplan–Meier estimates of (A) time to initiation of cytotoxic chemotherapy and (B) second progression-free survival.

apalutamide was observed despite crossover of 19% of patients from placebo to apalutamide, and a higher use of subsequent life-prolonging therapy in the placebo group (69% versus 40%). Sensitivity analyses accounting for patients who crossed over from placebo to apalutamide, using two independent methods (naive censoring and IPCW), revealed similar results. Finally, the treatment effect of apalutamide was consistent across pre-specified subgroups analyzed, although in some subgroups with smaller sample sizes, the 95% CI included 1.0.

These data suggest that the statistically significant improvement in MFS and time to symptomatic progression observed with apalutamide [10] may translate into a survival advantage in patients with nmCRPC. Furthermore, PFS2 continued to favor apalutamide at IA2 with an HR of 0.55 (0.45–0.68; $P < 0.0001$), translating into a 45% reduction in risk of secondary progression or death after the development of metastatic CRPC. These data similarly suggest that the effect of apalutamide might be observed at time points beyond the time of metastasis detection and closer to the OS end point.

While SPARTAN was not specifically designed to test the question of early versus delayed androgen-signaling inhibitor therapy, and PFS2 was an exploratory end point, the PFS2 data favoring apalutamide over placebo also support the hypothesis that early use of a next-generation androgen-signaling inhibitor in patients with CRPC, before the development of metastases, may provide an advantage over withholding this therapy until metastases develop.

We undertook a post-hoc analysis of the impact of prior definitive local therapy on the OS effect of apalutamide in SPARTAN, based on provocative results from the STAMPEDE trial evaluating the effect of definitive local therapy (consisting of prostate radiation) on OS in patients with metastatic (hormone-naive) prostate cancer treated with systemic therapy consisting of ADT [11]. While STAMPEDE failed to demonstrate improved survival

Table 1. Summary of adverse events and most frequent treatment-emergent adverse events (occurring in >15% in the apalutamide group)

	Apalutamide with ongoing ADT ($n = 803$)		Placebo with ongoing ADT ($n = 398$)		Placebo group to apalutamide group ($n = 76$)	
Median treatment duration (range), months	31.4 (0.1–62.5)		11.5 (0.1–37.2)		15.0 (1.0–16.9)	
Any AE, *n* (%)	781 (97.3)		373 (93.7)		65 (85.5)	
Grade 3 or 4 AE, *n* (%)	426 (53.1)		146 (36.7)		24 (31.6)	
Any serious AE, *n* (%)	269 (33.5)		99 (24.9)		12 (15.8)	
Any AE leading to treatment discontinuation, *n* (%)[a]	109 (13.6)		29 (7.3)		8 (10.5)	
AE leading to death, *n* (%)	17 (2.1)		2 (0.5)		2 (2.6)	
AE, *n* (%)	All grades	Grades 3–4	All grades	Grades 3–4	All grades	Grades 3–4
Fatigue	256 (31.9)	6 (0.7)	85 (21.4)	1 (0.3)	11 (14.5)	1 (1.3)
Hypertension	222 (27.6)	129 (16.1)	83 (20.9)	49 (12.3)	7 (9.2)	4 (5.3)
Diarrhea	178 (22.2)	10 (1.2)	61 (15.3)	2 (0.5)	9 (11.8)	1 (1.3)
Fall	168 (20.9)	21 (2.6)	38 (9.5)	3 (0.8)	5 (6.6)	0
Nausea	155 (19.3)	0	63 (15.8)	0	4 (5.3)	0
Arthralgia	154 (19.2)	3 (0.4)	33 (8.3)	0	7 (9.2)	1 (1.3)
Weight decreased	149 (18.6)	12 (1.5)	26 (6.5)	1 (0.3)	7 (9.2)	1 (1.3)
Back pain	129 (16.1)	10 (1.2)	61 (15.3)	6 (1.5)	7 (9.2)	0
Hot flush	121 (15.1)	0	34 (8.5)	0	6 (7.9)	0

Total patient-years of exposure were 1842.1 for the apalutamide group, 446.0 for the placebo group, and 85.5 for the crossover group. Patients are counted only once for any given event, regardless of the number of times they actually experienced the event. The event experienced by the patient with the worst toxicity grade is used. If a patient has all adverse events with missing toxicity grades, the patient is only counted in the total column.

[a]All AEs leading to discontinuation are reported. However, reported AEs may not be the primary reason for discontinuation.

AE, adverse event.

with the addition of curative intent prostatic radiation in the entire study population, a pre-specified analysis of patients with a low metastatic burden in this trial indicated that local treatment of the prostate with radiotherapy improved OS (HR 0.68 for low metastatic burden, 1.07 for high metastatic burden). The mechanism by which local therapy might impact survival in patients with metastatic prostate cancer is not known, but one plausible mechanism proffered is local tumor eradication and 'debulking' to prevent subsequent metastases from the primary tumor. Prospective clinical trials are testing whether radical prostatectomy has the same effect. Based on these results, we hypothesized that prior local therapy would modulate the OS effect of apalutamide in SPARTAN, which also included patients with minimal disease burden, albeit in a castration-resistant state. In the patients who had undergone prior definitive local therapy, the HR for OS favored apalutamide (HR 0.67; 95% CI 0.45–0.98), and there was a clear, early, and consistent separation of the Kaplan–Meier survival curves between apalutamide and placebo groups beginning at ~15 months. In patients who had not undergone definitive local therapy, the HR, while also favoring apalutamide, was 0.82, and the 95% CI overlapped 1.0 (0.60–1.11). The time to separation of the curves for apalutamide and placebo groups occurred later in treatment (near 30 months). Although data regarding prior local therapy were prospectively collected at the time of study enrollment, this analysis should be interpreted with caution as it is a retrospective, subset analysis. While baseline patient characteristics, including PSADT, were generally balanced in patients with and without prior local therapy, there were some subtle imbalances between the groups, and it is certainly possible that other known or unknown risk factors were not evenly distributed across the groups. Nevertheless, given the growing interest (and controversy) around the utility of definitive local therapy in patients with metastatic prostate cancer [12], this observation is intriguing, and warrants prospective testing.

After 20 additional months of median follow-up since IA1, the safety profile of apalutamide added to ongoing ADT remains unchanged, with no evidence of cumulative toxicity. The frequencies of AEs leading to permanent treatment discontinuation were low in both treatment groups, with disease progression the most common reason in both groups. The median duration of treatment on study was almost three times longer in the apalutamide group than in the placebo group, resulting in longer treatment exposure. With 20.7 months of additional data, the incidence of AEs of interest in the apalutamide group (event rates/100 patient-years) did not substantially change.

In summary, these data from IA2, with 67% of observed OS events, suggest that in addition to prolonging MFS, time to symptomatic progression and PFS2, apalutamide may prolong survival in patients with high-risk nmCRPC; a final survival analysis will be done once all requisite events have occurred. Furthermore, long-term follow-up suggests that these end points are achieved without any exacerbation of AEs.

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Disclosure

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