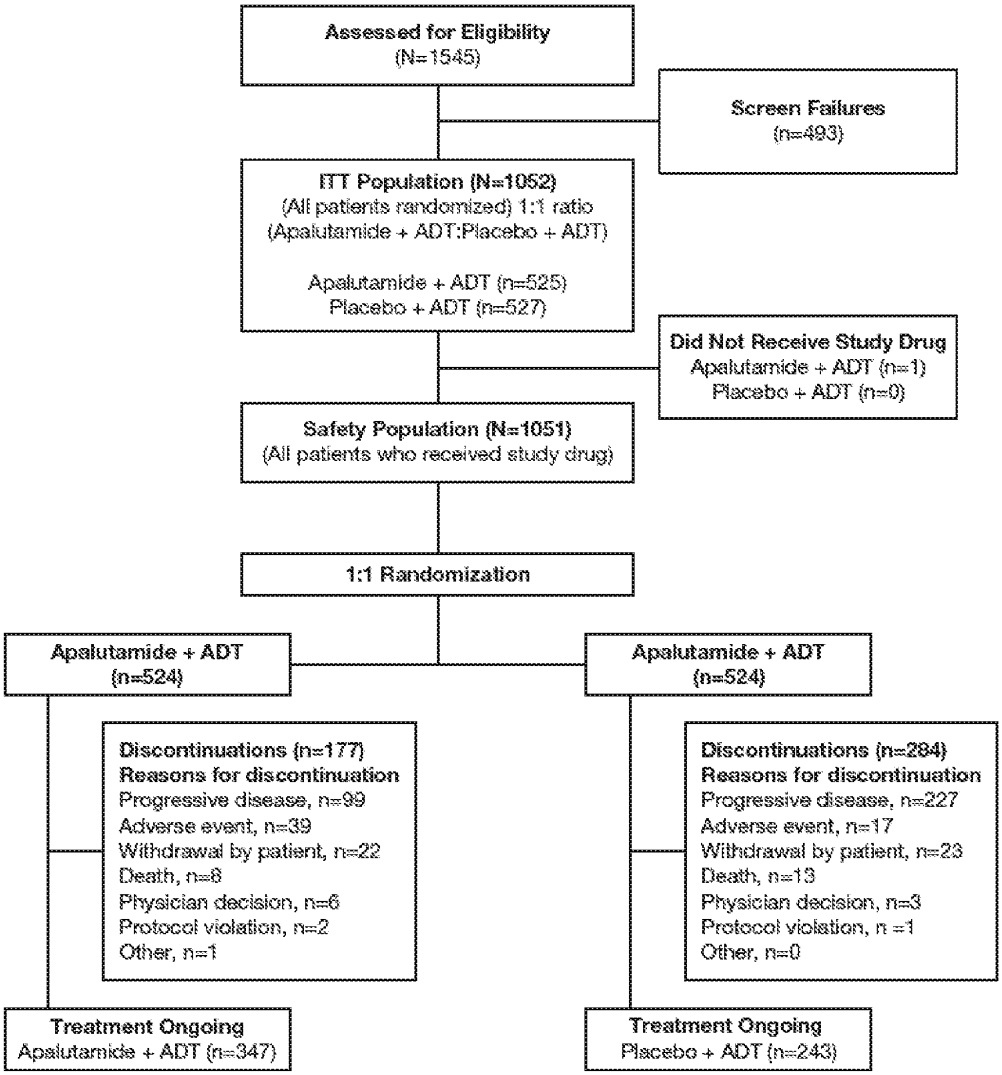

Assessed for Eligibility
(N=1545)
Screen Failures
(n=493)
ITT Population (N=1052)
(All patients randomized) 1:1 ratio
(Apalutamide + ADT:Placebo + ADT)
Apalutamide + ADT (n=525)
Placebo + ADT (n=527)
Did Not Receive Study Drug
Apalutamide + ADT (n=1)
Placebo + ADT (n=0)
Safety Population (N=1051)
(All patients who received study drug)
1:1 Randomization
Apalutamide + ADT
(n=524)
Apalutamide + ADT
(n=524)
Discontinuations (n=177)
Reasons for discontinuation
Progressive disease, n=99
Adverse event, n=39
Withdrawal by patient, n=22
Death, n=8
Physician decision, n=6
Protocol violation, n=2
Other, n=1
Discontinuations (n=284)
Reasons for discontinuation
Progressive disease, n=227
Adverse event, n=17
Withdrawal by patient, n=23
Death, n=13
Physician decision, n=3
Protocol violation, n =1
Other, n=0
Treatment Ongoing
Apalutamide + ADT (n=347)
Treatment Ongoing
Placebo + ADT (n=243)

FIG. 1

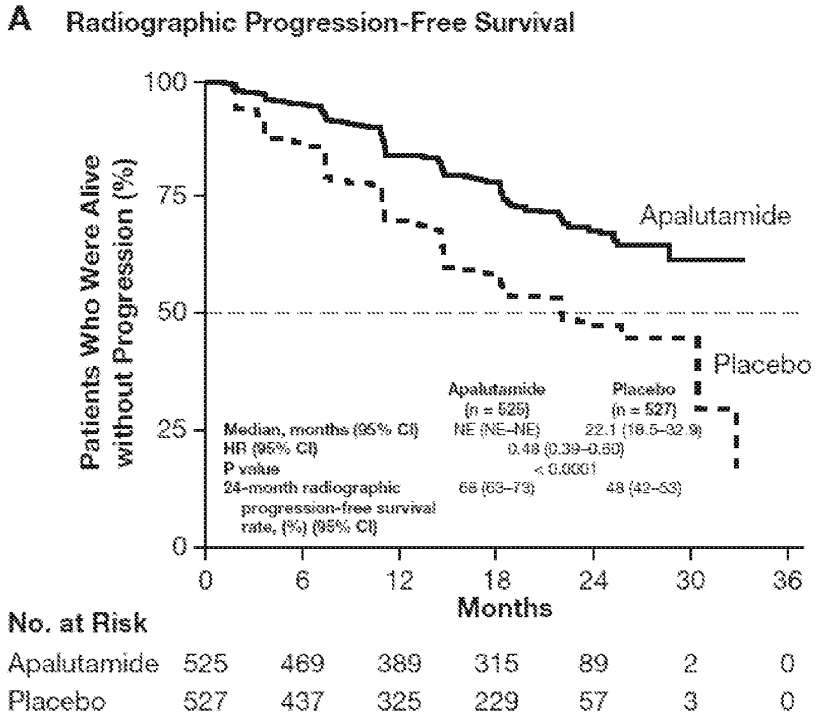

A Radiographic Progression-Free Survival
Patients Who Were Alive without Progression (%)
100
75
50
25
0
Apalutamide
Placebo
Apalutamide (n = 525)
Placebo (n = 527)
Median, months (95% CI) NE (NE–NE) 22.1 (16.5–32.9)
HR (95% CI) 0.48 (0.39–0.60)
P value < 0.0001
24-month radiographic progression-free survival rate, (%) (95% CI) 68 (63–73) 48 (42–53)
0 6 12 18 24 30 36
Months
No. at Risk
Apalutamide 525 469 389 315 89 2 0
Placebo 527 437 325 229 57 3 0

FIG. 2A

Variable	Apalutamide median (mo)	Placebo median (mo)	Hazard Ratio (95% CI)	Apalutamide events (no./No.)	Placebo events (no./No.)
All patients					
All	NE	22.1	0.49 (0.40–0.61)	134/525	231/527
Baseline ECOG performance status					
0	NE	30.5	0.52 (0.39–0.68)	79/328	142/348
1	28.7	15	0.42 (0.30–0.59)	55/197	89/179
Geographic region					
EU/NA	NE	30.5	0.43 (0.28–0.66)	32/173	67/173
Other	NE	21.4	0.51 (0.40–0.65)	102/352	164/354
Bone metastasis only at baseline					
Yes	NE	32.9	0.38 (0.27–0.54)	49/289	102/269
No	NE	18.2	0.60 (0.46–0.80)	85/236	129/258
Visceral disease and bone metastasis at baseline					
Yes	28.7	14.9	0.71 (0.43–1.18)	25/58	38/72
No	NE	23	0.46 (0.37–0.59)	109/469	193/455
Gleason score at diagnosis					
≤7	NE	30.5	0.53 (0.36–0.78)	41/174	65/169
>7	NE	18.8	0.48 (0.37–0.61)	93/351	166/358
Prior docetaxel use					
Yes	NE	22.1	0.47 (0.22–1.01)	10/58	19/55
No	NE	22	0.49 (0.39–0.62)	124/467	212/472
Age (years)					
<65	NE	18.4	0.45 (0.31–0.66)	40/149	85/182
≥65	NE	22	0.47 (0.34–0.64)	61/243	105/232
≥75	NE	32.9	0.65 (0.41–1.03)	33/133	41/113
Baseline PSA above median					
Yes	NE	15.4	0.51 (0.39–0.67)	92/265	119/241
No	NE	30.5	0.39 (0.27–0.56)	42/240	112/266
Baseline LDH above ULN					
Yes	22.4	14.6	0.57 (0.33–1.00)	21/60	30/60
No	NE	23	0.48 (0.38–0.61)	109/443	191/442
Baseline ALP above ULN					
Yes	22.4	14.7	0.54 (0.40–0.74)	69/177	98/180
No	NE	30.5	0.42 (0.31–0.57)	64/346	133/345
mCSPC disease volume					
High volume	NE	14.9	0.53 (0.41–0.67)	109/325	173/335
Low volume	NE	30.5	0.36 (0.22–0.57)	25/200	58/192
Metastasis stage at initial diagnosis					
M0	NE	NE	0.41 (0.22–0.78)	17/85	23/59
M1	22	NE	0.49 (0.39–0.63)	108/411	196/441

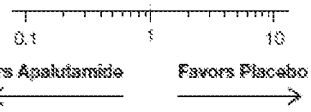


FIG. 2B

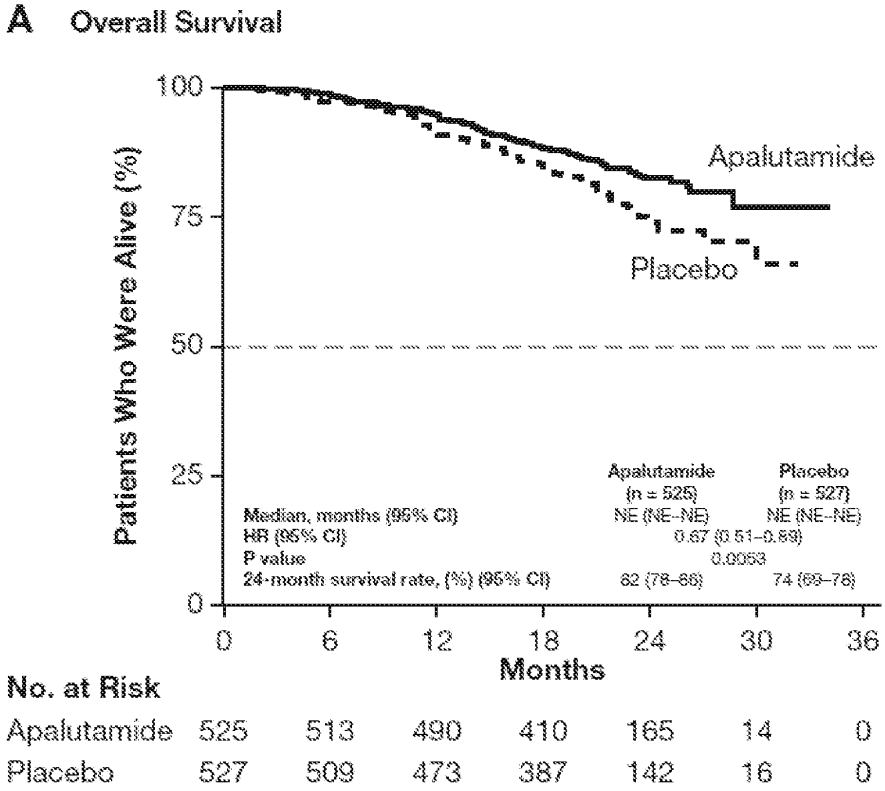

A Overall Survival
Patients Who Were Alive (%)
100
75
50
25
0
Apalutamide
Placebo
Apalutamide (n = 525)
Placebo (n = 527)
Median, months (95% CI)
NE (NE–NE)
NE (NE–NE)
HR (95% CI)
0.67 (0.51–0.89)
P value
0.0053
24-month survival rate, (%) (95% CI)
82 (78–86)
74 (69–78)
0
6
12
18
24
30
36
Months
No. at Risk
Apalutamide 525 513 490 410 165 14 0
Placebo 527 509 473 387 142 16 0

FIG. 3A

B

Variable	Apalutamide median (mo)	Placebo median (mo)	Hazard Ratio (95% CI)	Apalutamide events (no./No.)	Placebo events (no./No.)
All patients					
All	NE	NE	0.68 (0.51–0.90)	93/525	117/527
Baseline ECOG performance status					
0	NE	NE	0.71 (0.47–1.05)	41/328	60/348
1	NE	NE	0.59 (0.40–0.88)	42/197	57/178
Geographic region					
EU/NA	NE	NE	0.71 (0.40–1.25)	21/173	29/173
Other	NE	NE	0.66 (0.48–0.91)	62/352	88/354
Bone metastasis only at baseline					
Yes	NE	NE	0.47 (0.30–0.75)	28/289	53/269
No	NE	NE	0.89 (0.61–1.26)	55/236	64/258
Visceral disease and bone metastasis at baseline					
Yes	NE	28.6	0.99 (0.55–1.77)	20/56	25/72
No	NE	NE	0.63 (0.46–0.87)	83/469	92/455
Gleason score at diagnosis					
≤7	NE	NE	0.58 (0.33–0.97)	21/174	34/189
>7	NE	NE	0.73 (0.52–1.01)	62/351	83/338
Prior docetaxel use					
Yes	NE	NE	1.27 (0.52–3.09)	11/58	9/55
No	NE	NE	0.63 (0.47–0.85)	72/467	108/472
Age (years)					
<65	NE	NE	0.58 (0.33–0.94)	21/149	43/162
≥65	NE	NE	0.73 (0.48–1.10)	42/243	51/232
≥75	NE	NE	0.74 (0.41–1.35)	20/133	23/113
Baseline PSA above median					
Yes	NE	NE	0.68 (0.48–0.97)	58/285	86/241
No	NE	NE	0.58 (0.35–0.91)	25/240	51/286
Baseline LDH above ULN					
Yes	NE	NE	0.69 (0.37–1.24)	18/60	25/60
No	NE	NE	0.69 (0.49–0.95)	62/443	86/442
Baseline ALP above ULN					
Yes	NE	NE	0.63 (0.42–0.93)	40/177	61/180
No	NE	NE	0.73 (0.49–1.09)	43/346	56/345
mCSPC disease volume					
High volume	NE	NE	0.68 (0.50–0.92)	69/325	97/335
Low volume	NE	NE	0.67 (0.34–1.32)	14/200	20/192
Metastasis stage at initial diagnosis					
M0	NE	NE	0.40 (0.15–1.03)	7/85	11/59
M1	NE	NE	0.72 (0.53–0.98)	71/411	101/441

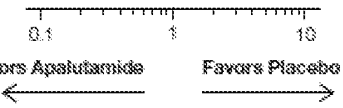


FIG. 3B

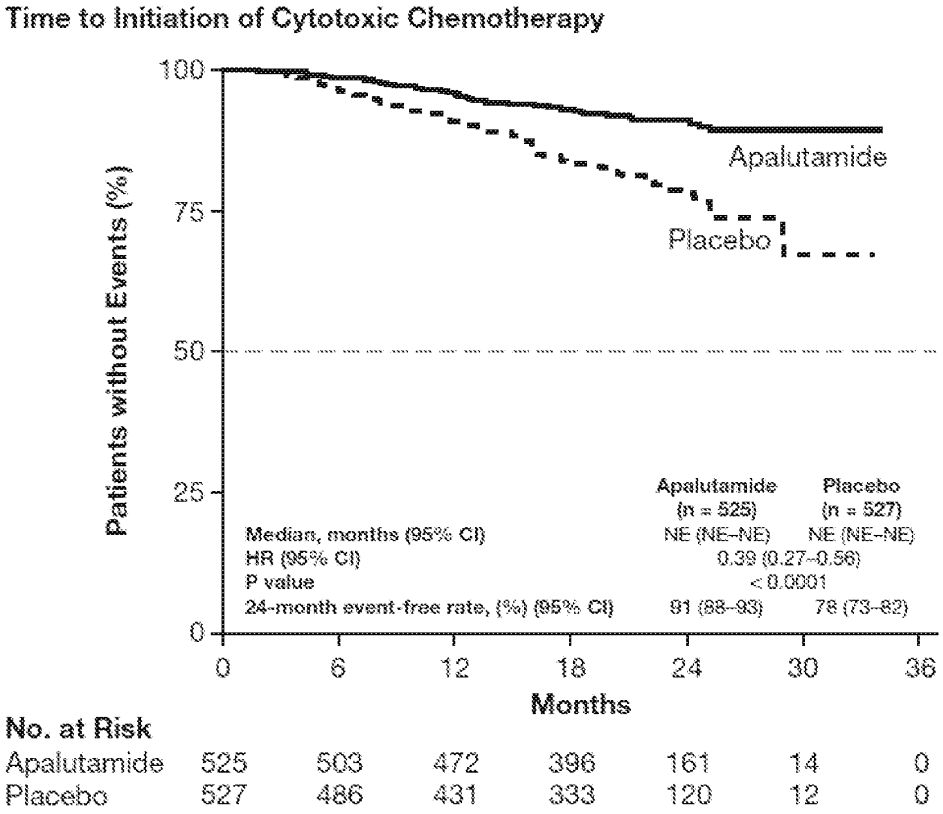

Time to Initiation of Cytotoxic Chemotherapy
Patients without Events (%)
100
75
50
25
0
Apalutamide
Placebo
Apalutamide (n = 525)
Placebo (n = 527)
Median, months (95% CI)
NE (NE–NE)
NE (NE–NE)
HR (95% CI)
0.39 (0.27–0.56)
P value
< 0.0001
24-month event-free rate, (%) (95% CI)
91 (88–93)
78 (73–82)
0
6
12
18
24
30
36
Months
No. at Risk
Apalutamide 525 503 472 396 161 14 0
Placebo 527 486 431 333 120 12 0

FIG. 4

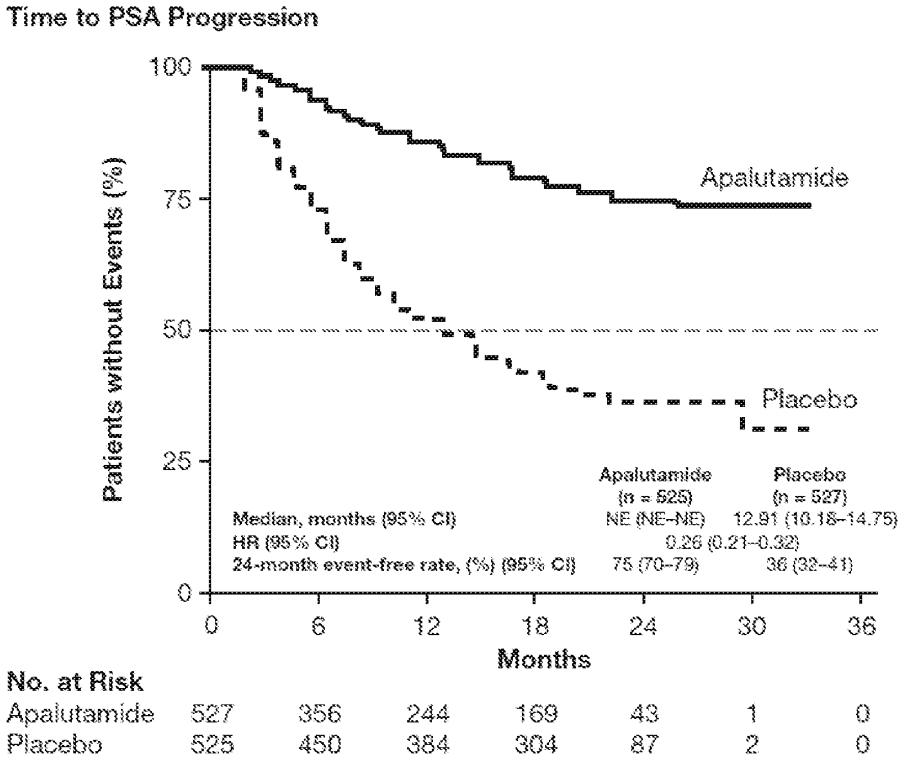

Time to PSA Progression
Patients without Events (%)
100
75
50
25
0
Apalutamide
Placebo
Apalutamide (n = 525)
Placebo (n = 527)
Median, months (95% CI) NE (NE–NE) 12.91 (10.18–14.75)
HR (95% CI) 0.26 (0.21–0.32)
24-month event-free rate, (%) (95% CI) 75 (70–79) 36 (32–41)
0 6 12 18 24 30 36
Months
No. at Risk
Apalutamide 527 356 244 169 43 1 0
Placebo 525 450 384 304 87 2 0

FIG. 5

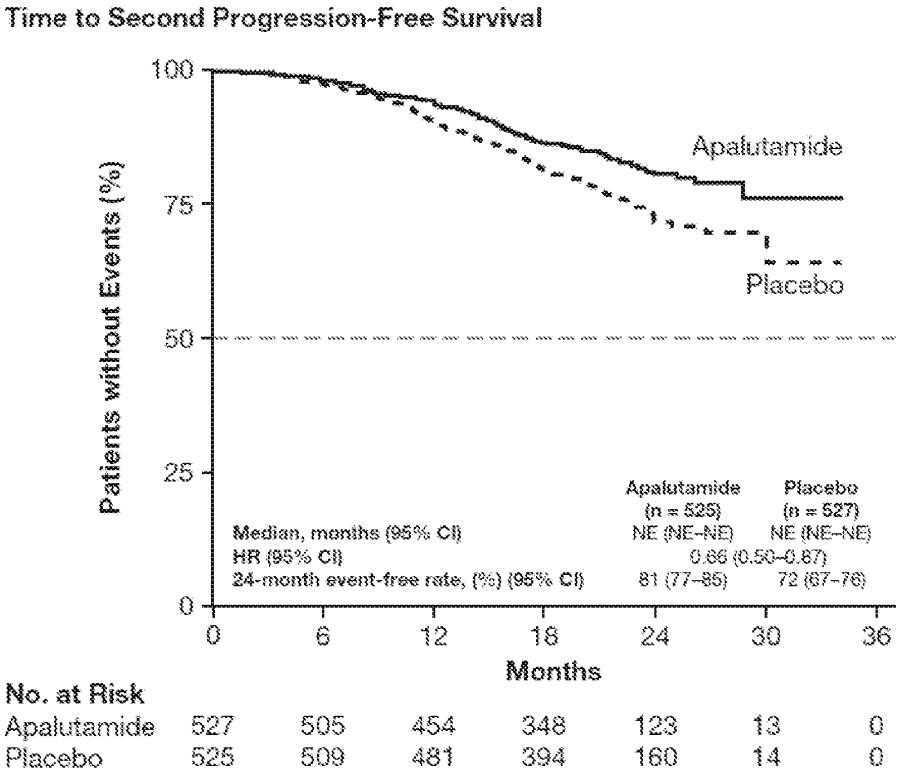

Time to Second Progression-Free Survival
Patients without Events (%)
100
75
50
25
0
Apalutamide
Placebo
Apalutamide (n = 525)
Placebo (n = 527)
Median, months (95% CI)
NE (NE–NE)
NE (NE–NE)
HR (95% CI)
0.66 (0.50–0.87)
24-month event-free rate, (%) (95% CI)
81 (77–85)
72 (67–76)
0
6
12
18
24
30
36
Months
No. at Risk
Apalutamide 527 505 454 348 123 13 0
Placebo 525 509 481 394 160 14 0

FIG. 6

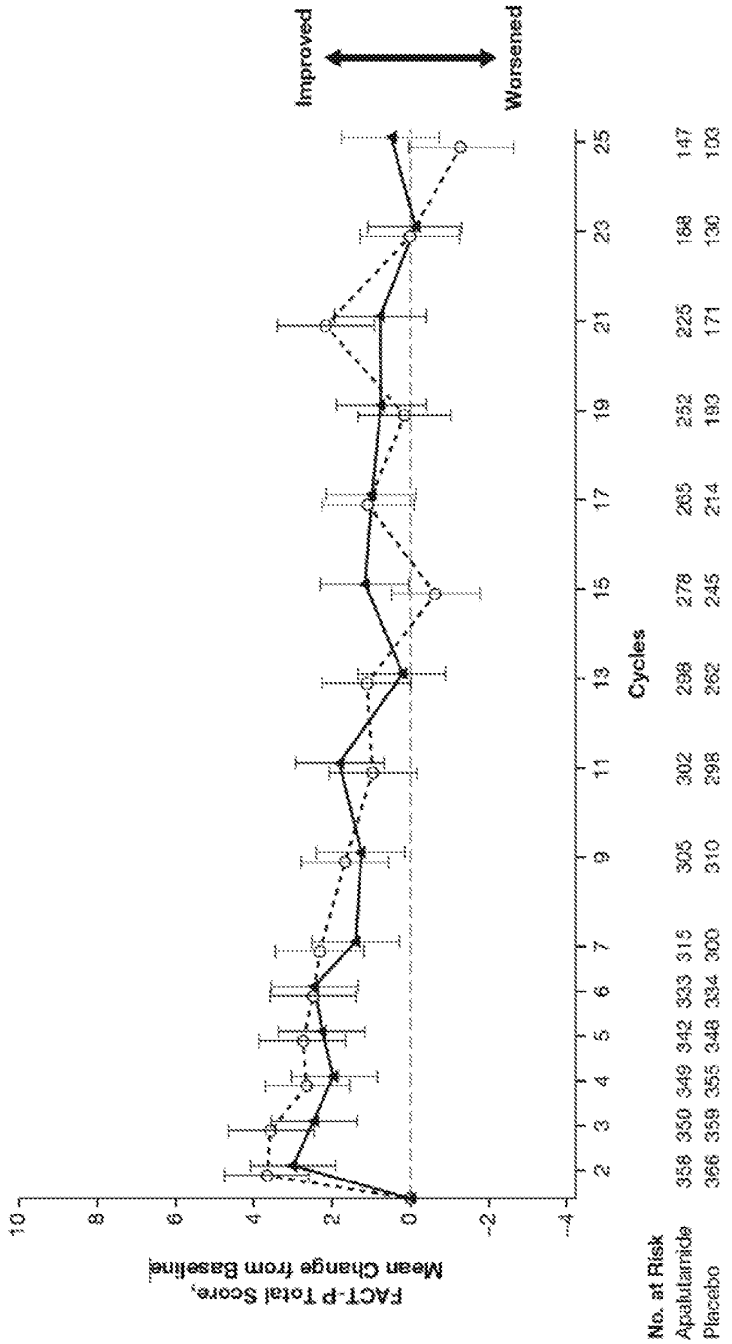
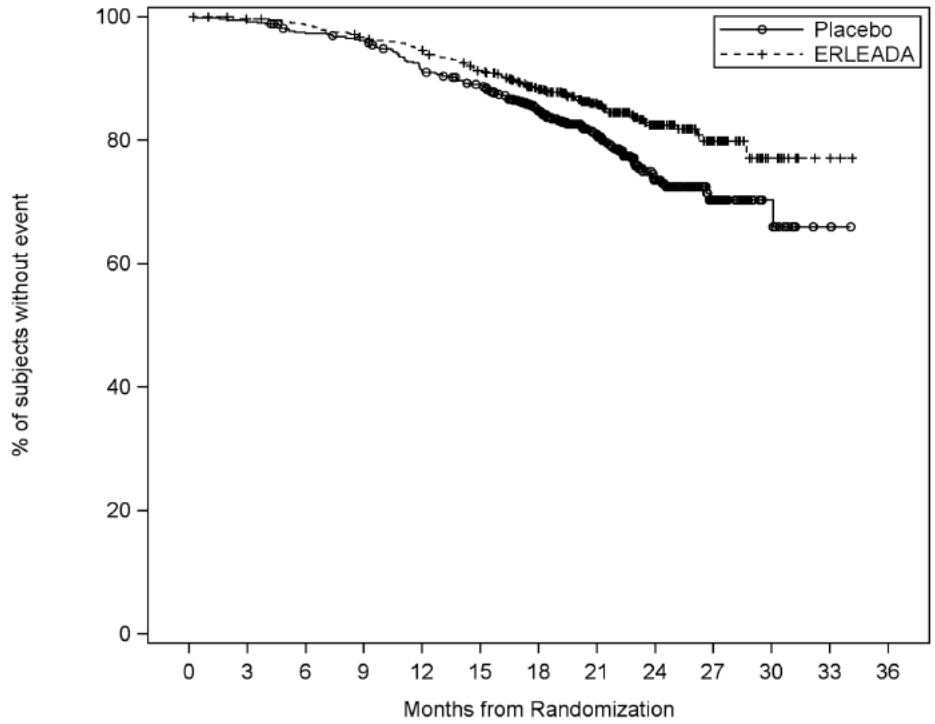

Improved
Worsened
FACT-P Total Score, Mean Change from Baseline
10
8
6
4
2
0
-2
-4
2 3 4 5 6 7 9 11 13 15 17 19 21 23 25
Cycles
No. at Risk
Apalutamide 358 350 349 342 333 315 305 302 288 278 265 252 225 168 147
Placebo 366 359 355 348 334 300 310 298 262 245 214 193 171 130 103
Placebo
Apalutamide

FIG. 7

Figure 8: Kaplan-Meier Plot of Overall Survival (OS); Intent-to-treat mCSPC Population (TITAN)



Subjects at risk

Placebo	527	524	509	502	473	456	387	263	142	59	16	3	0
ERLEADA	525	519	513	500	490	467	410	289	165	60	14	3	0

Figure 9: **Kaplan-Meier Plot of Radiographic Progression-Free Survival (rPFS); Intent-to-treat mCSPC Population (TITAN)**

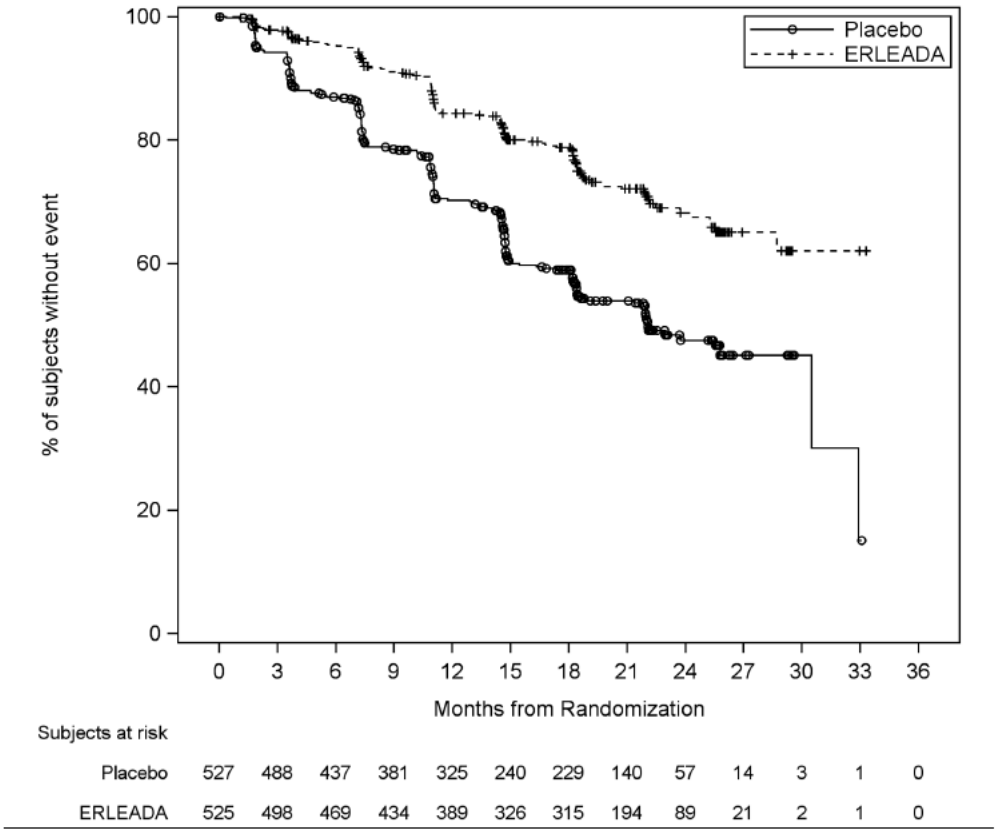
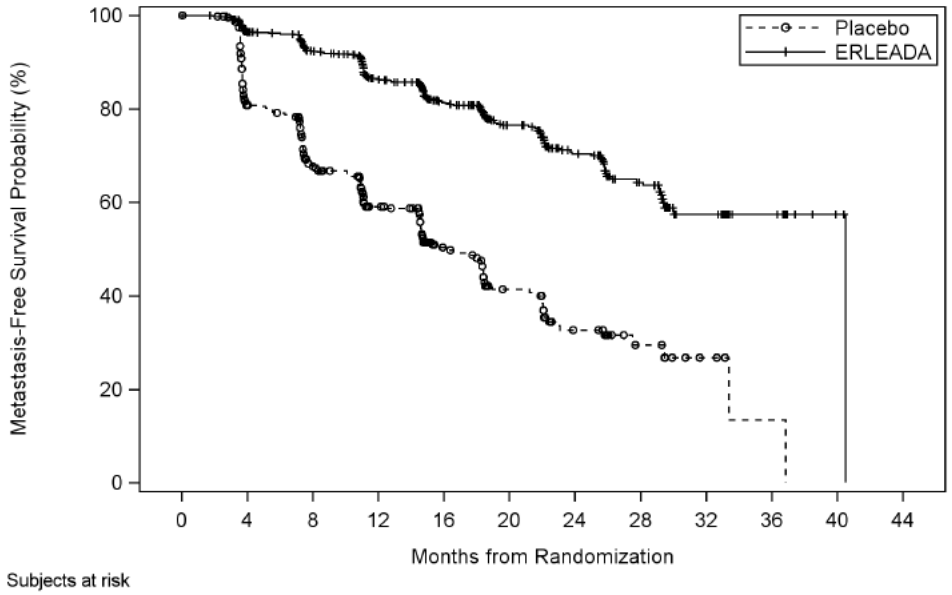


Figure 10: Kaplan-Meier Metastasis-Free Survival (MFS) Curve in SPARTAN (nmCRPC)



Subjects at risk

Placebo	401	291	220	153	91	58	34	13	5	1	0	0
ERLEADA	806	713	652	514	398	282	180	96	36	16	3	0