Supplementary Material

Supplementary Table S1. Multivariate analysis of radiographic progression-free survival by blinded independent central review in the *BRCA1/2* subgroup

	Model fit		HR
Model parameter	Coeff (SE)	*P* value	Estimate (95% CI)
Treatment (niraparib vs placebo)	−0.69 (0.18)	<0.0001	0.50 (0.35-0.71)
Presence of visceral disease (no vs yes)	−0.75 (0.20)	0.0001	0.47 (0.32-0.69)
Baseline PSA[a]	0.15 (0.04)	0.0001	1.16 (1.08-1.26)

CI, confidence interval; HR, hazard ratio; PSA, prostate-specific antigen; SE, standard error.

[a]The logarithmic value of PSA was used.

Supplementary Table S2. Subsequent therapy for prostate cancer in the *BRCA1/2* subgroup[a]

Therapy, *n* (%)	NIRA + AAP (*n* = 113)	PBO + AAP (*n* = 112)
Total	35 (31.0)	66 (58.9)
Chemotherapy	28 (24.8)	44 (39.3)
Docetaxel	18 (15.9)	36 (32.1)
Cabazitaxel	8 (7.1)	13 (11.6)
Carboplatin	6 (5.3)	4 (3.6)
Carboplatin/docetaxel	1 (0.9)	1 (0.9)
Carboplatin:etoposide	1 (0.9)	0
Cisplatin	1 (0.9)	2 (1.8)
Etoposide	1 (0.9)	1 (0.9)
Docetaxel/prednisone	0	1 (0.9)
Estramustine	0	1 (0.9)
Mitoxantrone	0	1 (0.9)
Vinorelbine	0	1 (0.9)
Other	11 (9.7)	18 (16.1)
Prednisone	4 (3.5)	9 (8.0)
Investigational drug	3 (2.7)	3 (2.7)
Lutetium (Lu 177)	2 (1.8)	2 (1.8)
Investigational antineoplastic drugs	1 (0.9)	2 (1.8)
Prednisolone	1 (0.9)	0
Radium Ra 223	1 (0.9)	1 (0.9)
Dexamethasone	0	4 (3.6)
Nivolumab	0	1 (0.9)
Novel AR-targeted therapy	7 (6.2)	11 (9.8)
Enzalutamide	7 (6.2)	10 (8.9)
Apalutamide	0	1 (0.9)
Hormonal	2 (1.8)	9 (8.0)
Abiraterone	2 (1.8)	6 (5.4)
Bicalutamide	0	2 (1.8)
Flutamide	0	1 (0.9)
PARPi	1 (0.9)	22 (19.6)
Olaparib	1 (0.9)	18 (16.1)
Fluzoparib	0	1 (0.9)
Niraparib	0	2 (1.8)
Rucaparib	0	1 (0.9)
Talazoparib	0	1 (0.9)

AAP, abiraterone acetate plus prednisone; AR, androgen receptor; NIRA, niraparib; /, poly adenosine diphosphate-ribose polymerase inhibitor; PBO, placebo.

[a]Recurrent medications were counted only once per patient.

Supplementary Table S3. Other endpoints in the *BRCA1/2* subgroup

	Median, months			Nominal
	NIRA + AAP (*n* = 113)	PBO + AAP (*n* = 112)	**HR (95% CI)**	***P* value**
Time to PSA progression	18.4	9.2	0.48 (0.33-0.70)	<0.0001
Objective response rates	28 (50.0)[a]	15 (31.3)[a]	1.60 (0.98-2.62)[b]	0.053
OS multivariate analysis	NA	NA	0.68 (0.45-1.05)	0.0793
PSA response,[c] *n* (%)	93 (82.3)	77 (68.8)	1.21 (1.02-1.43)[b]	0.023
Confirmed	89 (78.8)	73 (65.2)		
Unconfirmed	4 (3.5)	4 (3.6)		

AAP, abiraterone acetate with prednisone; AR, androgen receptor; CI, confidence interval; HR, hazard ratio; NA, not available; NIRA, niraparib; OS, overall survival; PBO, placebo; PSA, prostate-specific antigen.

[a]Responder is presented as *n* (%) and represents a complete or partial response, neither of which had to be confirmed.

[b]Relative risk (95% CI); relative risk >1 favors active treatment.

[c]PSA response rate was defined as the proportion of patients achieving a PSA decline of ≥50% and confirmed at 3-4 weeks later according to Prostate Cancer Working Group 3 criteria by week 12 and during the treatment period.

Supplementary Table S4. Multivariate analysis of OS by blinded independent central review in the HRR+ population

	Model fit		HR
Model parameter	Coeff (SE)	*P* value	Estimate (95% CI)
Treatment (niraparib vs placebo)	−0.21 (0.15)	0.1821	0.82 (0.60-1.10)
PSA[a]	0.09 (0.04)	0.0287	1.09 (1.01-1.18)
Lactate dehydrogenase[a]	0.52 (0.15)	0.0003	1.69 (1.27-2.25)
Alkaline phosphatase	0.28 (0.10)	0.0054	1.32 (1.09-1.61)
Age	0.03 (0.01)	0.0017	1.03 (1.01-1.05)
ECOG PS (0 vs 1)	−0.34 (0.16)	0.0339	0.71 (0.52-0.97)
Number of bone lesions at baseline (≤10 vs >10)	−0.60 (0.19)	0.0015	0.55 (0.38-0.80)
Presence of visceral disease (yes vs no)	0.43 (0.18)	0.0161	1.54 (1.08-2.18)

CI, confidence interval; ECOG PS, Eastern Cooperative Oncology Group performance status; HR, hazard ratio; HRR, homologous recombination repair; OS, overall survival; PSA, prostate-specific antigen; SE, standard error.

[a]The logarithmic value of PSA and lactate dehydrogenase was used.

Supplementary Table S5. Key efficacy endpoints by gene alteration in the HRR+ population

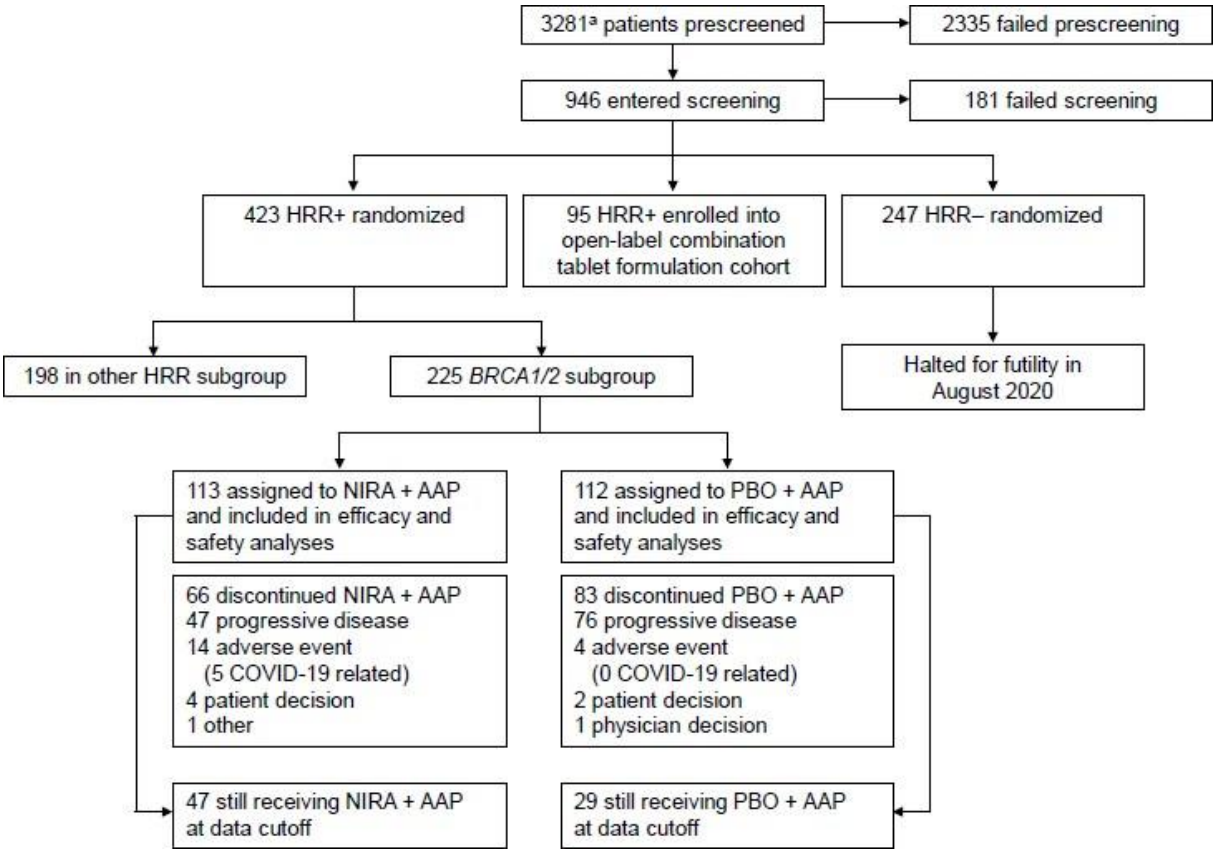
		rPFS		TSP		TCC		OS	
Gene	Treatment group	*N* (events)	HR (95% CI)	*N* (events)	HR (95% CI)	*N* (events)	HR (95% CI)	*N* (events)	HR (95% CI)
HRR-Fanconi Anemia (*PALB2*, *BRIP1*, *FANCA*)	NIRA + AAP PBO + AAP	17 (10) 14 (11)	0.68 (0.29-1.61)	17 (5) 14 (6)	0.61 (0.19-2.02)	17 (6) 14 (5)	0.73 (0.22-2.39)	17 (8) 14 (8)	0.71 (0.26-1.89)
PALB2	NIRA + AAP PBO + AAP	8 (6) 4 (4)	0.54 (0.14-2.03)	8 (1) 4 (2)	0.22 (0.02-2.42)	8 (3) 4 (1)	0.56 (0.05-6.41)	8 (4) 4 (3)	0.46 (0.10-2.08)
BRIP1	NIRA + AAP PBO + AAP	4 (2) 4 (3)	0.44 (0.07-2.65)	4 (2) 4 (1)	1.14 (0.10-13.27)	4 (2) 4 (0)	NE (NE)	4 (3) 4 (3)	0.40 (0.07-2.47)
FANCA	NIRA + AAP PBO + AAP	5 (2) 6 (4)	0.73 (0.13-4.06)	5 (2) 6 (3)	1.23 (0.17-8.74)	5 (1) 6 (4)	0.42 (0.04-4.03)	5 (1) 6 (2)	1.41 (0.09-22.82)
HRR associated (*CHEK2* + *HDAC2*)	NIRA + AAP PBO + AAP	20 (12) 23 (14)	0.77 (0.36-1.68)	20 (4) 23 (7)	0.55 (0.16-1.88)	20 (6) 23 (7)	0.76 (0.26-2.27)	20 (8) 23 (12)	0.63 (0.26-1.55)
CHEK2	NIRA + AAP PBO + AAP	18 (11) 20 (11)	0.87 (0.37-2.01)	18 (3) 20 (6)	0.48 (0.12-1.94)	18 (4) 20 (7)	0.49 (0.14-1.69)	18 (7) 20 (10)	0.66 (0.25-1.75)
HDAC2	NIRA + AAP PBO + AAP	2 (1) 3 (3)	0.71 (0.06-8.02)	2 (1) 3 (1)	0.71 (0.04-11.79)	2 (2) 3 (0)	NE (NE)	2 (1) 3 (2)	0.44 (0.04-5.13)
ATM	NIRA + AAP PBO + AAP	43 (32) 42 (25)	1.26 (0.74-2.13)	43 (9) 42 (11)	0.79 (0.33-1.90)	43 (9) 42 (16)	0.47 (0.21-1.06)	43 (17) 42 (14)	1.13 (0.56-2.30)
CDK12	NIRA + AAP PBO + AAP	11 (7) 16 (10)	0.89 (0.34-2.36)	11 (4) 16 (5)	1.05 (0.28-3.94)	11 (5) 16 (6)	1.32 (0.38-4.56)	11 (6) 16 (9)	1.30 (0.45-3.81)

AAP, abiraterone acetate with prednisone; CI, confidence interval; HR, hazard ratio; HRR, homologous recombination repair; NE, not estimable; NIRA, niraparib; OS, overall survival; PBO, placebo; PSA, prostate-specific antigen; rPFS, radiographic progression-free survival; TCC, time to initiation of cytotoxic chemotherapy; TSP, time to symptomatic progression.

Note: Nonestimable HRs are due to few or no events.

Supplementary Figure S1. CONSORT diagram.

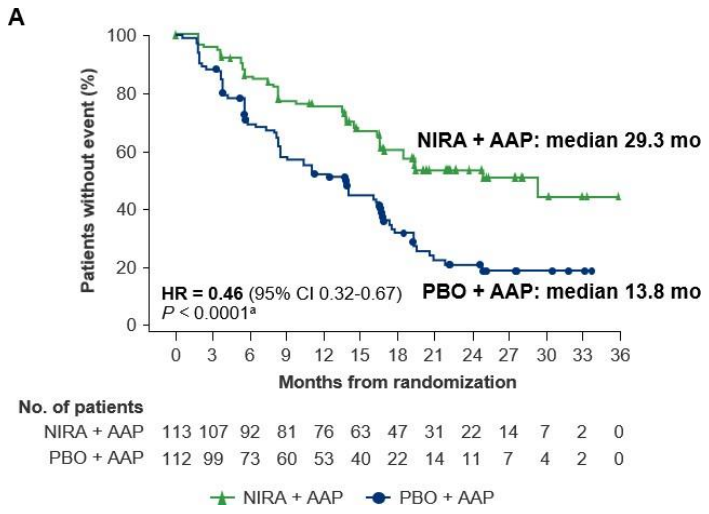
AAP, abiraterone acetate with prednisone; HRR, homologous recombination repair; NIRA, niraparib; PBO, placebo. [a]Included 3166 patients who entered prescreening *de novo* (did not have known HRR status).



Supplementary Figure S2. Radiographic progression-free survival at IA2 assessed (A) in the *BRCA1/2* subgroup as analyzed by investigator review, (B) in the HRR+ population as analyzed by blinded independent central review, and (C) in the HRR+ population as analyzed by investigator review.

AAP, abiraterone acetate with prednisone; CI, confidence interval; HR, hazard ratio; HRR, homologous recombination repair; IA2, second interim analysis; NIRA, niraparib; PBO, placebo.

[a]Nominal *P* value.



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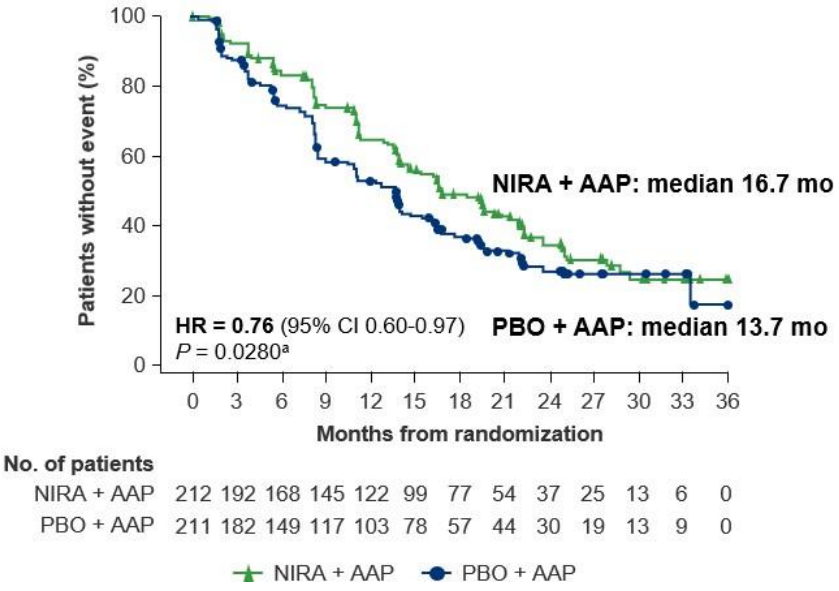
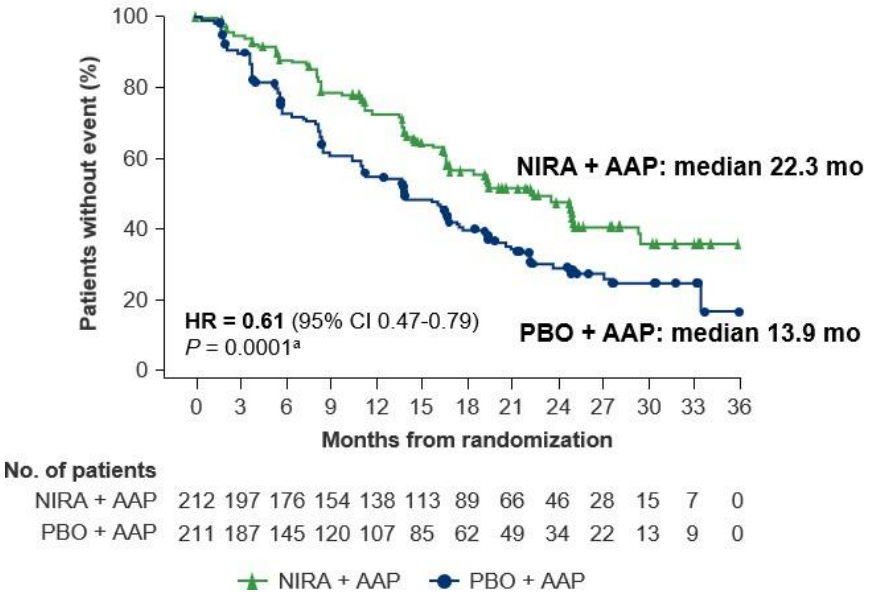
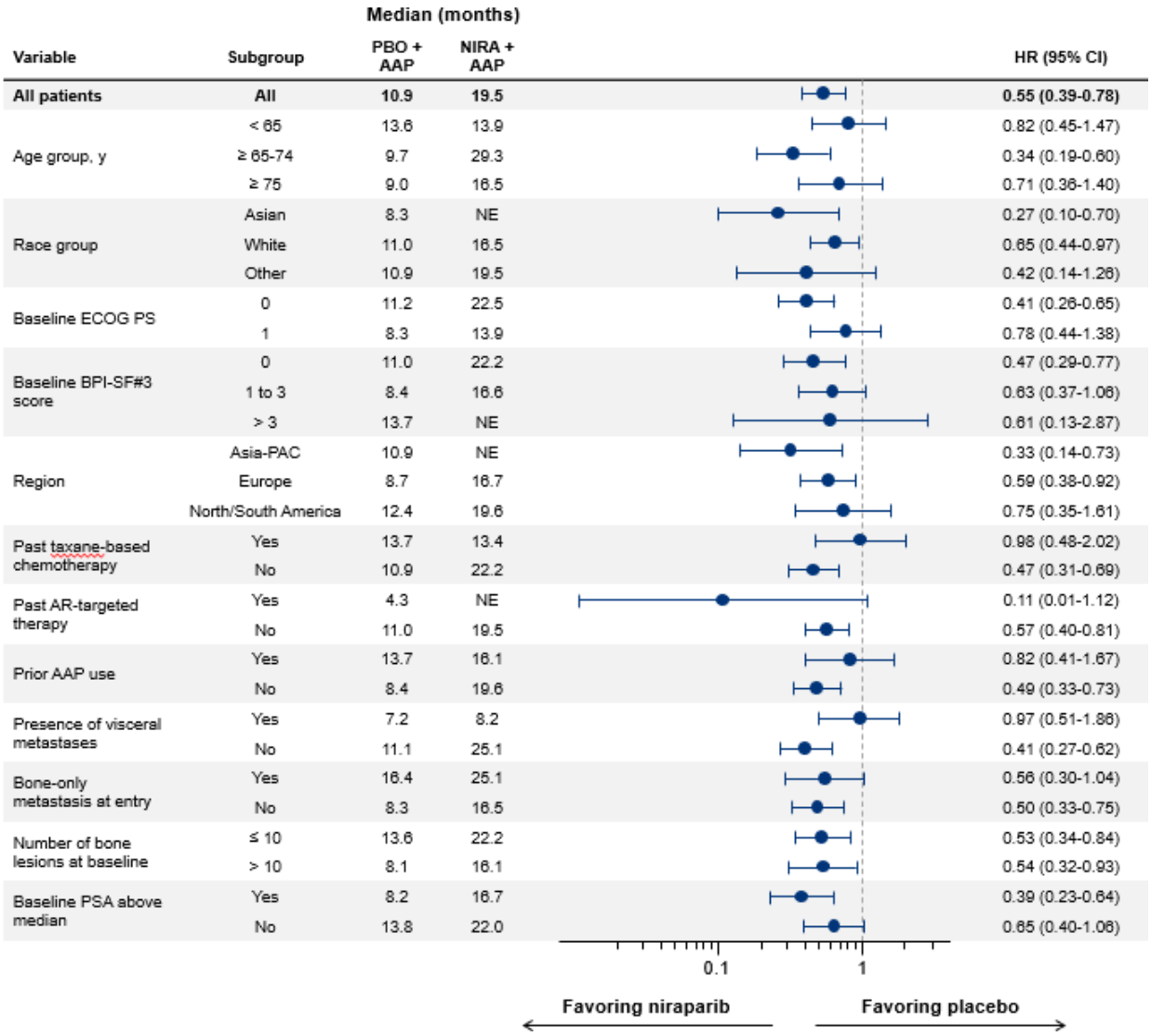

Patients without event (%)
100
80
60
40
20
0
NIRA + AAP: median 16.7 mo
HR = 0.76 (95% CI 0.60-0.97)
P = 0.0280a
PBO + AAP: median 13.7 mo
0 3 6 9 12 15 18 21 24 27 30 33 36
Months from randomization
No. of patients
NIRA + AAP 212 192 168 145 122 99 77 54 37 25 13 6 0
PBO + AAP 211 182 149 117 103 78 57 44 30 19 13 9 0
NIRA + AAP
PBO + AAP

C


Patients without event (%)
100
80
60
40
20
0
NIRA + AAP: median 22.3 mo
HR = 0.61 (95% CI 0.47-0.79)
P = 0.0001a
PBO + AAP: median 13.9 mo
0 3 6 9 12 15 18 21 24 27 30 33 36
Months from randomization
No. of patients
NIRA + AAP 212 197 176 154 138 113 89 66 46 28 15 7 0
PBO + AAP 211 187 145 120 107 85 62 49 34 22 13 9 0
NIRA + AAP
PBO + AAP

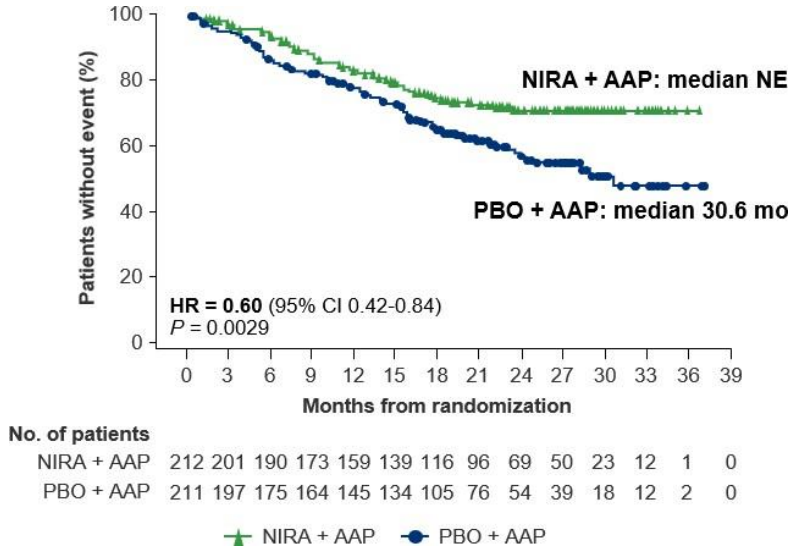
Supplementary Figure S3. Radiographic progression-free survival by baseline patient and disease characteristics for the *BRCA1/2* subgroup.

AAP, abiraterone acetate with prednisone; AR, androgen receptor; BPI-SF, Brief Pain Inventory-Short Form; CI, confidence interval; ECOG PS, Eastern Cooperative Oncology Group performance status; HR, hazard ratio; NE, not evaluable; PAC, Pacific; PSA, prostate-specific antigen.



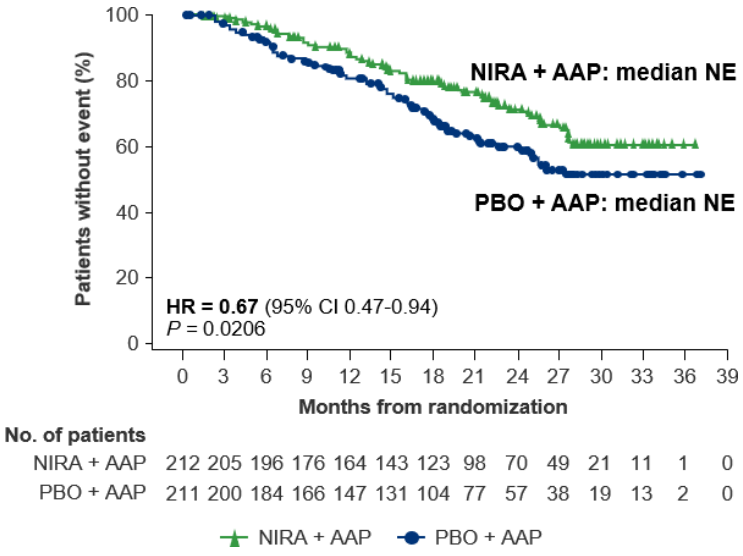
Supplementary Figure S4. Time to symptomatic progression at IA2 in the HRR+ population.

AAP, abiraterone acetate with prednisone; CI, confidence interval; HR, hazard ratio; HRR, homologous recombination repair; IA2, second interim analysis; NE, not evaluable; NIRA, niraparib; PBO, placebo.



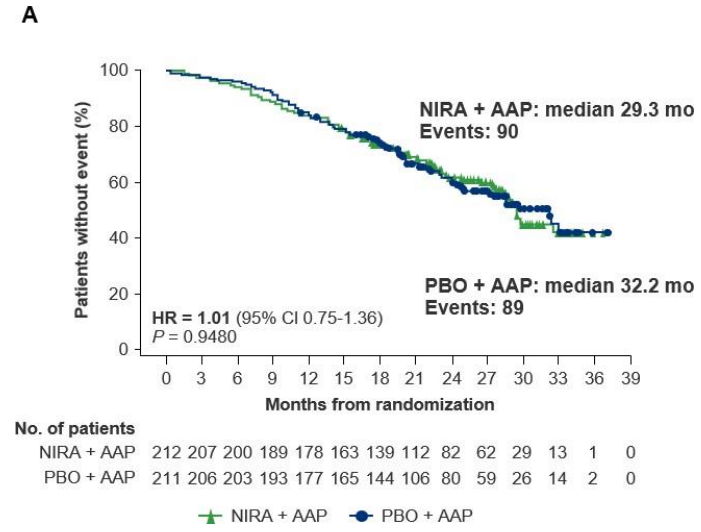
Supplementary Figure S5. Time to initiation of cytotoxic chemotherapy at IA2 in the HRR+ population.

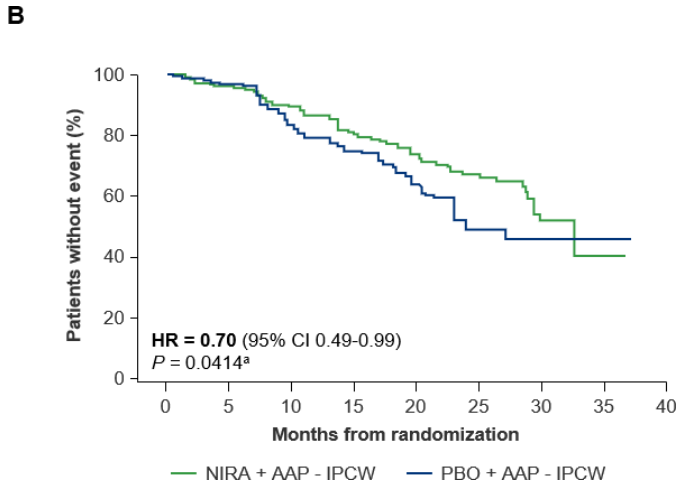
AAP, abiraterone acetate with prednisone; CI, confidence interval; HR, hazard ratio; HRR, homologous recombination repair; IA2, second interim analysis; NE, not evaluable; NIRA, niraparib; PBO, placebo.



Supplementary Figure S6. Overall survival at IA2 in the HRR+ population by (A) stratified analysis and (B) IPCW analysis.

AAP, abiraterone acetate with prednisone; CI, confidence interval; HR, hazard ratio; HRR, homologous recombination repair; IA2, second interim analysis; IPCW, inverse probability censoring weighting; NIRA, niraparib; PBO, placebo. [a]Nominal *P* value.





Supplementary Figure S7. Additional endpoints at IA2 in the *BRCA1/2* subgroup, including (A) time to pain progression and (B) time to BPI-SF pain interference.

AAP, abiraterone acetate with prednisone; BPI-SF, Brief Pain Inventory-Short Form; CI, confidence interval; HR, hazard ratio; IA2, second interim analysis; NE, not evaluable; NIRA, niraparib; PBO, placebo. [a]Nominal *P* value.