

# Efficacy of Niraparib and Abiraterone Acetate plus Prednisone in metastatic castration-resistant prostate cancer with *HRR* gene alterations identified by tissue vs plasma assay in MAGNITUDE study (final analysis)

Gerhardt Attard<sup>1</sup>, Usha Singh<sup>2</sup>, Victoria Zadorozhny<sup>2</sup>, Yaji Xu<sup>2</sup>, Lesley Farrington<sup>4</sup>, Katie Bell<sup>3</sup>, Daphne Wu<sup>4</sup>, Sharon McCarthy<sup>3</sup>, Fei Shen<sup>3</sup>, Songbai Wang<sup>2</sup>

<sup>1</sup>Institute of Cancer Research, University College, London, United Kingdom; <sup>2</sup>Johnson & Johnson, Raritan, NJ, USA; <sup>3</sup>Johnson & Johnson, Spring House, PA, USA; <sup>4</sup>Johnson & Johnson, Los Angeles, CA, USA

\*Presenting author

## Key Takeaway



These findings suggest that both, tissue and plasma assay can identify the *HRR+* and *BRCA1/2+* patients for treatment decisions

## Conclusions



In the MAGNITUDE study, mCRPC patients with *HRR+* alteration identified by either the Resolution ctDx plasma assay or the F1CDx tissue assay demonstrated comparable efficacy on rPFS, OS, TCC and TSP with NIRA+AAP treatment versus PBO+AAP



Clinically meaningful benefit with NIRA+AAP treatment was similar for *BRCA1/2+* patients detected by either plasma- or tissue-based assays



Please scan QR code

<https://www.congresshub.com/Oncology/ESMO2024/Niraparib/Attard>

Poster

Copies of this poster obtained through QR (Quick Response) and/or text key codes are for personal use only and may not be reproduced without written permission of the authors.

## Background

- Metastatic castration-resistant prostate cancer (mCRPC) with alterations in homologous recombination repair (*HRR*) genes, has a poor prognosis<sup>1,2</sup>
- Poly-ADP ribose polymerase inhibitors (PARPi) have demonstrated significant efficacy and clinical benefit in mCRPC patients with *HRR* gene alterations, particularly *BRCA* gene alterations<sup>3,4</sup>
- The MAGNITUDE study reported that the PARPi, niraparib in combination with abiraterone acetate and prednisone (AAP) for Line 1 mCRPC treatment significantly improved radiographic progression-free survival (rPFS) and other clinically relevant outcomes in patients with *HRR+* mCRPC<sup>5</sup>
- Niraparib plus abiraterone acetate with prednisone (NIRA+AAP) is approved for patients with *BRCA*+ mCRPC, as identified by an approved companion diagnostic tissue test, FoundationOne<sup>®</sup>CDx (F1CDx)

## Objective

- To evaluate the clinical efficacy outcomes based on the two different enrollment assays, the tissue-based F1CDx assay and the plasma-based Resolution Bioscience ctDx HRD<sup>™</sup> (Resolution ctDx) assay

## Methods

### Study Design

- The MAGNITUDE study (Figure 1) was a phase 3, double-blind, randomized, placebo-controlled study assessing NIRA+AAP versus placebo+AAP (PBO+AAP) for patients with mCRPC<sup>5</sup>
- Patients in the MAGNITUDE study provided both plasma and tissue samples for *HRR* biomarker testing using tissue-based F1CDx assay and the plasma-based Resolution ctDx assay to classify them into *HRR+* and *HRR-* groups for screening and cohort assignment
  - Tumor tissue and plasma were tested using local or central (FoundationOne<sup>®</sup>CDx (F1CDx) tissue or Resolution HRD<sup>™</sup> Plasma) assays
  - HRR+* pts (*BRCA1*, *BRCA2*, *FANCA*, *PALB2*, *CHEK2*, *BRIP1*, *HDAC2*, *ATM*, *CDK12*) were randomized 1:1 to receive NIRA+AAP or PBO+AAP
- A subgroup analysis was performed after final analysis to evaluate the efficacy of NIRA+AAP compared with PBO+AAP based on enrollment assays in *BRCA1* and *BRCA2* (*BRCA+*) and *HRR+* positive mCRPC patients as identified by the two assays (Figure 2)
  - The primary endpoint of radiographic progression-free survival (rPFS) and the secondary endpoints of time to cytotoxic chemotherapy (TCC), time to symptomatic progression (TSP), and overall survival (OS) were reported for each subgroup

## Statistical analysis

- The Kaplan–Meier product limit method and a stratified Cox model were used to estimate rPFS, TSP, TCC, and OS and to obtain hazard ratios (HRs) and associated 95% confidence intervals (CIs)

Figure 1: MAGNITUDE Study Design (NCT03748641)

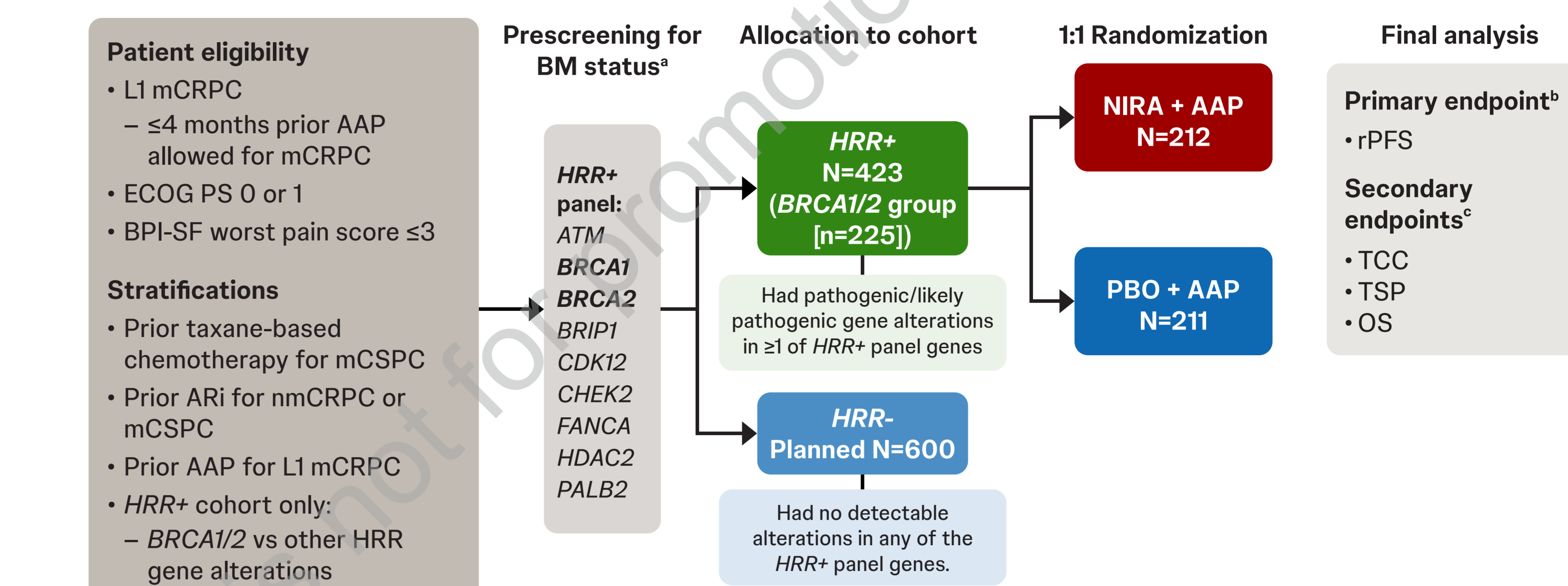
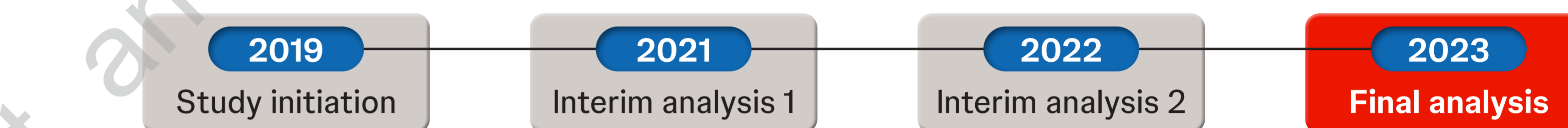


Figure 2: MAGNITUDE Study Timeline



Study duration: February 2019 - 2023

<sup>a</sup>Patients were prospectively tested by plasma, tissue, and/or saliva/whole blood. Patients were required to provide tissue and blood to confirm HRR BM status. Tissue and plasma assays used included FoundationOne tissue test (F1CDx), Resolution Bioscience liquid test (ctDNA), AmoyDx<sup>®</sup> germline (blood) and tissue assays, Invitae germline testing (blood/saliva), or local lab BM test results demonstrating a pathogenic germline or somatic alteration outlined in the study protocol. <sup>b</sup>As rPFS was found to be statistically significant at IA1, no formal statistical testing was performed for IA2. <sup>c</sup>Secondary endpoints did not cross the very conservative prespecified significance boundary at IA1 and were therefore formally tested in the *HRR+* population at IA2. ATM, ataxia-telangiectasia mutated; BRCA1, breast cancer gene 1; BRCA2, breast cancer gene 2; BPI-SF, brief pain inventory; BRIP1, BRCA1-interacting protein 1; BM, biomarker; CDK12, cyclin-dependent kinase 12; CHEK2, checkpoint kinase 2; ECOG, electrocardiography; FANCA, fanconi anemia; *HRR+*, homologous recombination repair positive; HDAC2, histone deacetylase 2; mCRPC, metastatic castration-resistant prostate cancer; nmCRPC, non-metastatic castration-resistant prostate cancer; NIRA, niraparib; PS, performance status; PALB2, partner and localizer of BRCA2; PBO, placebo; OS, overall survival; rPFS, radiographic progression free survival; TCC, transitional cell carcinoma; TSP, thrombospondin.

## Results

- Demographics and baseline characteristics were broadly comparable across both assay and biomarker groups (Table 1)

Table 1: MAGNITUDE enrollment with F1CDx tissue assay and Resolution ctDx plasma assay

Resolution ctDx assay (Plasma)	F1CDx assay (Tissue)					Total
	<i>BRCA</i>	<i>BRCA1/2</i>	Other <i>HRR</i>	Negative	No Result	
<i>BRCA</i>		96	5	12	37	150
Other <i>HRR</i>		6	52	26	43	127
Negative		56	68	0	3 <sup>a</sup>	127
No Result		4	4	0	11 <sup>b</sup>	19
<b>Total</b>		<b>162</b>	<b>129</b>	<b>38</b>	<b>94</b>	<b>423</b>

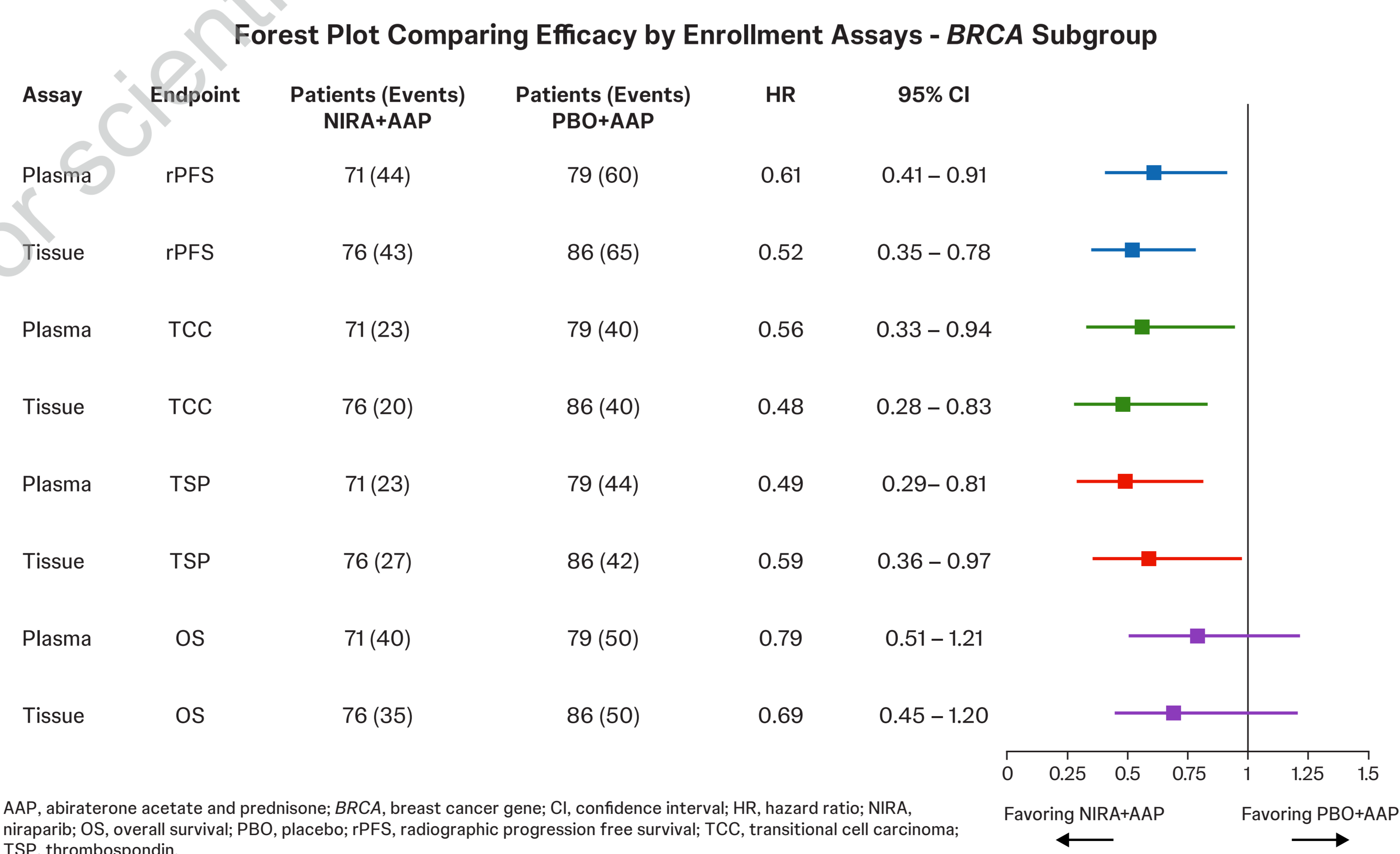
Demographics and baseline clinical disease characteristics were broadly comparable across both assay and biomarker (*HRR* and *BRCA1/2*) groups

<sup>a</sup>Enrolled by local tissue assays through Foundation Medicine, no tissue collected for tissue central confirmation

<sup>b</sup>Enrolled in China (by local AmoyDx test) and all of them are *BRCA2* positive. *BRCA*, breast cancer gene; *HRR+*, homologous recombination repair positive.

- Efficacy based on rPFS in the *BRCA1/2+* subgroup of patients with NIRA+AAP treatment versus PBO+AAP was comparable for the Resolution ctDx plasma assay and the F1CDx tissue assay (Figure 3)
- Efficacy based on TCC, TSP, and OS in the *BRCA1/2+* subgroup of patients with NIRA+AAP treatment versus PBO+AAP were comparable for the Resolution ctDx plasma assay and the F1CDx tissue assay (Figure 3)

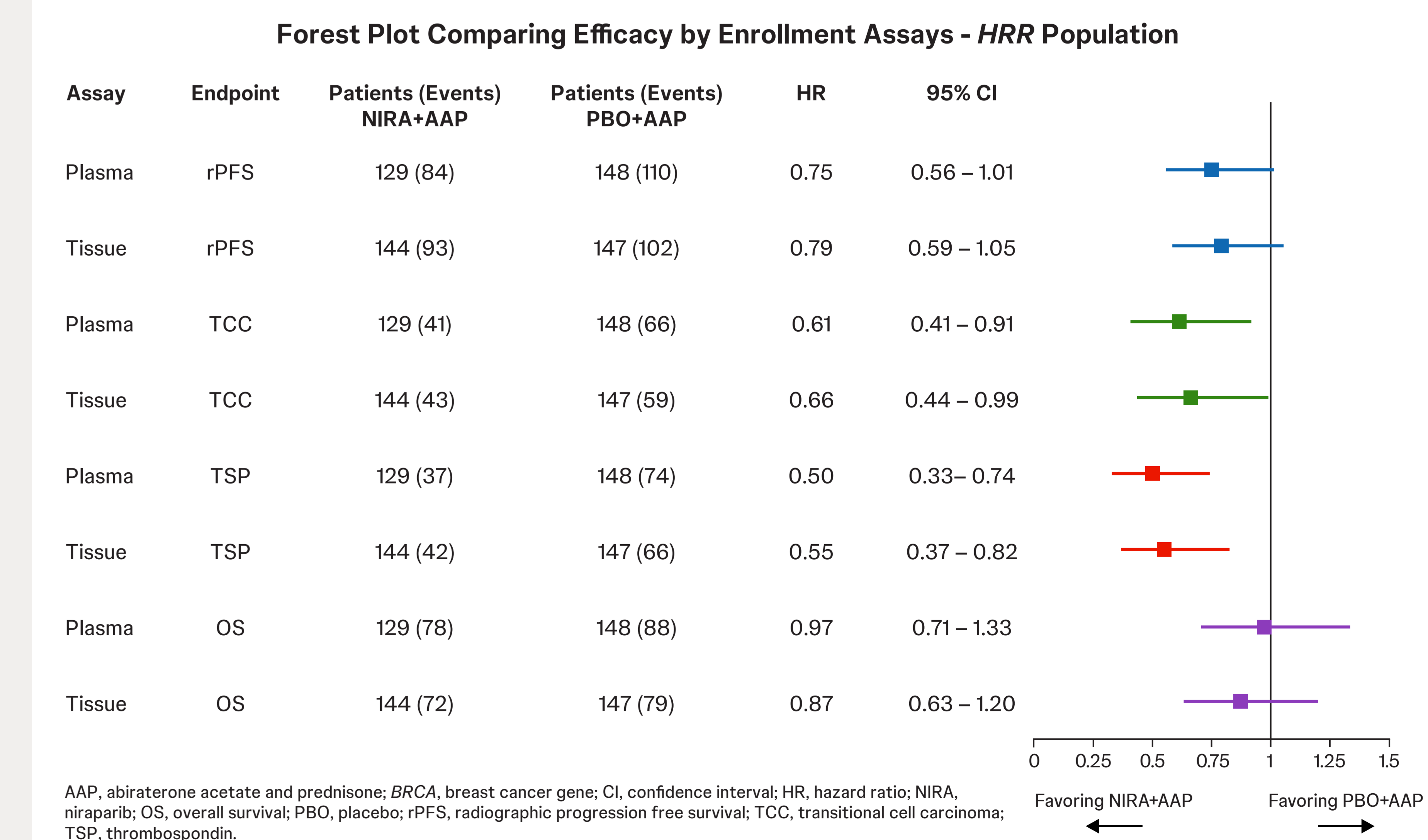
Figure 3: Efficacy by enrollment assays for *BRCA1/2+* status



AAP, abiraterone acetate and prednisone; *BRCA*, breast cancer gene; CI, confidence interval; HR, hazard ratio; NIRA, niraparib; OS, overall survival; PBO, placebo; rPFS, radiographic progression free survival; TCC, transitional cell carcinoma; TSP, thrombospondin.

- Efficacy based on rPFS in all *HRR+* patients with NIRA+AAP treatment versus PBO+AAP was comparable for the Resolution ctDx plasma assay and the F1CDx tissue assay
- Efficacy based on TCC, TSP, and OS in all *HRR+* patients with NIRA+AAP treatment versus PBO+AAP were comparable for the Resolution ctDx plasma assay and the F1CDx tissue assay (Figure 4)

Figure 4: Efficacy by enrollment assays for *HRR+* status



AAP, abiraterone acetate and prednisone; *BRCA*, breast cancer gene; CI, confidence interval; HR, hazard ratio; NIRA, niraparib; OS, overall survival; PBO, placebo; rPFS, radiographic progression free survival; TCC, transitional cell carcinoma; TSP, thrombospondin.

## References

- Castro E, et al. *J Clin Oncol*. 2019;20:37:490–503.
- Jayaram A, et al. *Ann Oncol*. 2021;32:726–735.
- Mateo J, et al. *Lancet Oncol*. 2020;21:162–174.
- De Bono J, et al. *Lancet Oncol*. 2021;22:1250–1264.
- Chi K, et al. *J Clin Oncol*. 2023;41:3339–3351.

Prostate Cancer

