



Investor science conference  
call: American Society of  
Clinical Oncology  
Genitourinary (ASCO GU)  
Cancers Symposium 2022

Conference call for investors and analysts

23 February 2022



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# Speakers



## **Dr Fred Saad**

Principal Investigator PROpel,  
Professor and Chief of Urology,  
University of Montreal Hospital  
Centre, Canada



## **Dave Fredrickson**

Executive Vice President,  
Oncology Business Unit



## **Andy Barnett**

Global Franchise Head, GU and  
GYN Cancers, DDR and  
Established Oncology (for Q&A)



## **Susan Galbraith**

Executive Vice President,  
Oncology R&D



## **Sunil Verma**

Senior Vice President,  
Global Head of Oncology,  
Medical (for Q&A)



# Agenda

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Closing and Q&A



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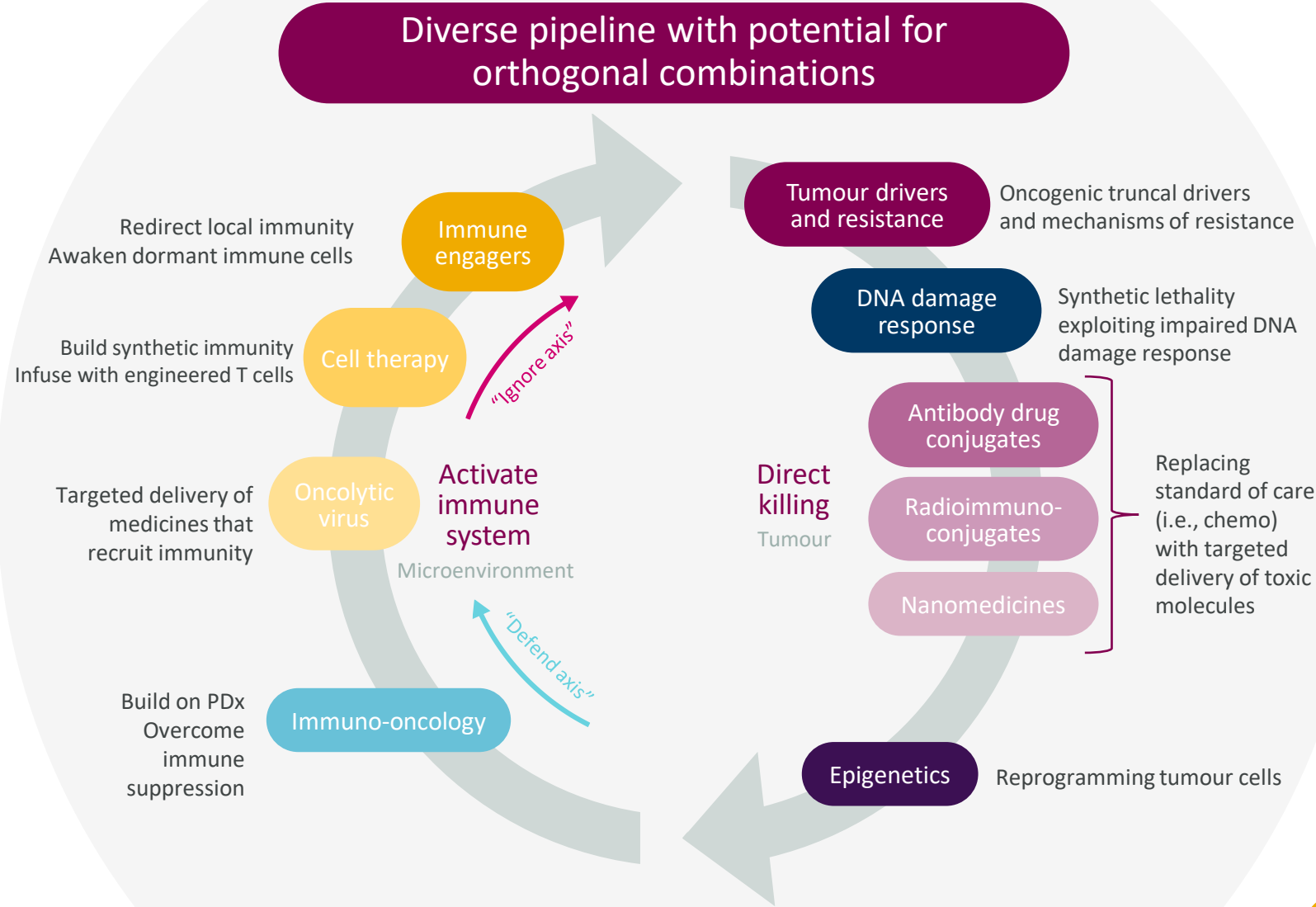
# Introduction

Susan Galbraith

Executive Vice President,  
Oncology R&D



# Comprehensive portfolio to combat cancer



Source: AstraZeneca.



# ASCO GU 2022

ASCO® Genitourinary  
Cancers Symposium

## 19 abstracts with three oral presentations

- **Two** Oral presentations
- **One** Mini-oral presentation
- **16** Posters
- **19** Abstracts accepted

## Data highlights

- ***Lynparza* + abiraterone  
in 1st-line mCRPC**  
PROpel Phase III trial
- ***Lynparza* + *Imfinzi*  
in 1st-line urothelial carcinoma**  
BAYOU Phase II trial
- ***Enhertu* + nivolumab  
in HER2+ urothelial carcinoma**  
U105 Phase Ib trial

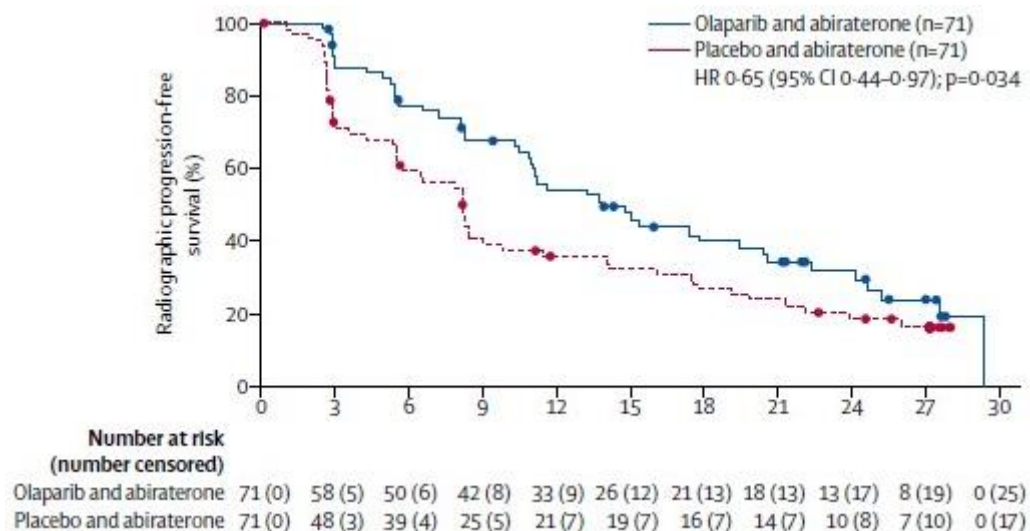


# Lynparza and abiraterone

Success in Study 08 paved the way for PROpel in 1st-line mCRPC

## Study 08<sup>1</sup>

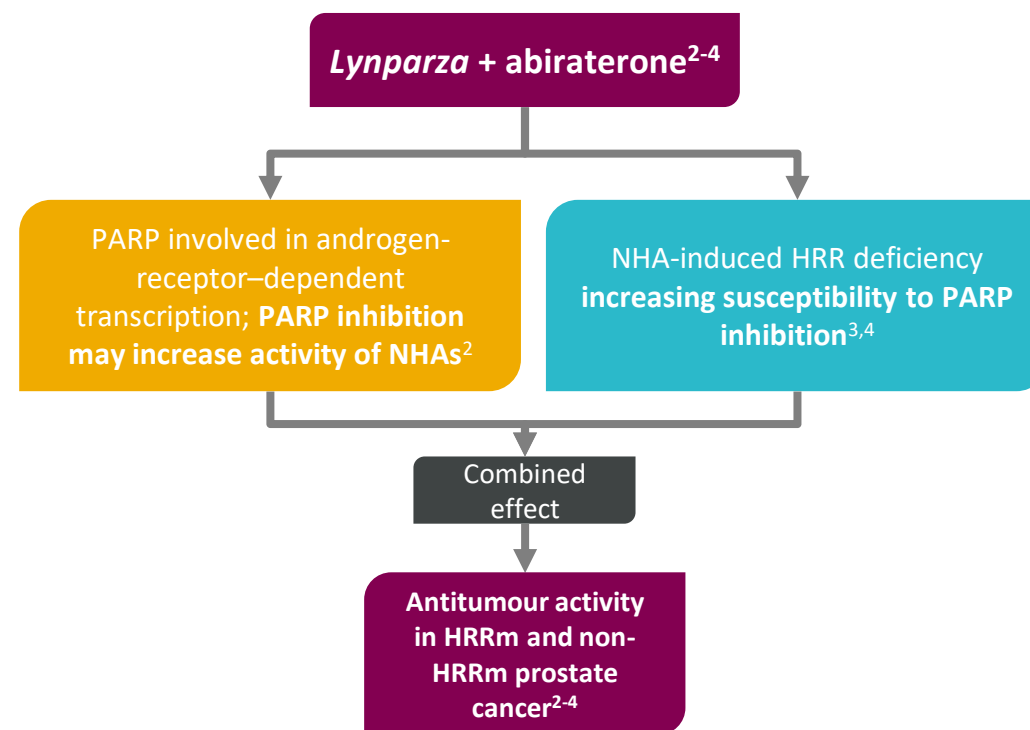
Phase II trial



**35% risk reduction**  
**Significant rPFS benefit regardless of HRRm status**

## PARP-signaling and AR-signaling pathway interaction

may explain combined effect





2

# *Lynparza* PROpel

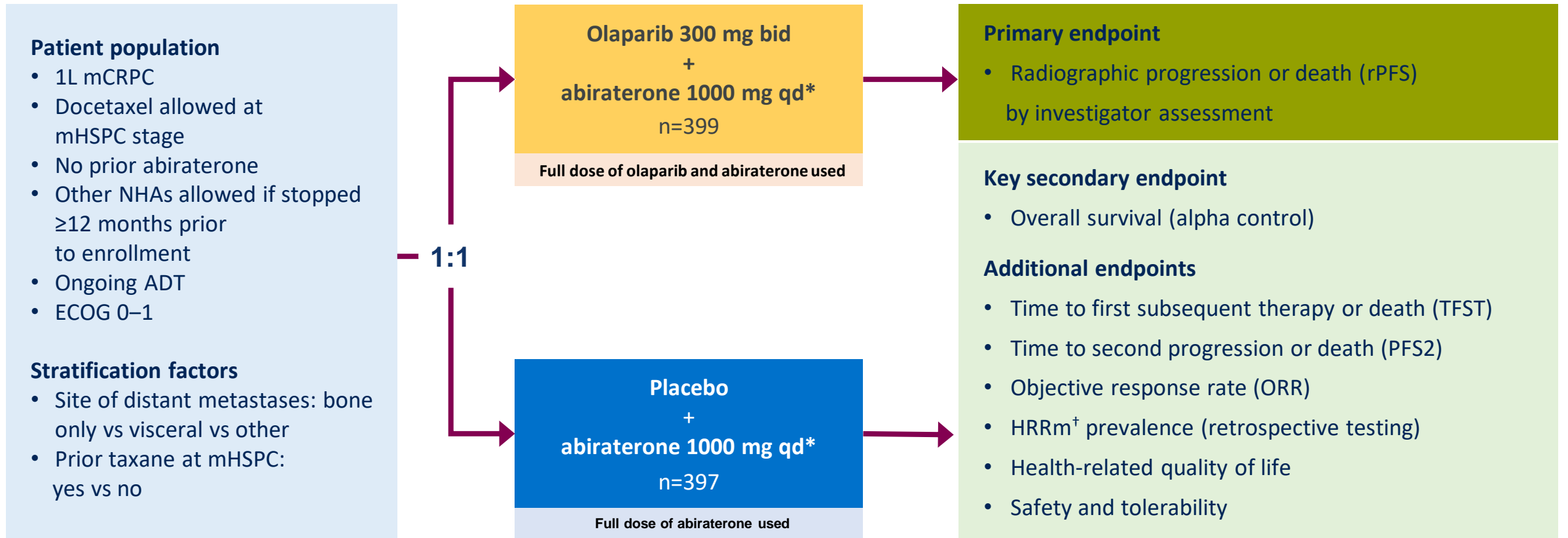
Dr Fred Saad

Principal Investigator,  
PROpel Phase III trial



# PROpel

## A global randomised double-blind Phase III trial



First patient randomized: Nov 2018; Last patient randomized: Mar 2020; DCO1: July 30, 2021, for interim analysis of rPFS and OS.

Multiple testing procedure is used in this study: 1-sided alpha of 0.025 fully allocated to rPFS. If the rPFS result is statistically significant, OS to be tested in a hierarchical fashion with alpha passed on to OS.

†Please access the Supplement at <https://bit.ly/3r50msO> for more details.

10 \*In combination with prednisone or prednisolone 5 mg bid. †HRRm, homologous recombination repair mutation, including 14 genes panel.

ADT = androgen deprivation therapy; bid = twice daily; ECOG = Eastern Cooperative Oncology Group; mHSPC = metastatic hormone sensitive prostate cancer.



# Baseline patient characteristics

Well-balanced between treatment arms

	Olaparib + abiraterone (n=399)	Placebo + abiraterone (n=397)
Median (range) age, years	69.0 (43–91)	70.0 (46–88)
ECOG performance status, n (%)		
0	286 (71.7)	272 (68.5)
1	112 (28.1)	124 (31.2)
Symptomatic,* n (%)	103 (25.8)	80 (20.2)
Site of metastases, n (%)		
Bone	349 (87.5)	339 (85.4)
Distant lymph nodes	133 (33.3)	119 (30.0)
Locoregional lymph nodes	82 (20.6)	89 (22.4)
Lung	40 (10.0)	42 (10.6)
Liver	15 (3.8)	18 (4.5)
Docetaxel treatment at mHSPC stage, n (%)	90 (22.6)	89 (22.4)
Median PSA, ug/L (IQR)	17.90 (6.09–67.00)	16.81 (6.26–53.30)
HRRm status <sup>†</sup>		
HRRm	111 (27.8)	115 (29.0)
Non-HRRm	279 (69.9)	273 (68.8)
HRRm unknown	9 (2.3)	9 (2.3)

\*Patients with symptomatic pain at baseline: BPI-SF item #3 score  $\geq 4$  and/or opiate use at baseline.

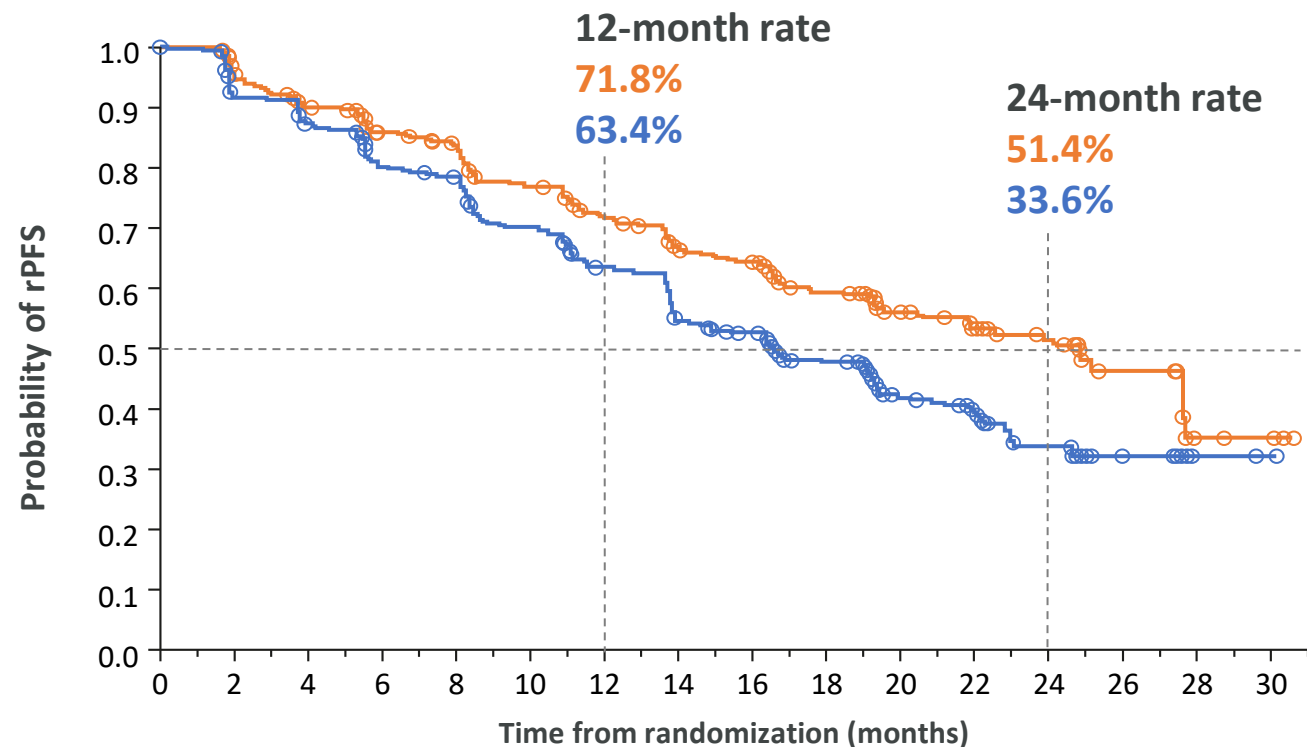
<sup>†</sup>The HRRm status of patients in PROpel was determined retrospectively using results from tumor tissue and plasma ctDNA HRRm tests. Patients were classified as HRRm if (one or more) HRR gene mutation was detected by either test; patients were classified as non-HRRm if no HRR gene mutation was detected by either test; patients were classified as unknown HRRm if no valid HRR test result from either test was achieved. Please access the Supplement via the QR code at the end of this presentation for more details.

BPI-SF = Brief Pain Inventory – Short Form; ctDNA = circulating tumor DNA; IQR = interquartile range; PSA = prostate-specific antigen.



# Primary endpoint: rPFS by investigator-assessment

34% risk reduction of progression or death with olaparib + abiraterone



No. at risk	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30																
Olaparib + abiraterone	399	395	367	354	340	337	313	309	301	277	274	265	251	244	277	221	219	170	167	163	104	100	87	59	57	28	26	25	5	4	4	0
Placebo + abiraterone	397	393	359	356	338	334	306	303	297	266	264	249	232	228	198	190	186	143	141	137	87	84	73	45	43	21	17	16	2	2	1	0

	Olaparib + abiraterone (n=399)	Placebo + abiraterone (n=397)
Events, n (%)	168 (42.1)	226 (56.9)
Median rPFS (months)	24.8	16.6
HR (95% CI)	0.66 (0.54–0.81); P<0.0001	

Pre-specified 2-sided alpha: 0.0324

**Median rPFS improvement of 8.2 months favors olaparib + abiraterone\***

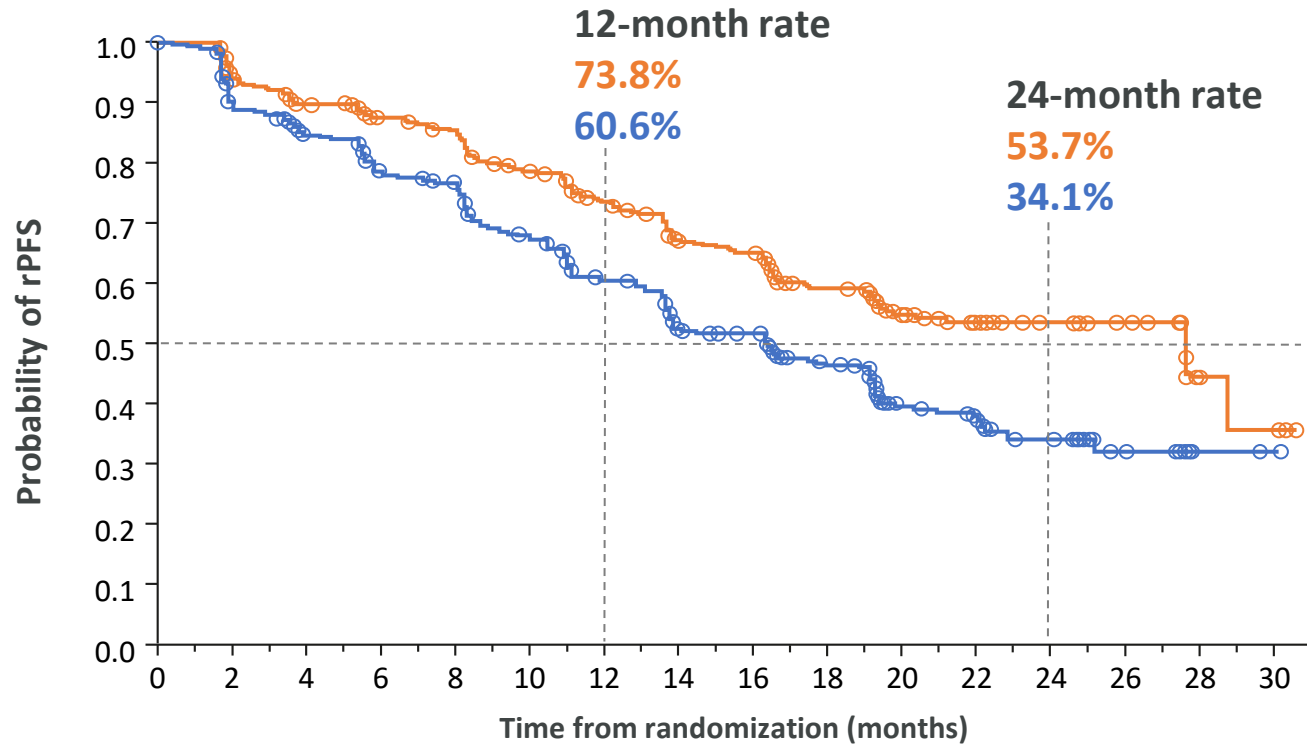
Events: 394; Maturity 49.5%

12 \*In combination with prednisone or prednisolone  
 CI = confidence interval; HR = hazard ratio.



# Secondary endpoint: rPFS by blinded independent central review\*

39% risk reduction of progression or death, highly consistent with the primary analysis



	Olaparib + abiraterone (n=399)	Placebo + abiraterone (n=397)
Events, n (%)	157 (39.3)	218 (54.9)
Median rPFS (months)	27.6	16.4
HR (95% CI)	0.61 (0.49–0.74) P<0.0001 <sup>†</sup>	

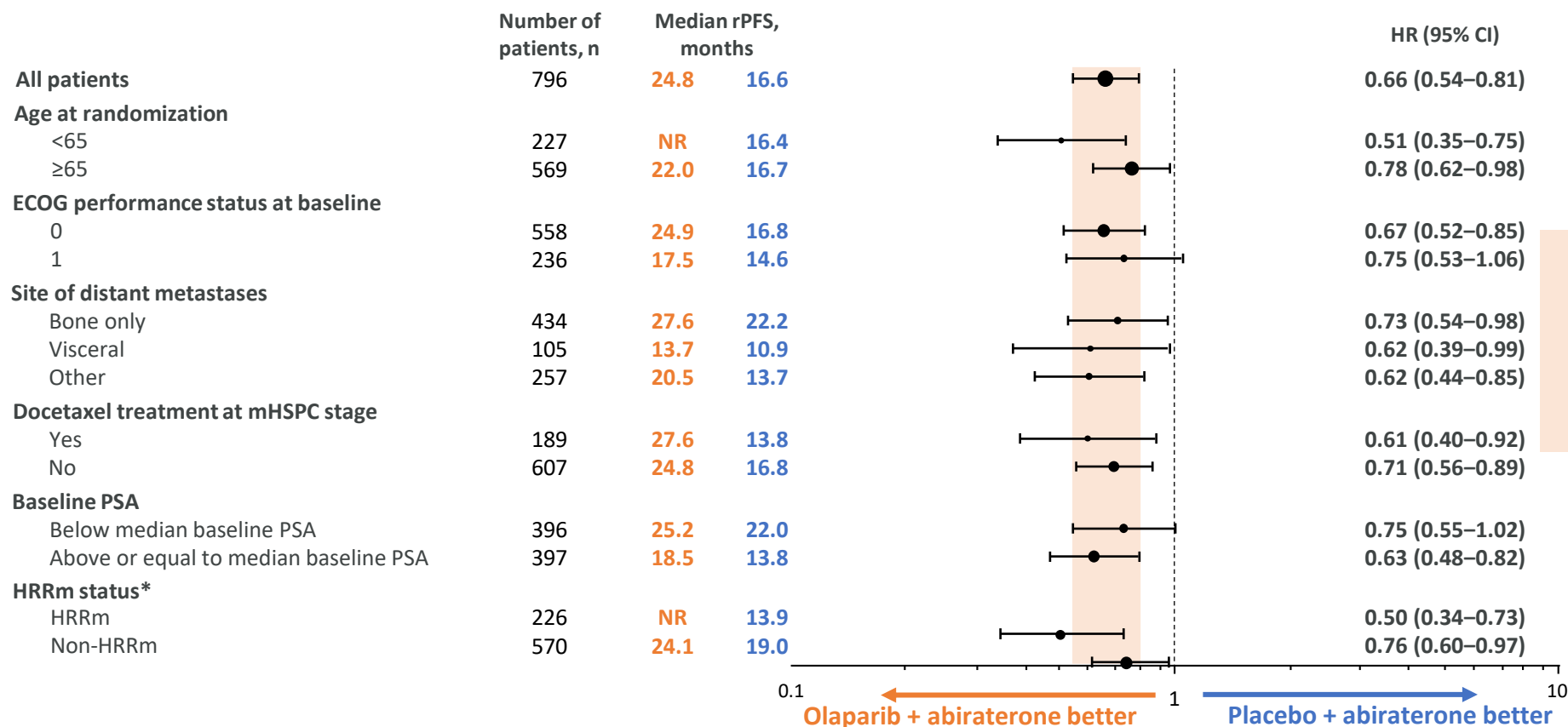
Median rPFS improvement of 11.2 months favors olaparib + abiraterone<sup>‡</sup>

No. at risk	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30																
Olaparib + abiraterone	399	389	353	347	332	331	314	309	303	283	275	267	249	240	221	217	215	165	161	159	96	89	80	55	53	30	28	26	5	4	4	0
Placebo + abiraterone	397	388	345	340	322	319	294	289	282	251	245	226	209	204	177	172	168	131	126	124	73	70	62	39	38	21	16	15	2	2	1	0



# Subgroup analysis of rPFS

rPFS benefit observed across all pre-specified subgroups



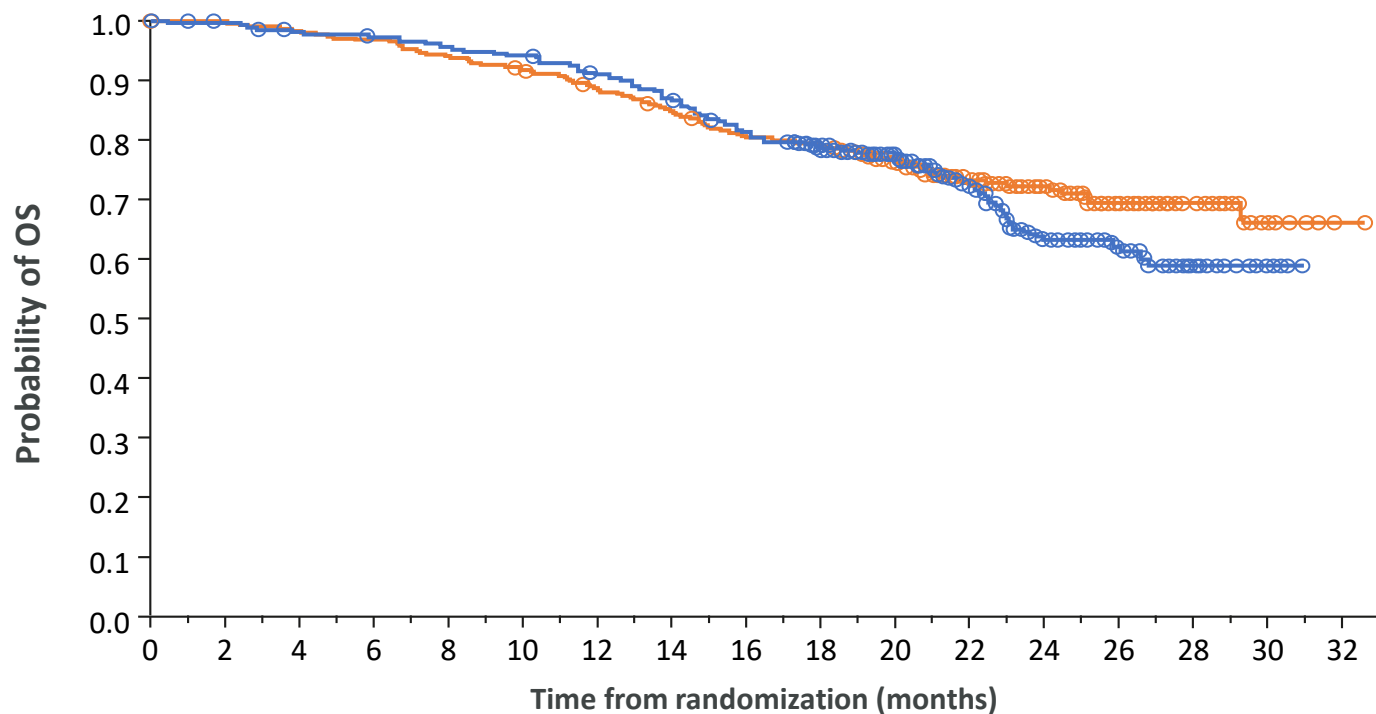
**Global interaction test not significant**

Global interaction test not significant at 10% level. \*The HRRm status of patients in PROpel was determined retrospectively using results from tumor tissue and plasma ctDNA HRRm tests. Patients were classified as HRRm if (one or more) HRR gene mutation was detected by either test; patients were classified as non-HRRm patients if no HRR gene mutation was detected by either test; patients were classified as unknown HRRm if no valid HRR test result from either test was achieved. 18 patients did not have a valid HRR testing result from either a tumor tissue or ctDNA test and were excluded from the subgroup analysis. This subgroup analysis is post hoc exploratory analysis. Please access the Supplement via the QR code at the end of this presentation for more details. NR = not reached.



# Secondary endpoint: overall survival

28.6% maturity; trend towards improved OS with olaparib + abiraterone



No. at risk	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32																	
Olaparib + abiraterone	399	398	398	394	391	387	385	379	374	369	364	359	349	343	333	322	316	313	290	263	231	193	159	135	116	92	73	51	37	24	11	4	1	0
Placebo + abiraterone	397	394	392	386	385	383	381	377	374	371	368	363	353	345	335	322	314	308	286	258	223	186	151	121	104	88	63	44	22	13	6	0	0	0

	Olaparib + abiraterone (n=399)	Placebo + abiraterone (n=397)
Events, n (%)	107 (26.8)	121 (30.5)
Median OS (months)	NR	NR
HR (95% CI)	0.86 (0.66–1.12) P=0.29	

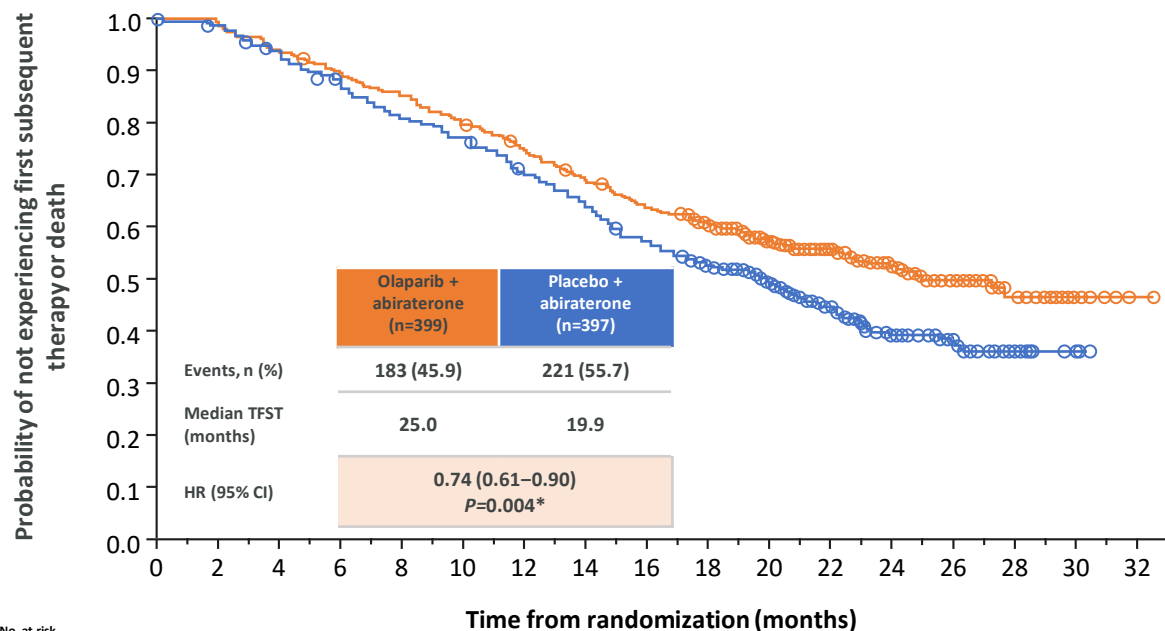
Pre-specified 2-sided alpha: 0.001



# Secondary endpoints: TFST and PFS2

TFST and PFS2 results support longer-term benefit with olaparib + abiraterone

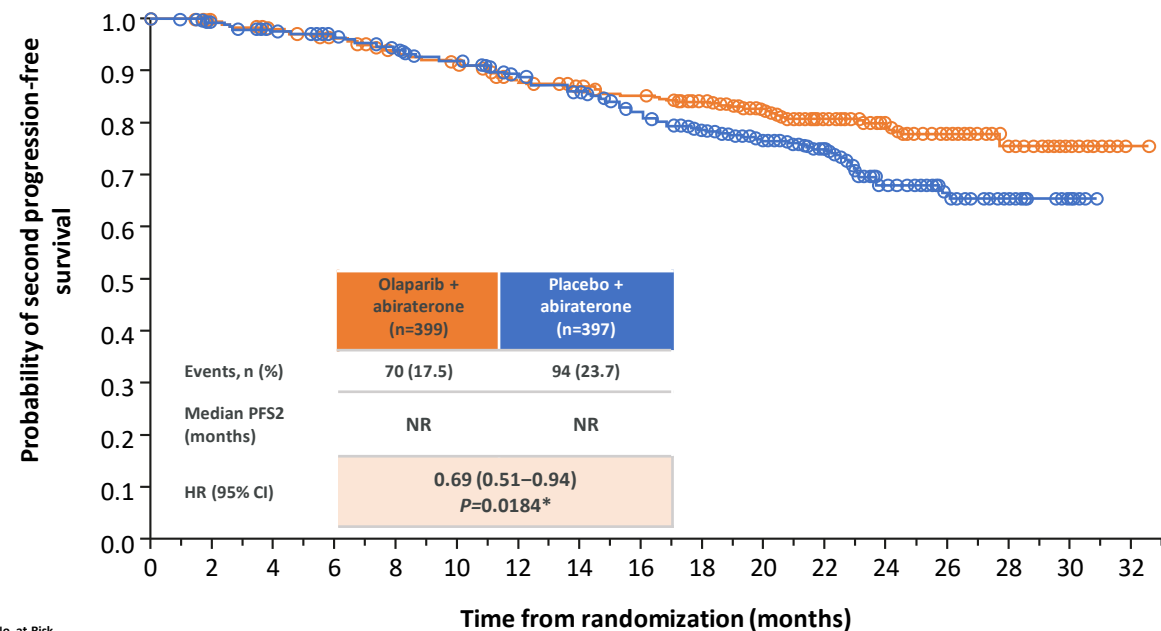
### Time to first subsequent therapy or death (TFST)



No. at risk

	399	398	396	385	374	365	358	345	338	328	317	308	295	285	272	260	250	245	222	202	174	148	124	104	87	67	53	41	28	19	8	3	1	0
Olaparib + abiraterone	399	398	396	385	374	365	358	345	338	328	317	308	295	285	272	260	250	245	222	202	174	148	124	104	87	67	53	41	28	19	8	3	1	0
Placebo + abiraterone	397	394	390	377	368	354	345	329	319	313	303	292	273	261	250	231	222	214	191	174	147	121	98	76	63	53	38	25	12	6	4	0	0	0

### Time to second progression or death (PFS2)



No. at Risk

	399	396	387	383	372	366	353	347	338	326	318	311	300	297	291	284	282	279	261	237	209	177	148	126	106	85	68	49	34	22	10	4	1	0
Olaparib + abiraterone	399	396	387	383	372	366	353	347	338	326	318	311	300	297	291	284	282	279	261	237	209	177	148	126	106	85	68	49	34	22	10	4	1	0
Placebo + abiraterone	397	394	381	374	367	363	351	346	339	322	320	312	300	294	286	276	269	259	239	212	179	152	124	99	85	71	50	36	18	11	5	0	0	0





# Overall safety profile

A relatively small increase in discontinuations for olaparib vs placebo, discontinuation with abiraterone was similar between treatment arms

n (%)	Olaparib + abiraterone (n=399)	Placebo + abiraterone (n=397)
Any AE	387 (97.2)	376 (94.9)
Any AE CTCAE Grade $\geq$ 3	188 (47.2)	152 (38.4)
<b>Death due to an AE</b>	<b>16 (4.0)</b>	<b>17 (4.3)</b>
Any AE leading to:		
Dose interruption of <b>olaparib/placebo</b>	178 (44.7)	100 (25.3)
Dose reduction of <b>olaparib/placebo</b>	80 (20.1)	22 (5.6)
<b>Discontinuation of olaparib/placebo</b>	<b>55 (13.8)</b>	<b>31 (7.8)</b>
<b>Discontinuation of abiraterone</b>	<b>34 (8.5)</b>	<b>35 (8.8)</b>

## AEs of special interest for olaparib

- No MDS/AML reported
- Incidence of new primary malignancies and pneumonitis were balanced between treatment arms



# Cardiac and thromboembolic adverse events

Cardiac failure and arterial thromboembolic events were balanced between the two arms

Numerically higher venous thromboembolic events were reported for olaparib + abiraterone

Pulmonary embolism was the most commonly reported venous thromboembolic event

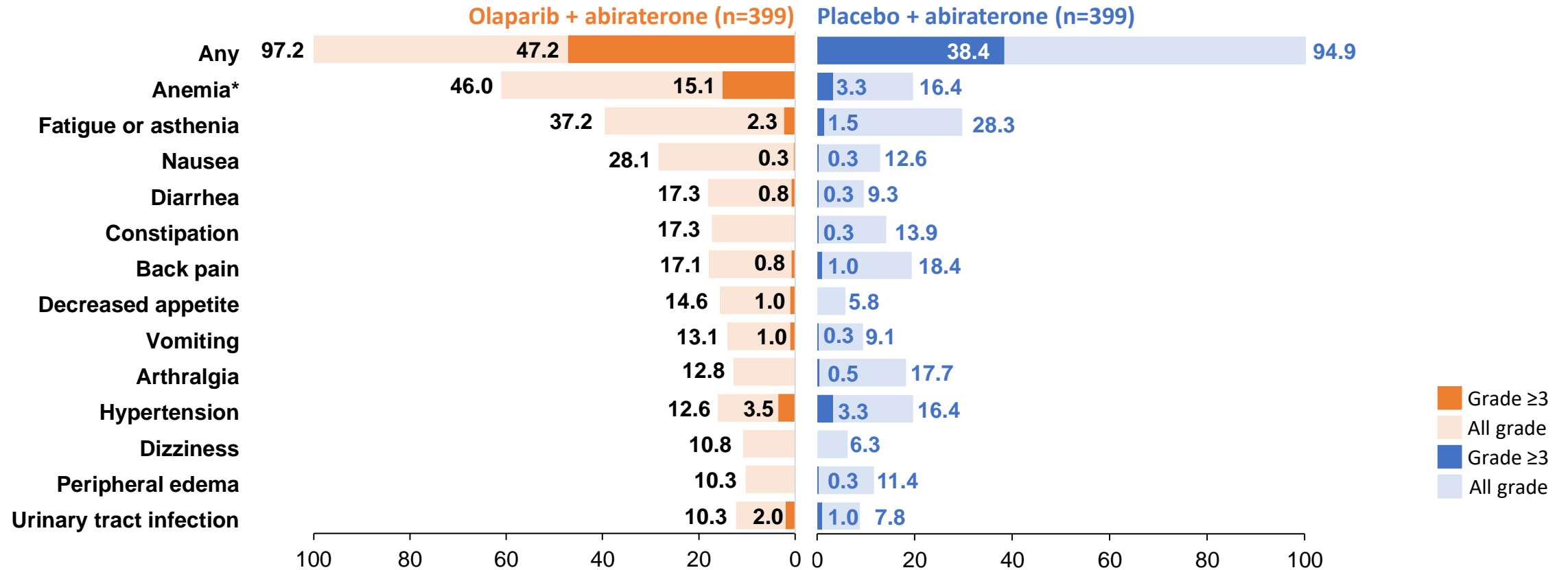
Pulmonary embolism events were mostly incidental findings by CT scans and did not lead to discontinuation of olaparib or abiraterone

n (%)	Olaparib + abiraterone (n=399)	Placebo + abiraterone (n=397)
Cardiac failure SMQ	6 (1.5)	5 (1.3)
Embolic and thrombotic events, arterial SMQ	8 (2.0)	10 (2.5)
Embolic and thrombotic events, venous SMQ	29 (7.3)	13 (3.3)
Pulmonary embolism	26 (6.5)	7 (1.8)



# Most common adverse events

AE profile was consistent with the known toxicity profiles for the individual drugs



Safety was assessed through the reporting of AEs according to the National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE v4.03) and laboratory assessments.

19 \*Anemia category includes anemia, decreased hemoglobin level, decreased red-cell count, decreased hematocrit level, erythropenia, macrocytic anemia, normochromic anemia, normochromic normocytic anemia, and normocytic anemia.



# Conclusions

**Olaparib + abiraterone** led to a **significant and clinically meaningful improvement in rPFS (HR 0.66 [95% CI 0.54–0.81])** over placebo + abiraterone in 1L mCRPC

Benefit observed led to a **median rPFS beyond 2 years**

Benefit was observed **irrespective of HRRm status**

**Secondary and exploratory endpoints support the treatment benefit** of olaparib + abiraterone over placebo + abiraterone in the overall patient population

The safety profile of olaparib + abiraterone was **consistent with the safety profile for the individual drugs** and there was **no detriment to quality of life** allowing most patients to stay on therapy

The Phase III PROpel study is the first combination approach to deliver consistent **clinical benefits for patients in the 1L mCRPC setting, irrespective of HRRm status**



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## Opportunity and unmet need in mCRPC

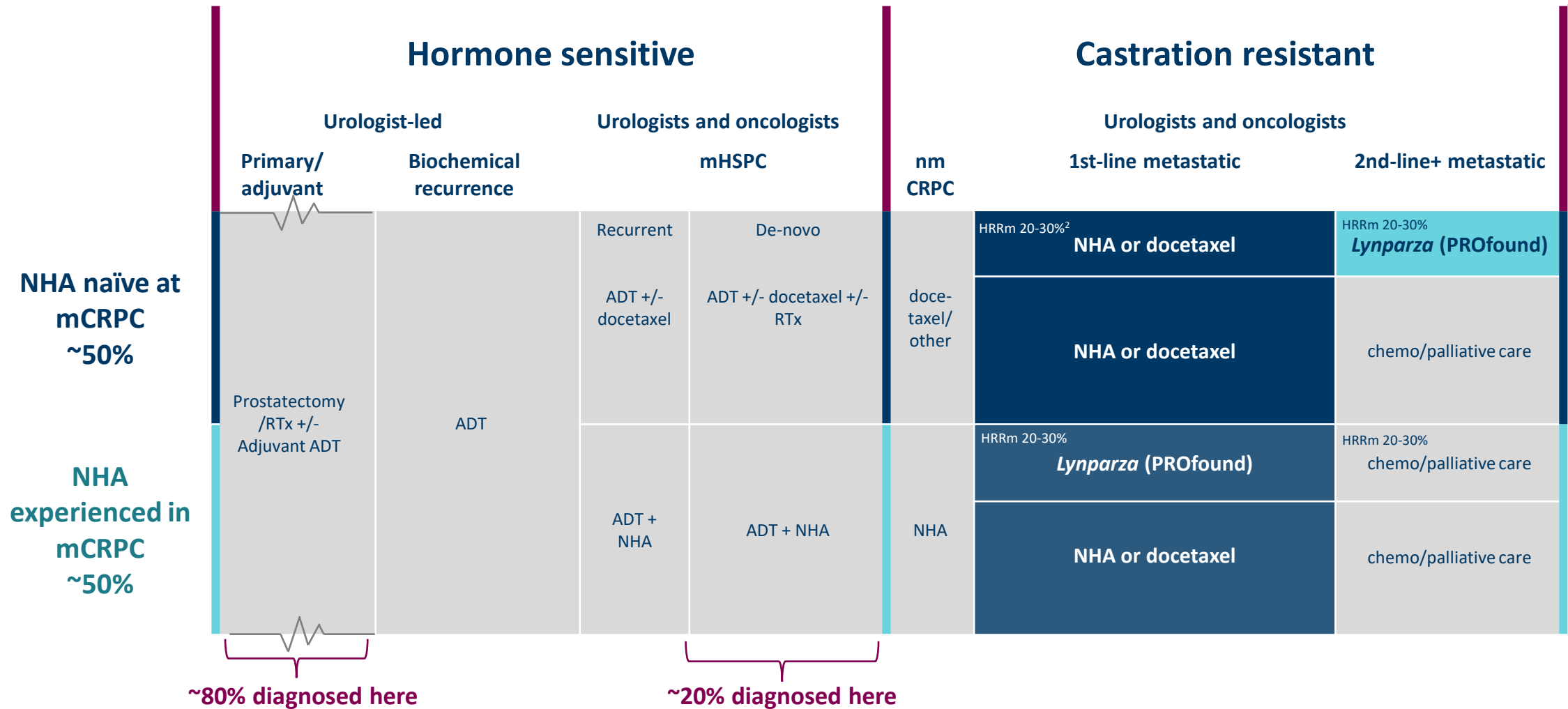
Dave Fredrickson

Executive Vice President,  
Oncology Business Unit



# Prostate is the second most common cancer in male patients

mCRPC therapies are limited; mostly monotherapy, including in first line



# PROpel - unprecedented clinical benefit without compromising quality of life - a potential new SoC in mCRPC

## Outcomes remain poor

in advanced prostate cancer

**40%**

of patients with prostate cancer will develop metastatic disease<sup>1-3</sup>

**30%**

the 5-year survival rate for patients with metastatic disease<sup>4</sup>

**3 years**

median OS for mCRPC patients in the first-line setting<sup>5-9</sup>

**50%**

of patients receive only one line of active therapy in mCRPC<sup>10</sup>

## PROpel

building on the success of PROfound

- Representative **real-world** population - **simple** trial design
- **All-comers** ITT population
- Retrospective **HRR testing** via tissue and ctDNA testing<sup>11</sup>
- Primary endpoint: **radiographic progression free survival**
- Key secondary endpoints: **Overall survival, time to first subsequent therapy, time to second progression or death**

300 mg **Lynparza**<sup>™</sup> + abiraterone  
olaparib 

a potential new standard of care

- **Clinically meaningful and consistent efficacy** across subgroups
- Despite OS immaturity, **strong secondary endpoint results** provide confidence
- **Class-leading tolerability** - full 300mg *Lynparza* dose in combination with abiraterone
- **Quality of life maintained**, allowing adoption of upfront combination therapy

**8.2-month median rPFS benefit over abiraterone alone**

1. Beltran H, Beer TM, Carducci MA, et al. *Eur Urol.* 2011;60(2):279-290. 2. Sciarra A, Salciccia S. *Eur Urol.* 2014;65(5):905-906. 3. Sartor O, de Bono JS. *N Engl J Med.* 2018;378(7):645-657. 4. Cancer of the Prostate - *Cancer Stat Facts.* SEER. Accessed November 6, 2019. 5. Kelly WK et al. *J Clin Oncol.* 2012;30:1534-40. 6. Quinn DI et al. *Lancet Oncol.* 2013;14:893-900. 7. Araujo JC et al. *Lancet Oncol.* 2013;14:1307-16. 8. Ryan CJ et al. *N Engl J Med.* 2013;368:138-48. 9. Beer TM et al. *N Engl J Med.* 2014;371:424-33. 10. Shore ND et al. *Adv Ther.* 2021;38:4520-40. 11. Tumour tissue and blood samples were collected at baseline for biomarker tests. HRRm status was determined using a tumour tissue test (FoundationOne<sup>®</sup>CDX) and/or a circulating tumour (ctDNA) based test (FoundationOne<sup>®</sup>Liquid CDx test).

OS = overall survival; ITT = intent-to-treat.





After almost a decade, the addition of *Lynparza* achieves a similar absolute rPFS improvement compared to the pivotal trial that established abiraterone as first-line SoC

	COU-AA-302 <sup>1</sup> (2012)			PROpel (2022)		
	control	abiraterone	Dif.	abi	<i>Lynparza</i> + abiraterone	Dif.
<b>Median rPFS</b>	8.2m	16.4m	<b>8.2m</b>	16.6m	24.8m	<b>8.2m</b>

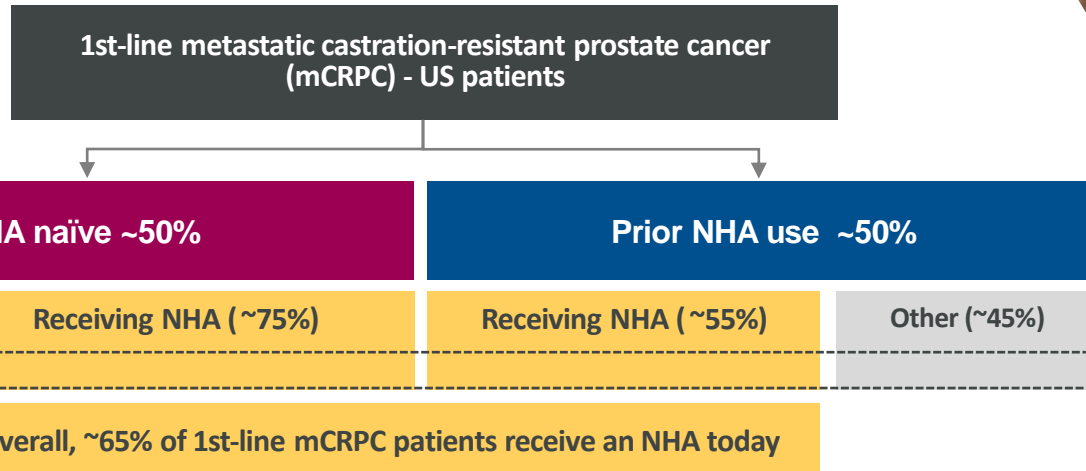
PROpel median rPFS	abiraterone	<i>Lynparza</i> + abiraterone	HR
Investigator assessment	16.6m	24.8m	0.66 (0.54-0.81)
HRRm	13.9m	NR	0.50 (0.34-0.73)
Non-HRRm	19.0m	24.1m	0.76 (0.60-0.97)
<b>BICR</b>	16.4m	27.6m	0.61 (0.49-0.74)

1. Mulders et al. *N Engl J Med* 2013; 368:138-148. Dif. = difference; NR = not reached; HR = hazard ratio.





# PROpel: a new treatment approach in 1st-line mCRPC



## Lynparza + abiraterone (PROpel)<sup>1</sup>

*Lynparza* and abiraterone demonstrates a **clear clinical benefit** vs. abiraterone alone in first line patients who are NHA naïve

For NHA experienced patients, *Lynparza* and abiraterone offers a **well tolerated, chemo-free treatment option**

A clear option for NHA-naïve patients regardless of HRRm status

The first combination trial to demonstrate consistent clinical benefit in 1st-line mCRPC



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## Other ASCO GU highlights

Susan Galbraith

Executive Vice President,  
Oncology R&D



# New advances in urothelial carcinoma

Phase II data advancing understanding of this aggressive cancer

## *Imfinzi + Lynparza: Phase II BAYOU trial*

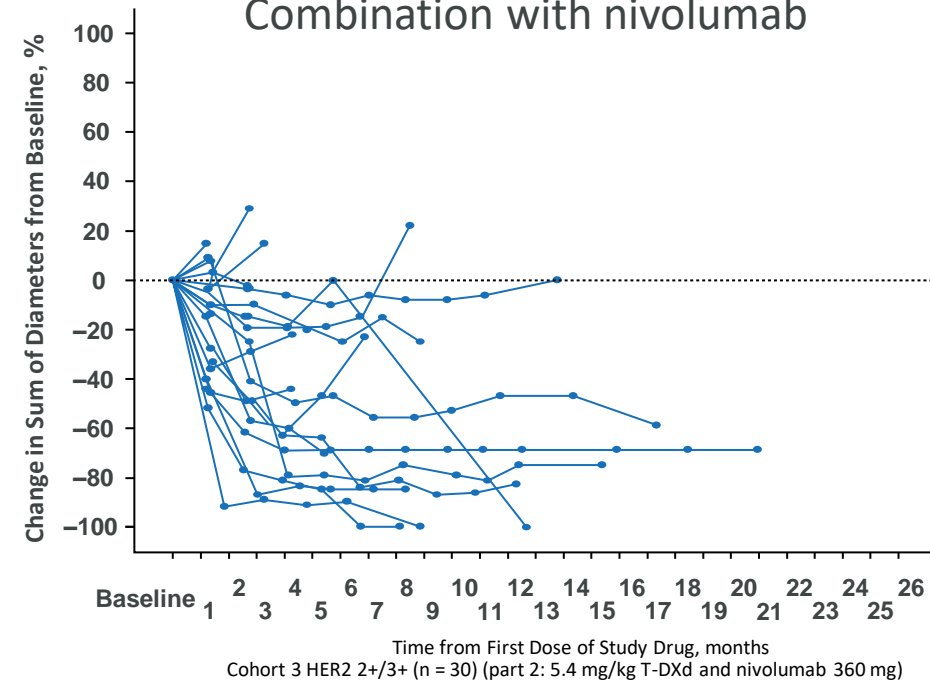
Platinum-ineligible patients with mUC

### Primary and secondary PFS analyses

	D+O	D+PBO
ITT population	n=78	n=76
Median PFS, mo (95% CI)	4.2 (3.6–5.6)	3.5 (1.9–5.1)
HR (95% CI)	0.94 (0.64–1.39)	
Log-rank p-value	0.789	
HRRm subset*	n=17	n=14
Median PFS, mo (95% CI)	5.6 (1.9–8.1)	1.8 (1.7–2.2)
HR (95% CI)	0.18 (0.06–0.47)	
Log-rank p-value	<0.001	

## *Enhertu: Phase II U105 trial*

Combination with nivolumab



Data suggests a role for PARP inhibition in HRRm UC

HER2+ UC included in DESTINY-PanTumor02



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Closing and Q&A



# Investor Relations



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# Appendix



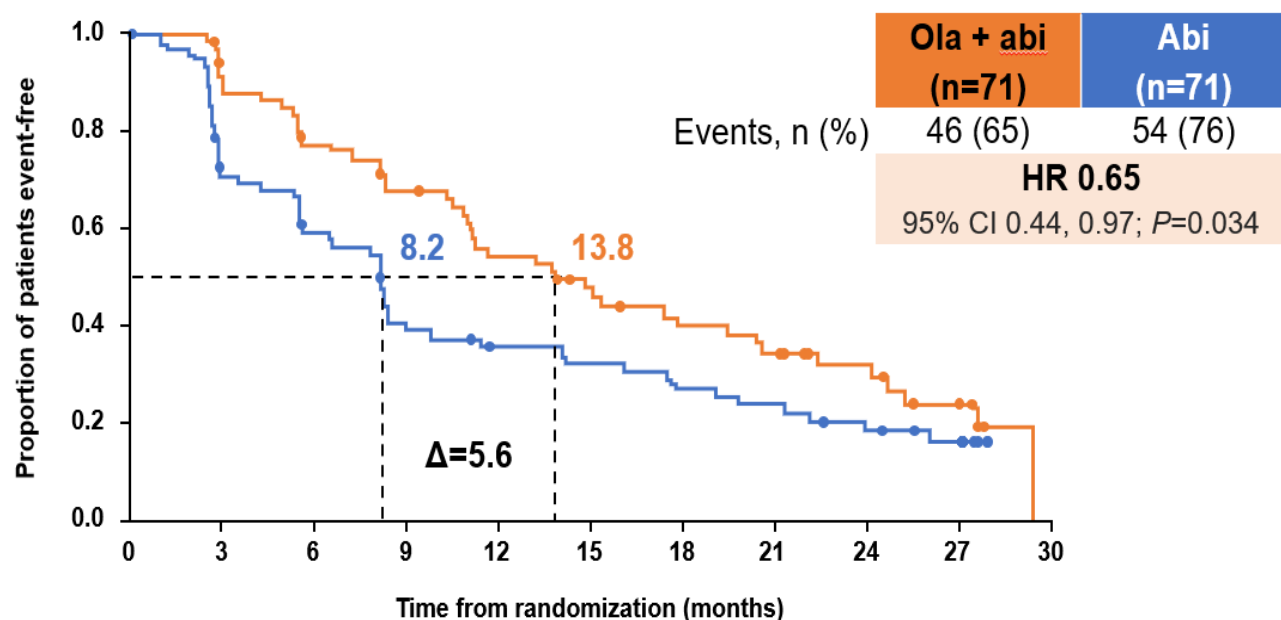
PROpel



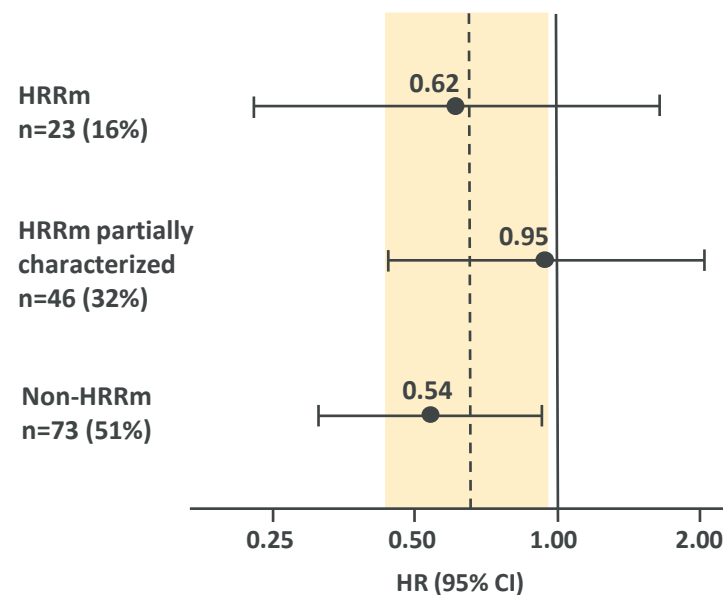
# Olaparib and abiraterone: A randomised Phase II trial

- Patients with mCRPC, unselected by HRRm status, with prior docetaxel treatment
- Randomized 1:1 to full dose of olaparib + abiraterone vs placebo + abiraterone
- Statistically significant improvement in rPFS with olaparib + abiraterone, irrespective of HRRm status<sup>1</sup>

Investigator-assessed rPFS<sup>1</sup>



rPFS by HRRm subgroup<sup>2\*</sup>



1. Clarke N et al. *Lancet Oncol* 2018;19:975–86. 2. Carr TH et al. *Cancers* 2021;13:5830

\*Dashed line and shaded area show HR and 95% CI, respectively, for the intent to treat population.

Please access the Supplement at <https://bit.ly/3r50msO> for more details including the full citations and further details on the HRRm partially characterised subgroup.



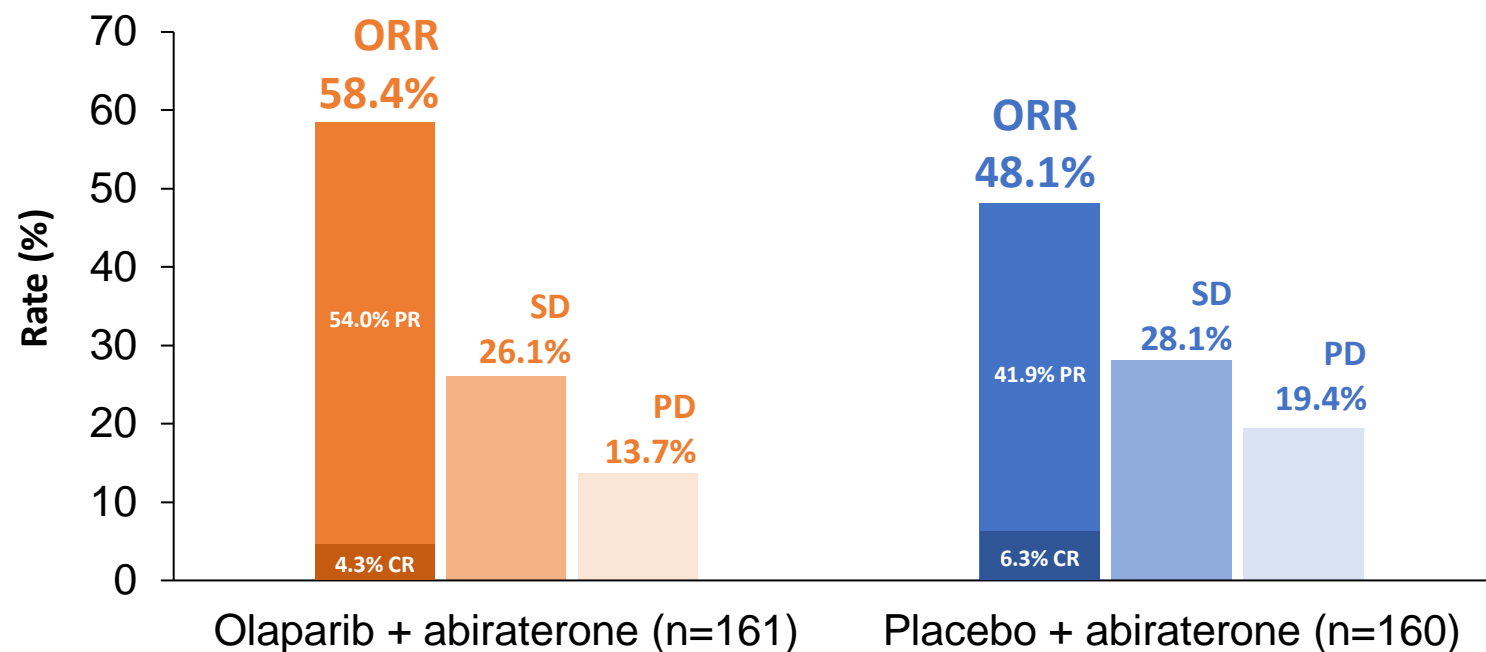


# ORR in patients with measurable disease

## 10% improvement in ORR with olaparib + abiraterone

OR 1.60 (95% CI 1.02–2.53)

*P*=0.0409\*

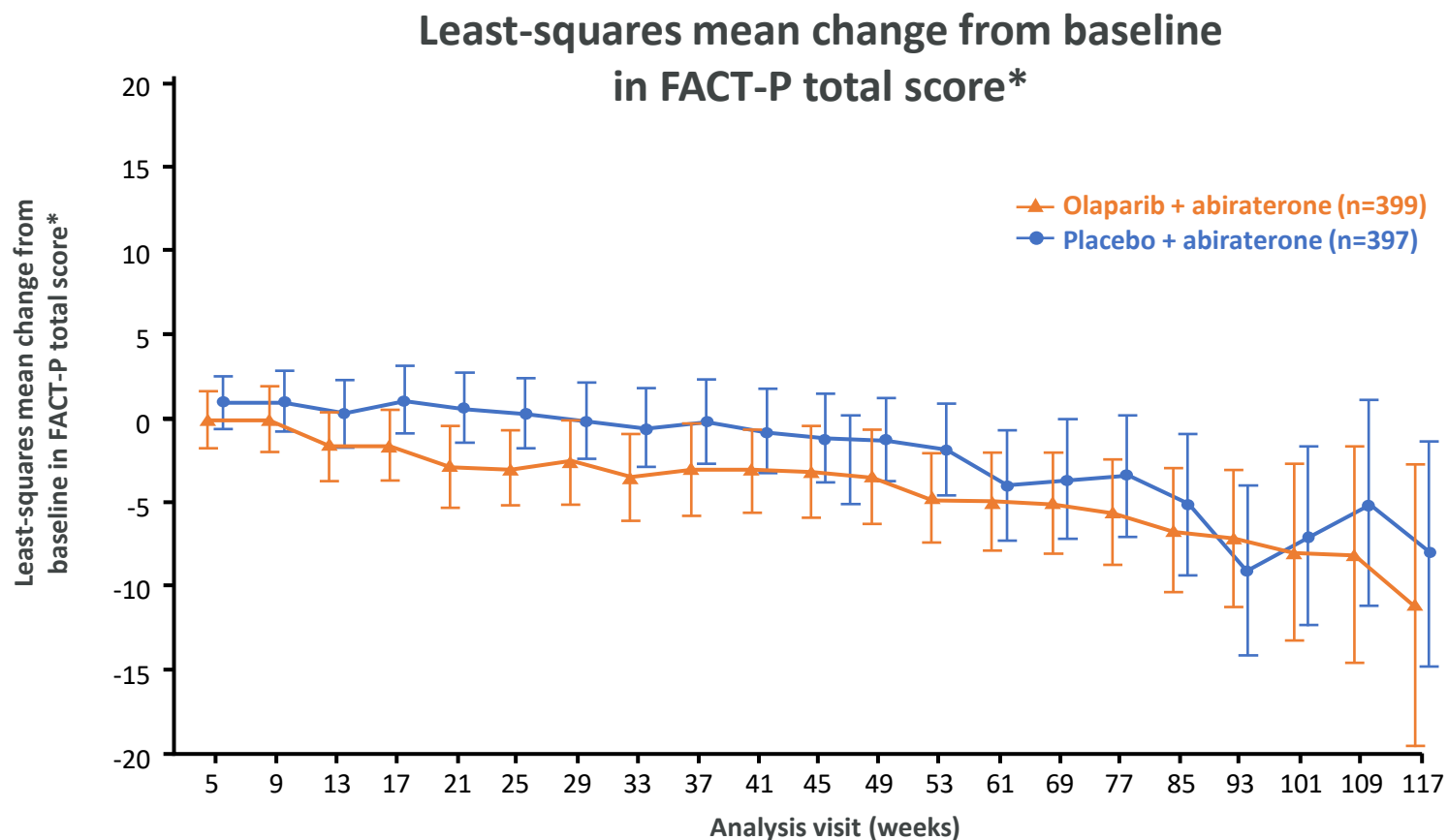


321/796 patients (40.3%)  
had measurable disease  
by RECIST v1.1 criteria  
at baseline



# FACT-P quality of life over time

Quality of life comparable between treatment arms



\*Plot includes 95% confidence limits. FACT-P total score change from baseline values can be a minimum of -156 and a maximum of 156. A clinically meaningful change in FACT-P total score is 1015,16



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