Weill Cornell Medicine
Englander Institute
for Precision Medicine

Weill Cornell Medicine
Meyer Cancer Center

Precision Medicine for Prostate Cancer

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Precision Medicine or Personalized Medicine

Increases survival rates

Targets tumors with greater accuracy

Mitigates unnecessary treatments

Identifies new treatment possibilities

Germline BRCA2 prostate cancer

Instead of using a one-size-fits-all approach
Aims to customize healthcare
Medical Decisions
Treatments
Products tailored to the individual patient

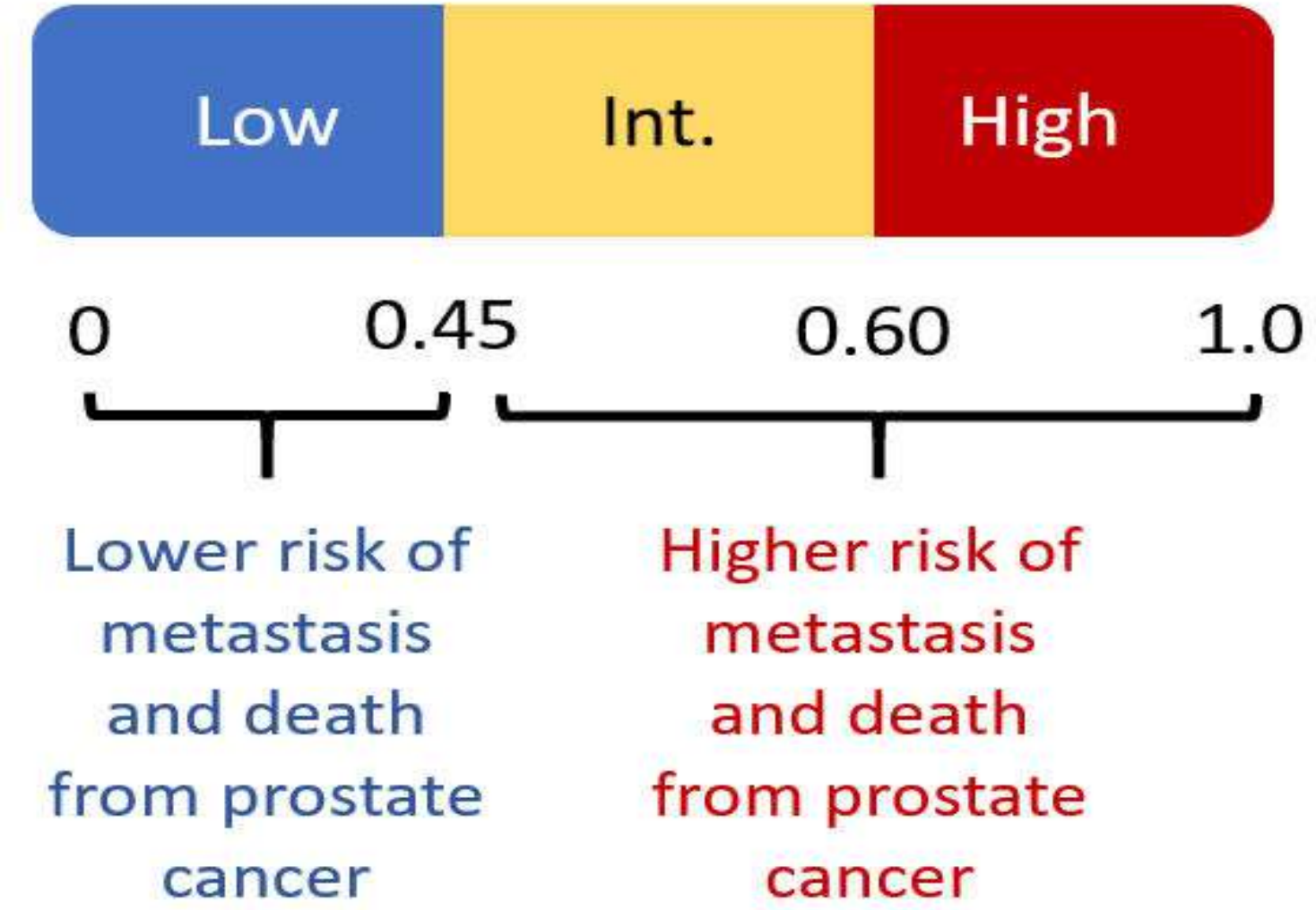
Precision Medicine in Prostate Cancer
Topics Today

- Risk Stratification
- Genetic Profiling of Prostate Cancer
- Targeted Therapies (PARPi)
- PSMA Theranostics

Genomic Decipher Scores

Evaluates the expression of 22 RNA biomarkers from multiple different biological pathways

<u>Goes beyond PSA and Gleason Score</u>



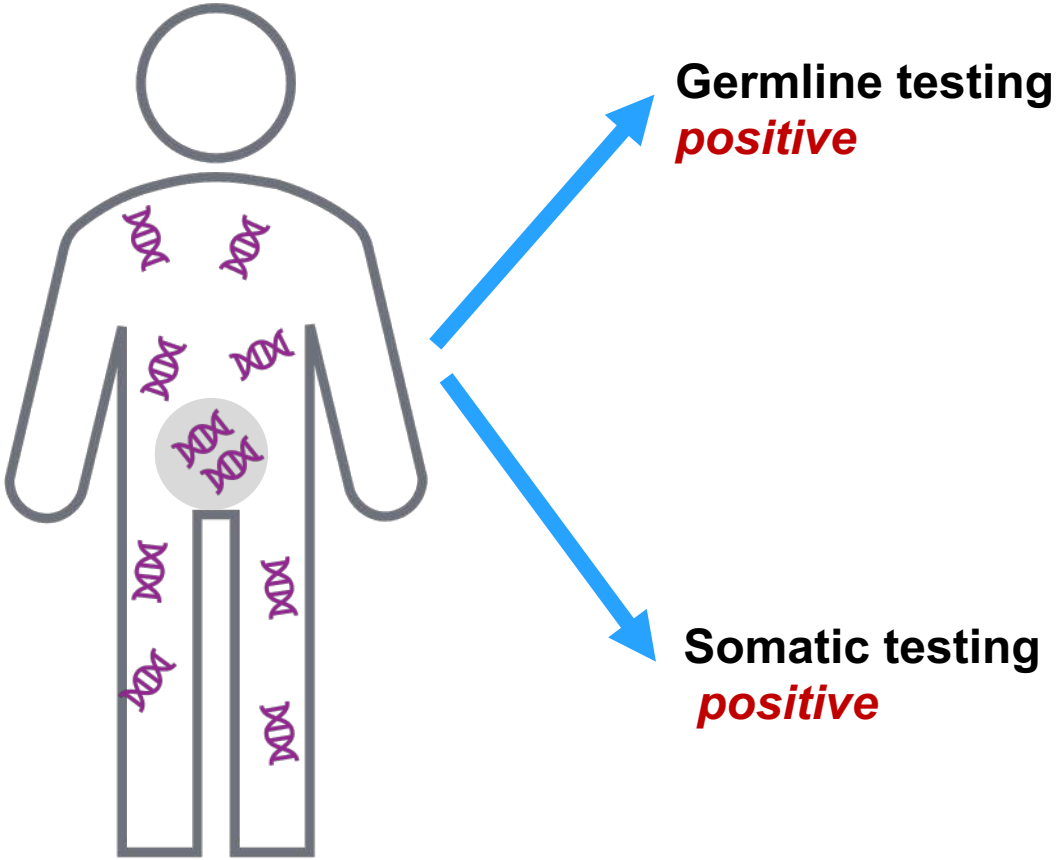
POST-BIOPSY		
Clinical Decision	**Decipher Risk**	**May Consider**
Active Surveillance Protocol	Low	Less Intense [1-6]
	High	More Intense [1-6]
Active Surveillance OR Definitive Therapy	Low	Active Surveillance [1-6]
	High	Definitive Therapy [1-6]
Radiation OR Radiation + ADT	Low	Radiation [1,4-7]
	High	Radiation + ADT [1,4-8]
Duration of Hormone Therapy with Radiation	Low	Radiation + Short-Term ADT [6-8]
	High	Radiation + Long-Term ADT [6-9]

POST-RADICAL PROSTATECTOMY		
Clinical Decision	**Decipher Risk**	**May Consider**
Monitoring Protocol	Low	Less Intense [10-12]
	High	More Intense [10-12]
PSA Monitoring OR Treatment	Low	PSA Monitoring [10-12]
	High	Treatment [10-12]
Radiation OR Radiation + ADT	Low	Radiation Alone [13-15]
	High	Radiation + ADT [13-15]

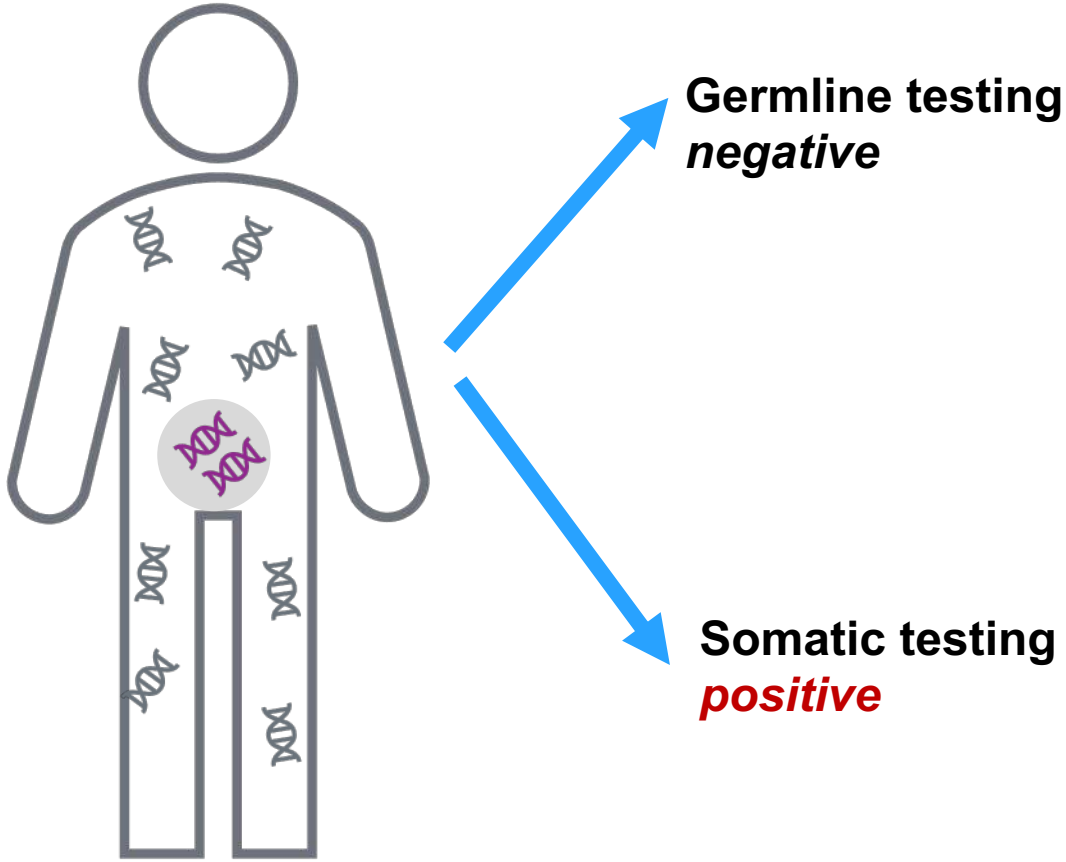
Marrone M et al. PLoS Curr. 2015 November 17; 7

Germline and somatic testing: ~50% of HRRm detected in prostate tumor tissue are germline, rest are somatic

Somatic testing detects somatic and most germline mutations but does not distinguish between the two mutation types



Germline testing if negative can miss somatic mutations present in the tumor

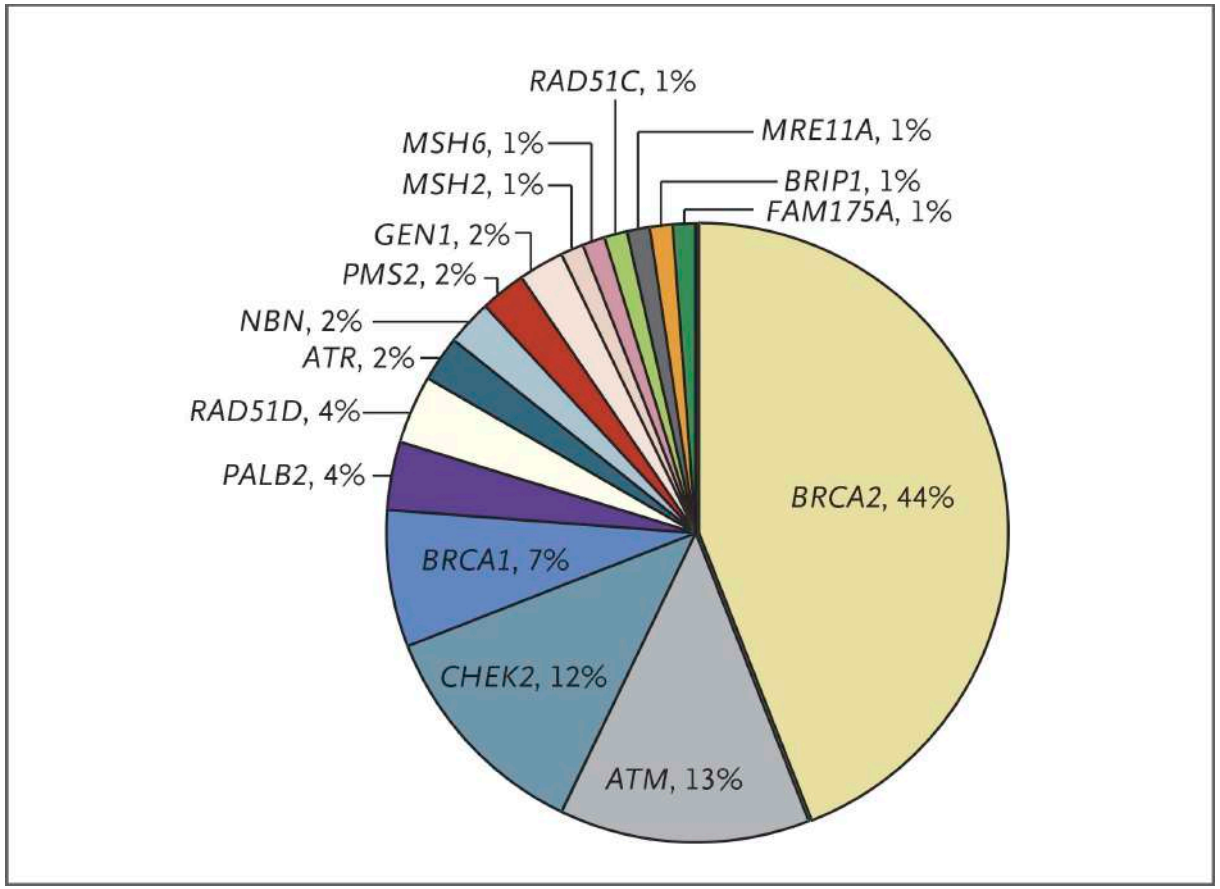


HRRm - homologous recombination repair gene mutations

Mateo et al. *New Engl J Med*. 2015 2. Robinson et al. *Cell.* 2015.

Pathogenic DNA repair germline mutations

Incidence of germline mutations in genes mediating DNA-repair: 11.8%



Selected DNA repair germline mutations from targeted panel and WES reveal 10-20% frequency

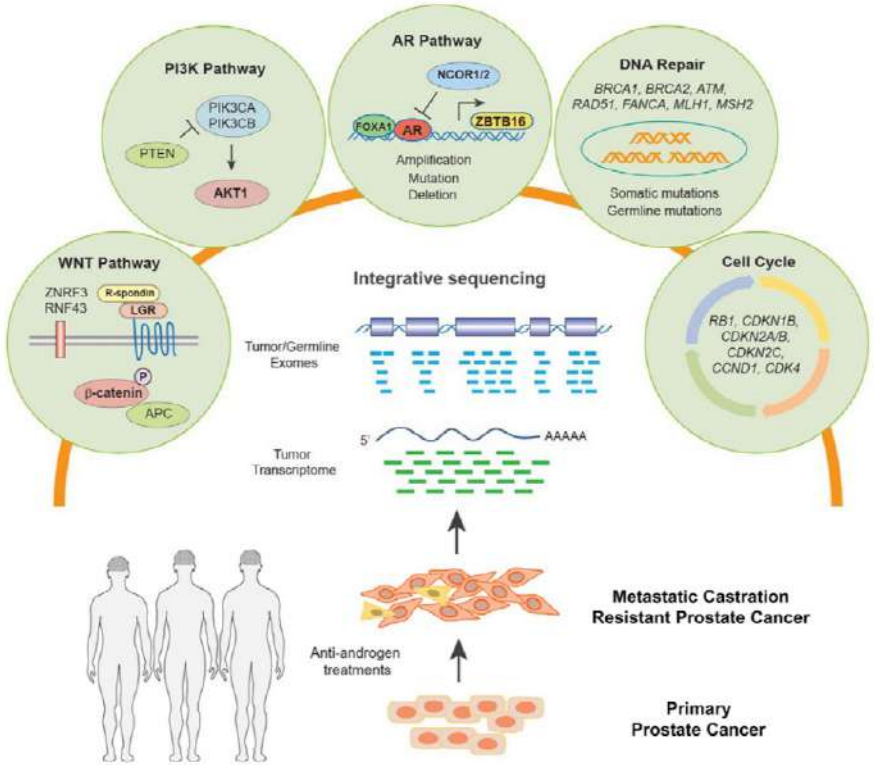
Distribution of 16 germline mutations: Most common BRCA2, ATM and CHEK2

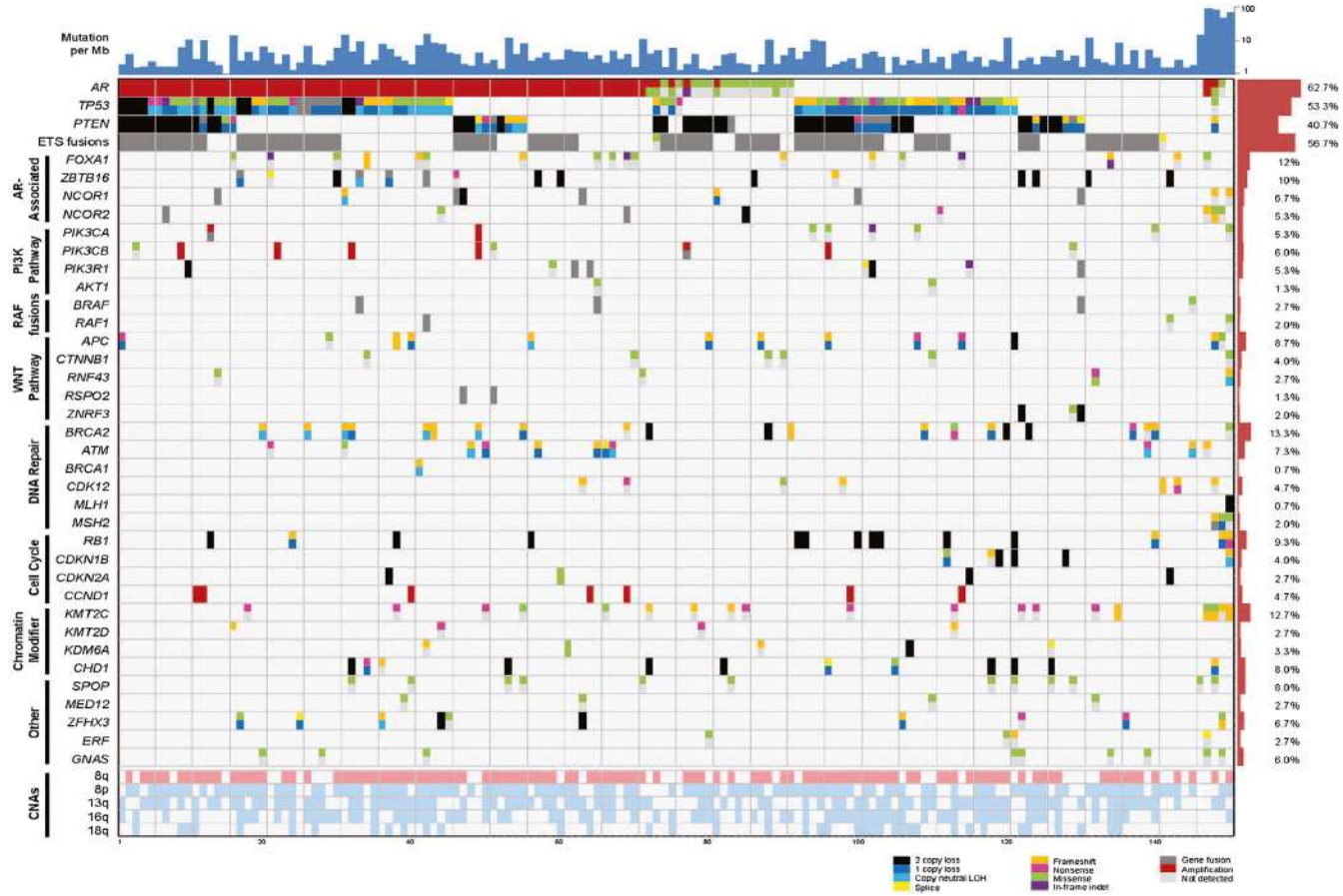
692 men with documented metastatic prostate cancer who were unselected for family history of cancer or age at diagnosis

Pritchard CC et al. N Engl J Med 2016;375:443-53

Genomic Alterations in mCRPC

- **90% of mCRPC harbor clinically actionable molecular alterations**
- **20% of mCRPC harbor DNA repair pathway aberrations (BRCA2, BRCA1, ATM and others)**

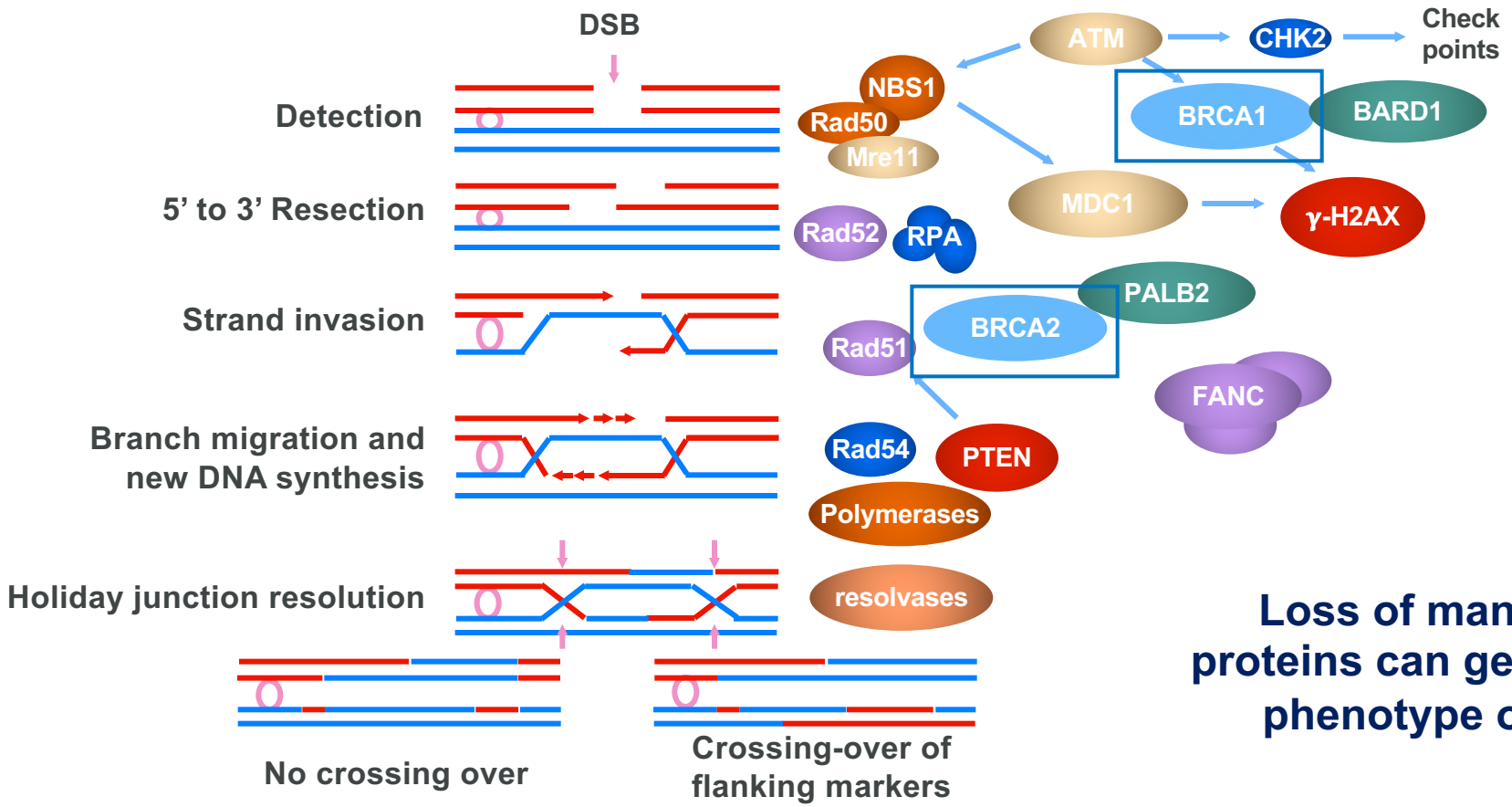




- Signaling pathways identified

Robinson D et al. Cell 2015;161:1215-28

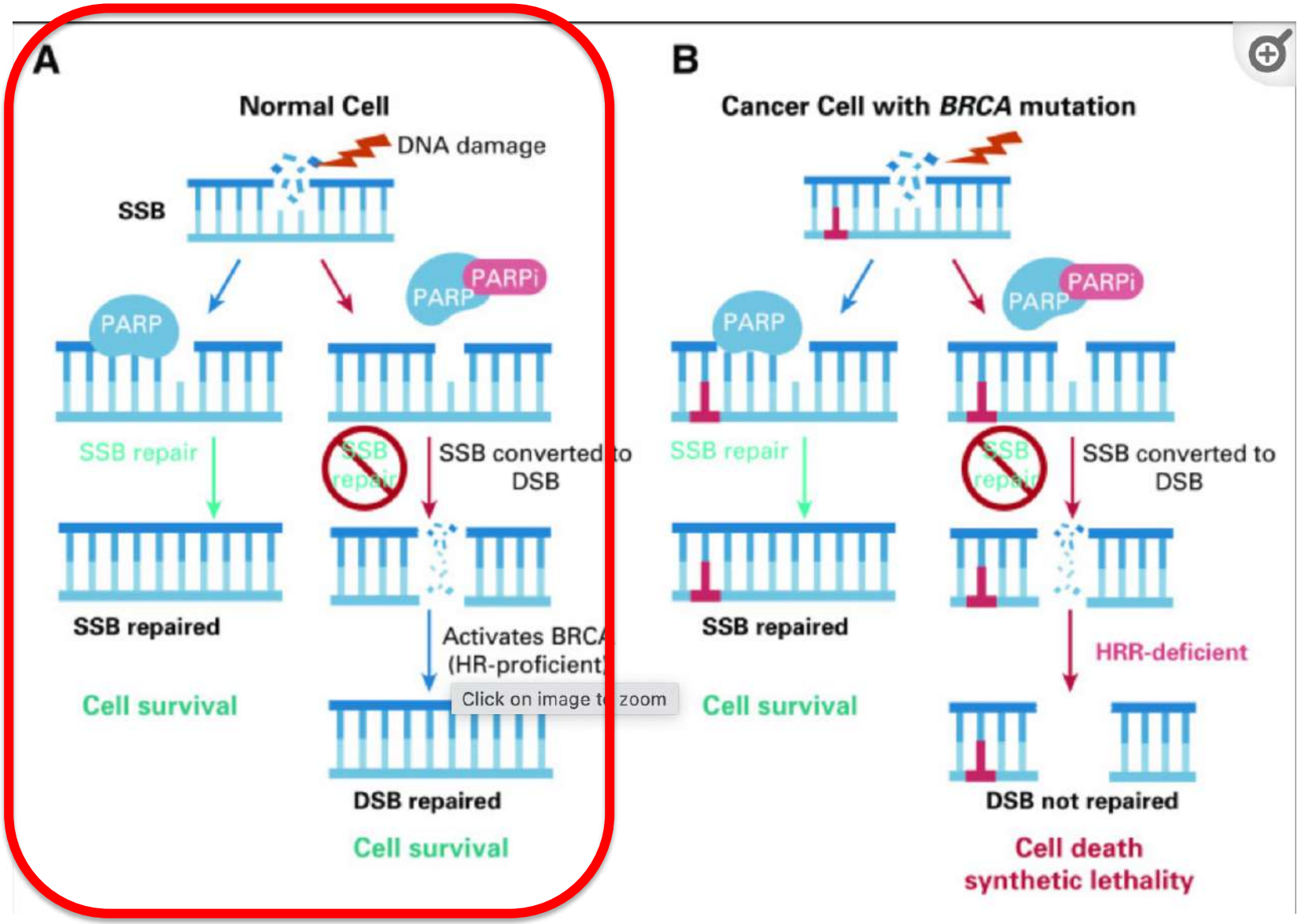
Homologous recombination DNA repair requires multiple proteins not just BRCA1/2



Loss of many DNA repair proteins can generate the same phenotype of BRCA*ness*

Nelson P, ASCO 2016 Annual Meeting; Pritchard CC et al. N Engl J Med 2016;375:443-53

Cell response to DNA damage +/- *BRCA* mutation and when treated with PARPi



DSB, double-strand breaks; **HRR, homologous recombination**; PARP, poly (ADP-ribose) polymerase; PARPi, poly (ADP-ribose) polymerase inhibition; SSB, single-strand breaks

von Werdt A et al, JCO Precision Oncology 2021 51639-1649

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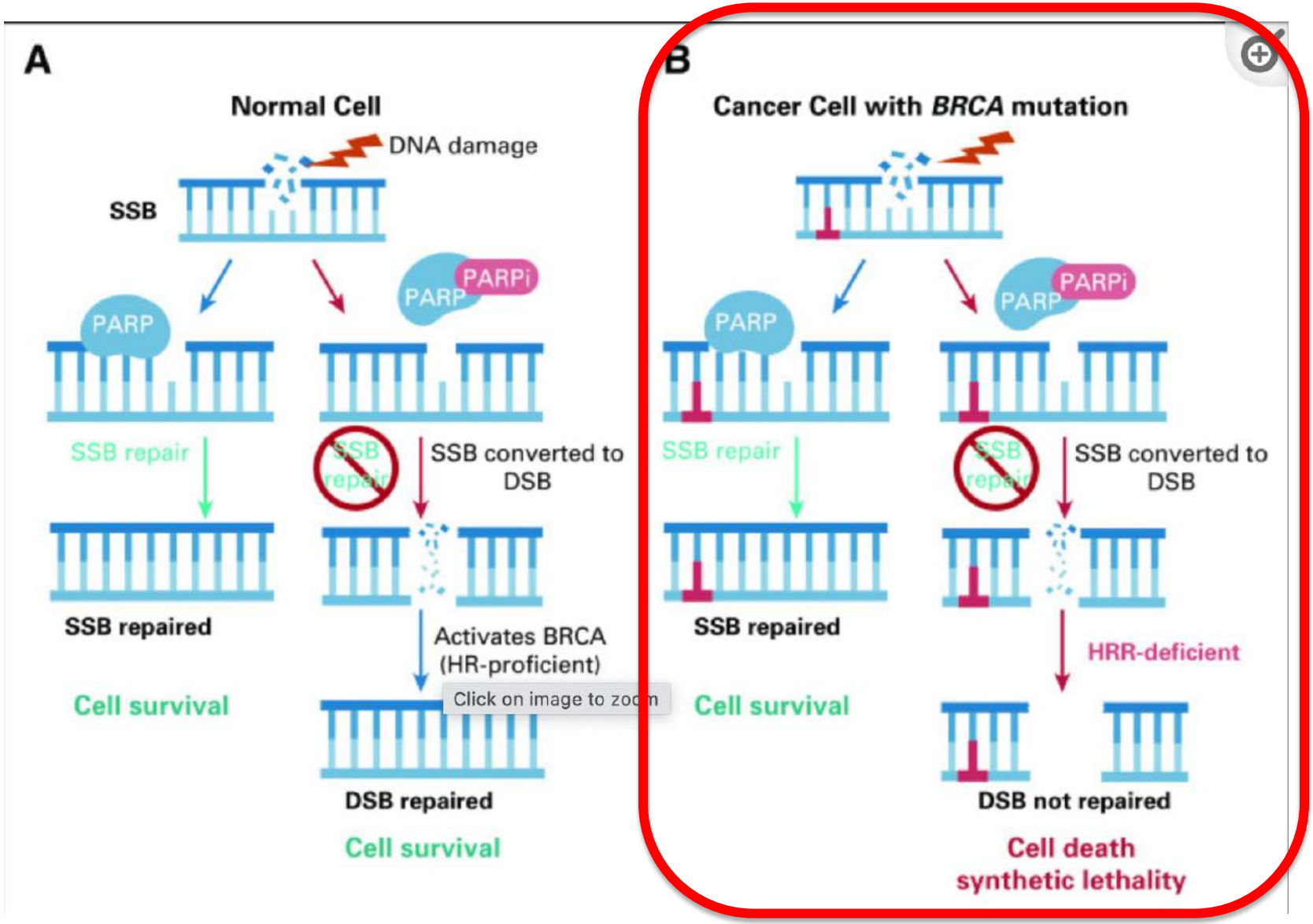

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von Werdt A et al, JCO Precision Oncology 2021 51639-1649

HRRm can be detected in archival samples

Tumor testing success rates in the PROfound study

	Proportion of samples with successful test (%)
For archived vs. newly collected samples	
Archived (n=4365)	56.9
Newly collected (n=438)	63.9
For primary vs. metastatic tumor samples	
Primary (n=4059)	56.3
Metastatic (n=775)	63.7
By sample age	
<1 year (n=368)	70.9
1-3 years (n=1133)	66.9
3-5 years (n=1139)	57.7
5-10 years (n=1446)	51.8
>10 years (n=727)	47.0

Majority (79.7%) of primary tumor samples in the study were archived samples

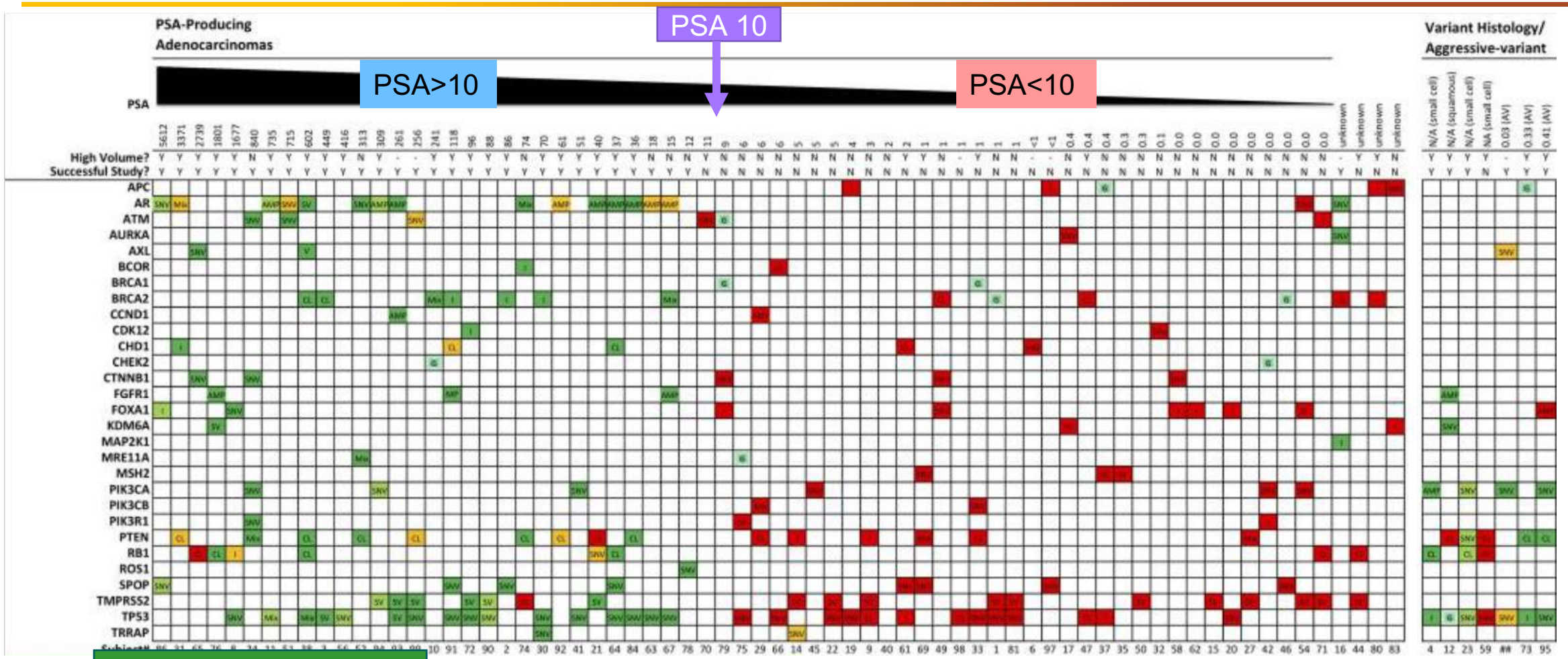
Other studies have shown HRR gene alterations detected in primary tumor tissue to be consistent and stable with matched metastatic tumor tissue

Successful tests were obtained in a proportion of samples that were 10+ years old[1]

HRRm - homologous recombination repair gene mutations

Hussain et al. *ASCO GU. 2020.* Mateo et al. *J Clin Invest.* 2020. Schweizer et al. *JAMA Oncol.* 2021.

Both tumor tissue and liquid based ctDNA tests are important in metastatic Prostate Cancer, but tissue is the gold standard



ctDNA and Tumor

Tumor Tissue only

ctDNA only

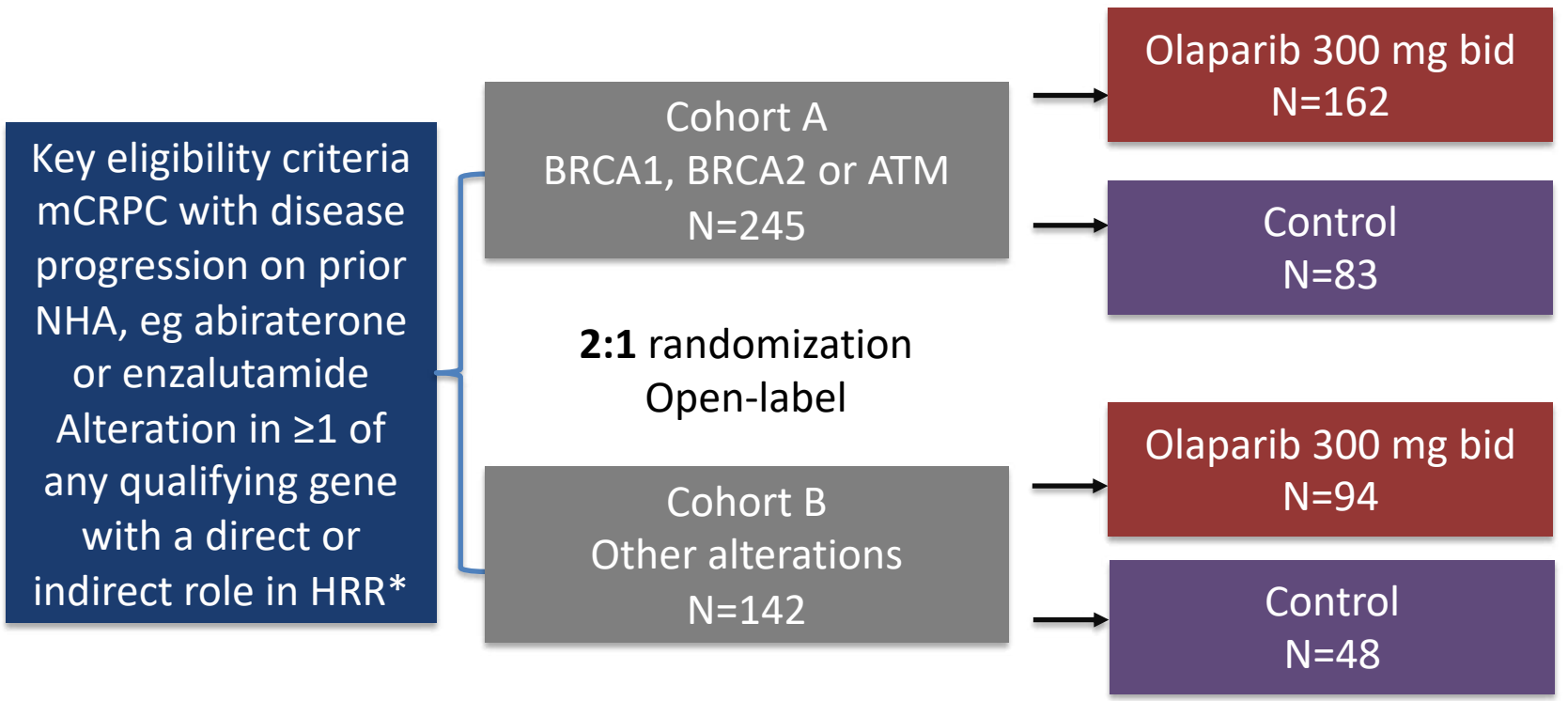
For patients with PSA<10, findings of single nucleotide variants, structural variants, indels, Copy Loss, Gene Amplifications, or Mutations are often found in tumor tissue only; not commonly found via ctDNA.

ctDNA – circulating tumor DNA

Schweizer et al. Prostate. 2019.

PROfound: Phase III Trial of Olaparib in mCRPC with HRR mutations

Study design



Primary endpoint

rPFS in cohort A (RECIST 1.1 &PCWG3 by BICR)

Key secondary endpoints

- ✓ rPFS in cohort A+B
- ✓ Confirmed radiographic ORR in cohort A
- ✓ OS in cohort A

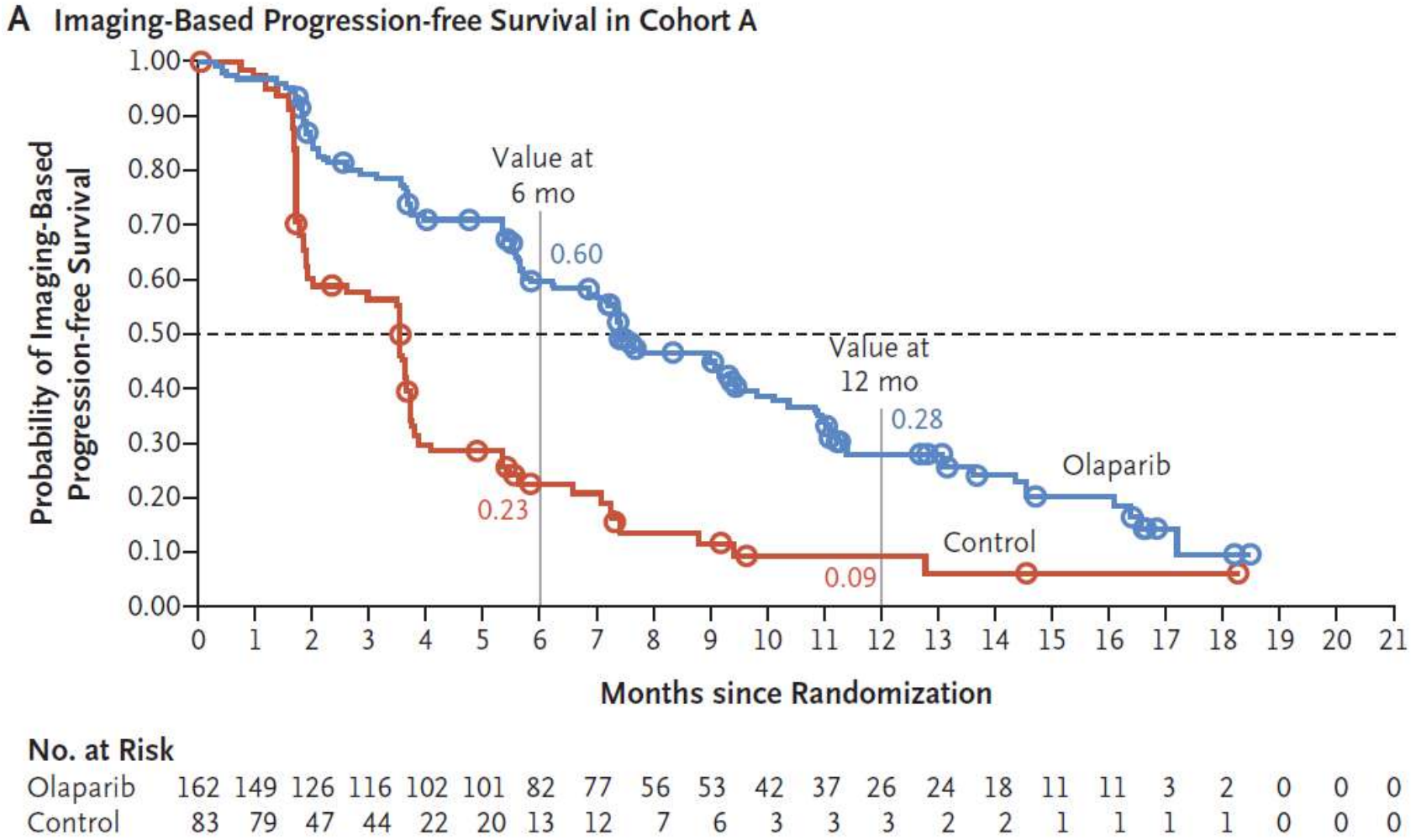
***An investigational clinical trial assay, based on the foundation medicine Inc, and used to prospectively select pts harboring alterations in BRCA1/2, ATM, BARD1, BRIP1, CDK12, CHEK1, CHEK2, FANCL, PALB2, PPP2R2A, RAD51B, RAD51C, RAD51D and/ or RAD54L in their tumor tissue.**

†Physician's choice of either enzalutamide (160 mg qd) or abiraterone (1000 mg qd plus prednisone [5 mg bid]).
BICR, blinded independent central review; bid, twice daily; HRR, homologous recombination repair; RECIST 1.1, Response Evaluation Criteria in Solid Tumors version 1.1; TTPP, time to pain progression.

de Bono J, et al. N Engl J Med. 2020 May 28;382(22):2091-2102.

PROfound: Phase III Trial of Olaparib in mCRPC with HRR mutations

Primary endpoint: rPFS by BICR in cohort A (BRCA1/2 and ATM)



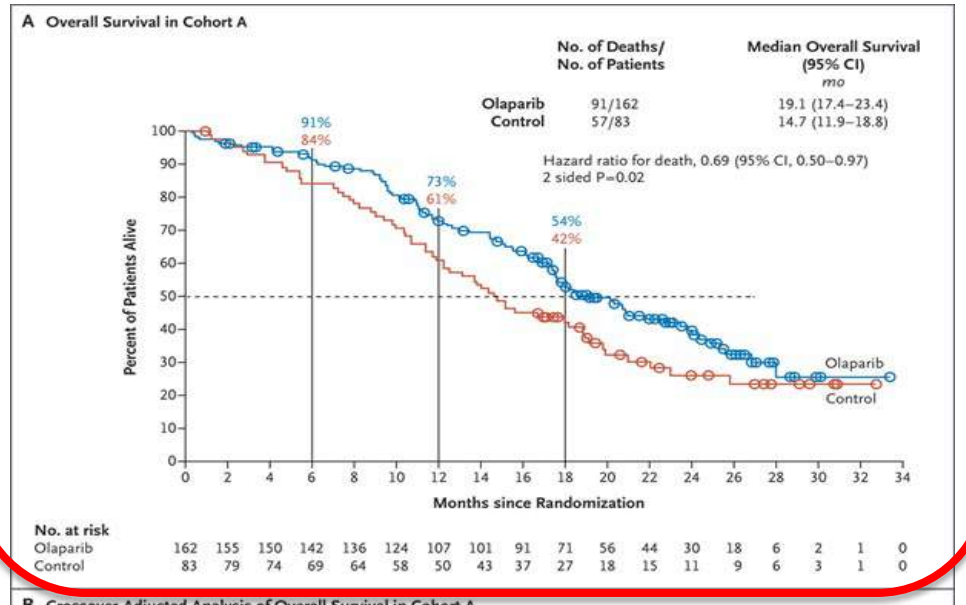
	Median *mo*
Olaparib	7.4
Control	3.6

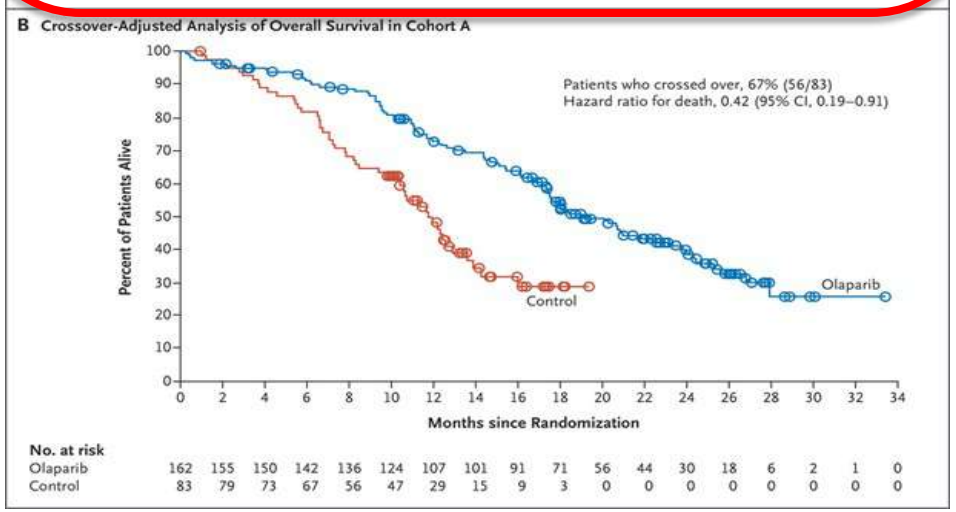
Hazard ratio for progression or death, 0.34 (95% CI, 0.25–0.47)
P<0.001

de Bono J, et al. N Engl J Med. 2020 May 28;382(22):2091-2102.

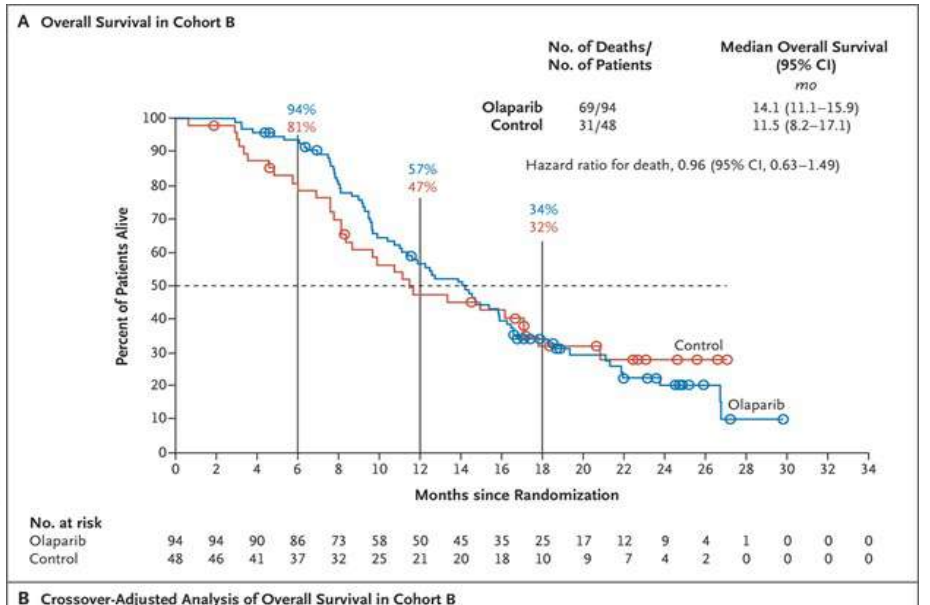
Overall Survival & Corresponding Crossover-Adjusted Sensitivity Analyses

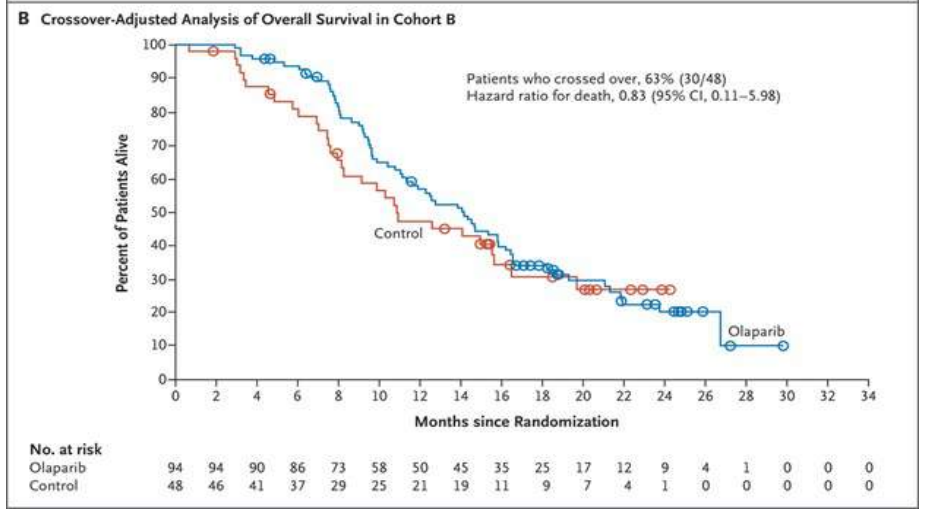
Cohort A:BRCA1, BRCA2, or ATM





Cohort B

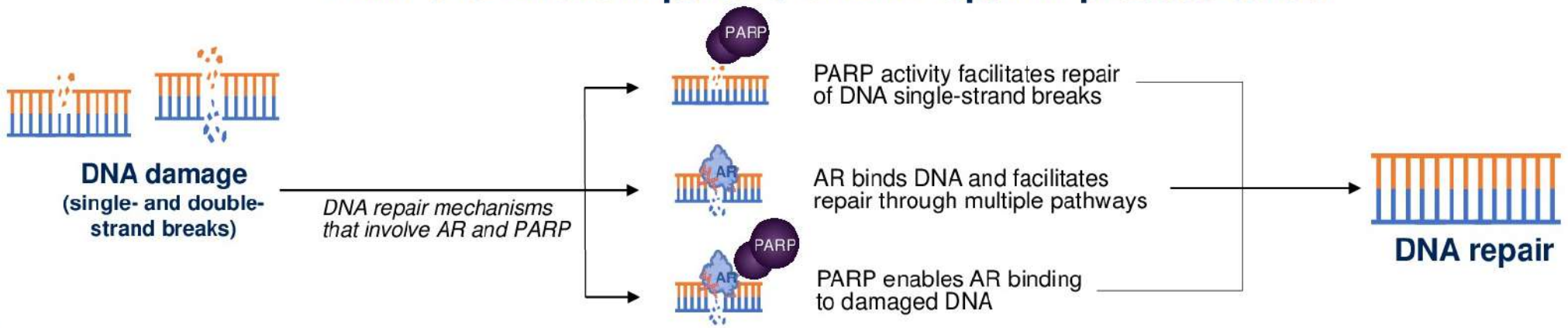




Hussain M et al, N Engl J Med 2020;383:2345-57

Preclinical rationale for a combined effect of PARP and AR inhibition

PARP and AR are important for DNA repair in prostate cancer



AR, androgen receptor; DNA, deoxyribonucleic acid; NHA, next-generation hormonal agent; PARP, poly(ADP-ribose) polymerase.

1. Chaudhuri *et al. Nat Rev Mol Cell Biol* 2017;18:610–21; 2. Polkinghorn *et al. Cancer Discov* 2013;3:1245–53; 3. Lord *et al. Science* 2017;355:1152–8 ; 4. Pommier *et al. Sci Transl Med* 2016;8:p362ps17; 5. Schiewer *et al. Cancer Discov* 2012;2:1134–49; 6. Asim *et al. Nat Commun* 2017;8:374; 7. Li *et al. Sci Signal* 2017;10.

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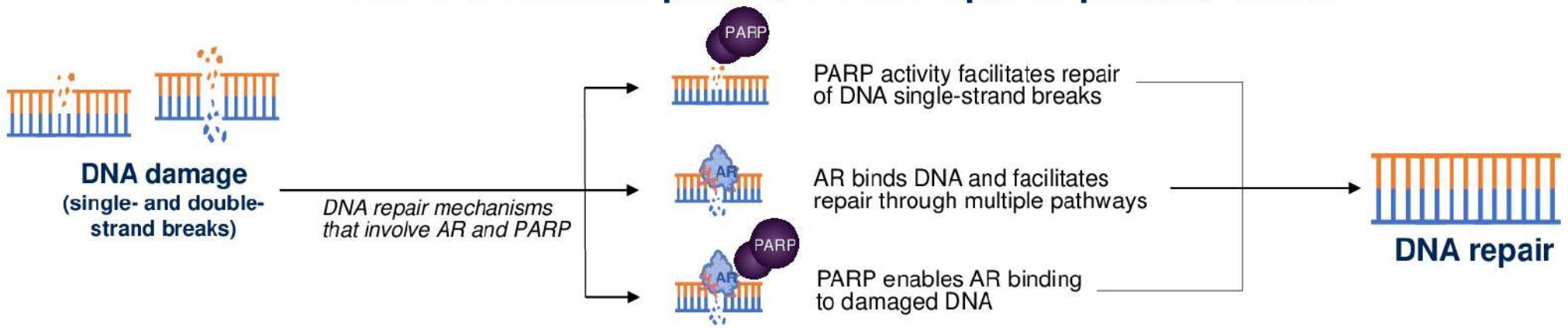
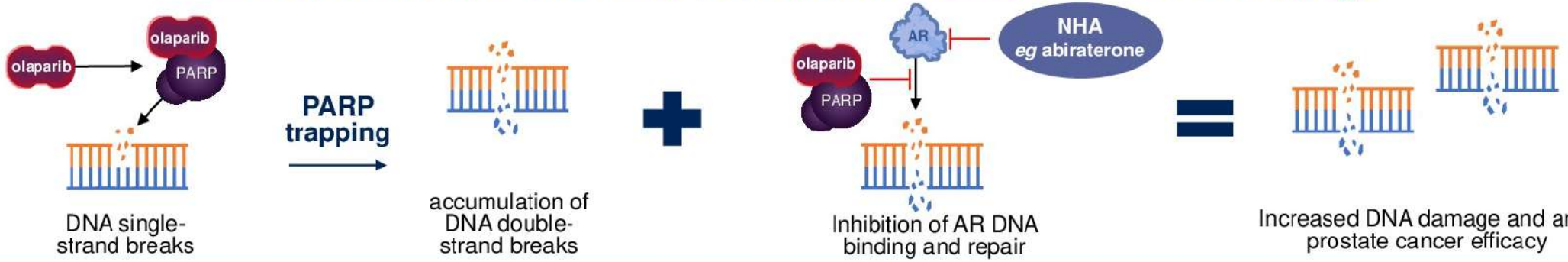


Inhibition of PARP and AR in combination results in more DNA damage



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PROpel: Phase III trial design

Patient population

- 1L mCRPC
- **Asymptomatic, mildly symptomatic, symptomatic**
- No prior abiraterone
- **Other NHAs allowed if stopped ≥12 months prior to enrollment**
- ECOG 0–1

Stratification factors

- Site of distant metastases: bone only vs visceral vs other
- Prior taxane at mHSPC: yes vs no

1:1

Abiraterone 1000 mg qd* + olaparib 300 mg bid
n=399
Full dose of abiraterone and olaparib

Abiraterone 1000 mg qd* + placebo
n=397
Full dose of abiraterone

Primary endpoint

- rPFS by investigator assessment (sensitivity analysis by blinded independent central review)

Key secondary endpoint

- OS

Additional preplanned analyses:

- TFST
- PFS2
- HRQoL
- HRRm status (by tissue and ctDNA after randomization and before primary analysis; see supplement)
- Safety and tolerability

Analysis timeline:

DCO1: 30 July 2021
rPFS (primary)

DCO2: 14 March 2022
OS (interim)

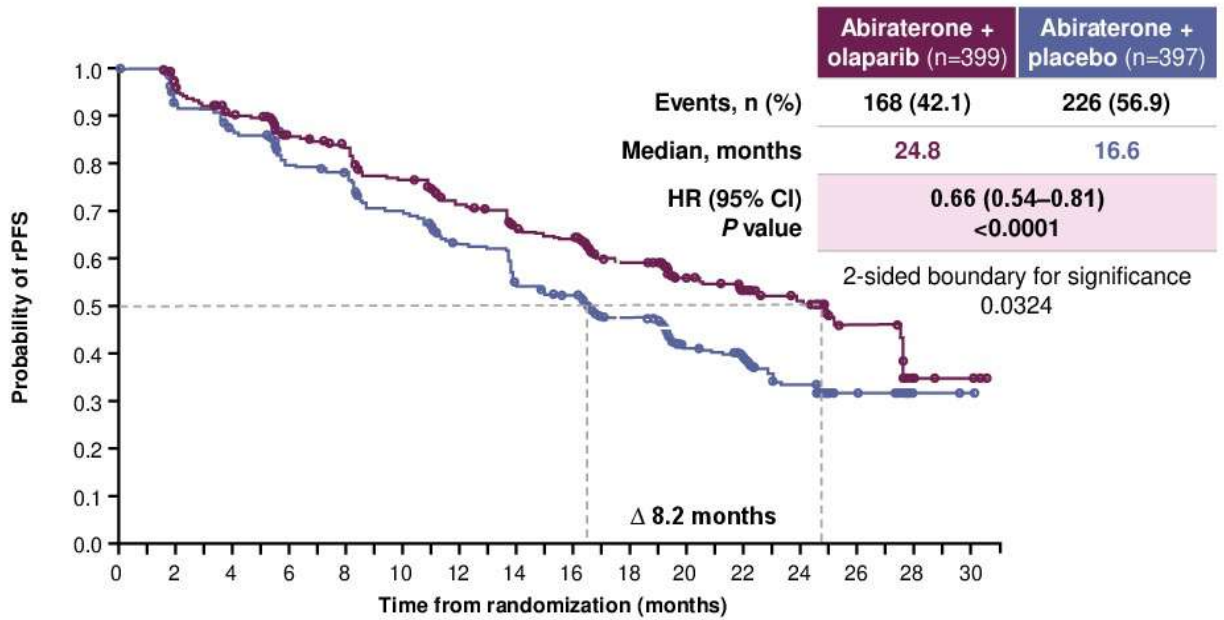
DCO3: 12 October 2022
OS (final) *current dataset*

*In combination with prednisone or prednisolone 5 mg bid.
bid, twice daily; ctDNA, circulating tumor DNA; DCO, data cut-off; ECOG, Eastern Cooperative Oncology Group; HRRm, homologous recombination repair mutation; HRQoL, health-related quality of life; mHSPC, metastatic hormone-sensitive prostate cancer; PFS2, time to second progression or death; qd, once daily; TFST, time to first subsequent therapy or death.

PROpel: primary rPFS results (DCO1)[1]

Abiraterone + olaparib significantly prolonged rPFS versus abiraterone + placebo in the ITT population

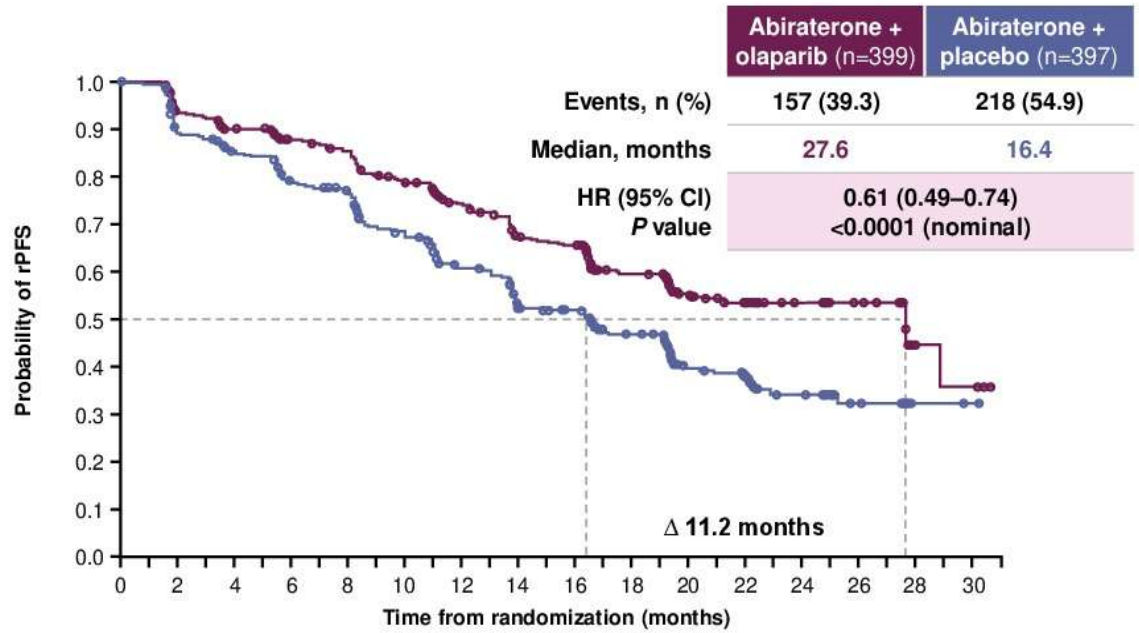
rPFS by investigator assessment (INV)



Number of patients at risk:

Abiraterone + olaparib	399	367	340	313	301	274	251	227	219	167	104	87	57	26	5	4
Abiraterone + placebo	397	359	338	306	297	264	232	198	186	141	87	73	43	17	2	1

rPFS by blinded independent central review (BICR)



Number of patients at risk:

Abiraterone + olaparib	399	353	332	314	303	275	249	221	215	161	96	80	53	28	5	4
Abiraterone + placebo	397	345	322	294	282	245	209	177	168	126	73	62	38	16	2	1

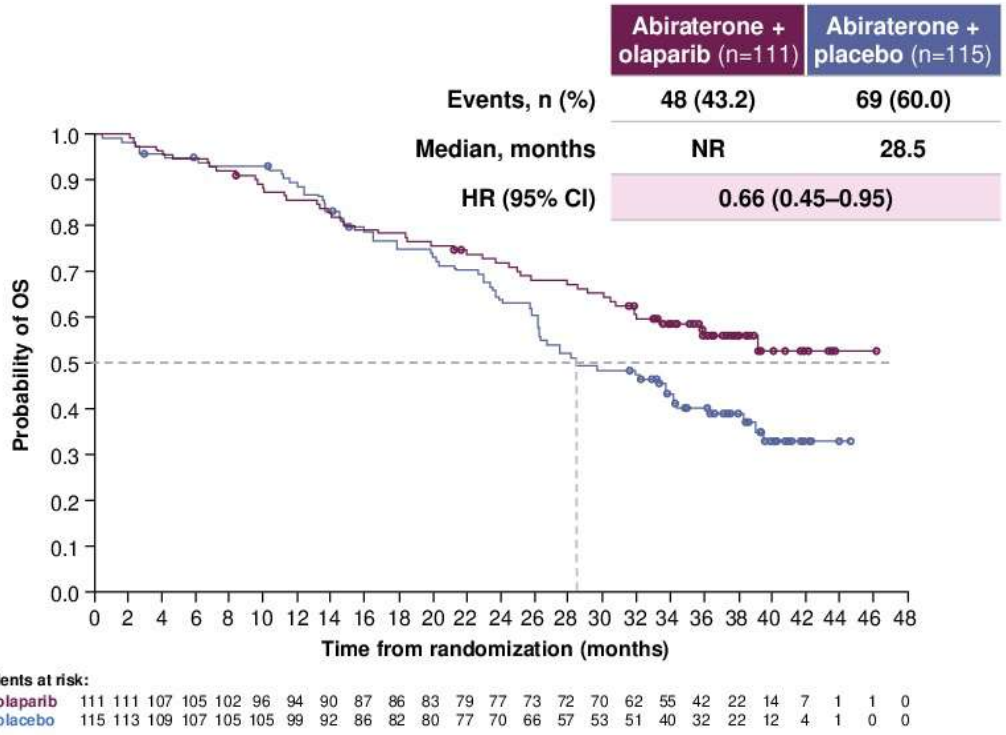
DCO1: 30 July 2021.
Median duration of follow-up for investigator-assessed rPFS for censored patients was 19.3 months in the abiraterone and olaparib arm, and 19.4 months in the abiraterone and placebo arm (19.3 and 19.2 months, respectively, for BICR).
ITT, intention-to-treat.

1. Clarke N *et al. NEJM Evidence* 2022; 1: EVIDoa2200043.

PROpel: OS in HRRm and non-HRRm subgroups (DCO3)

A trend towards OS benefit was observed across HRRm and non-HRRm subgroups ?

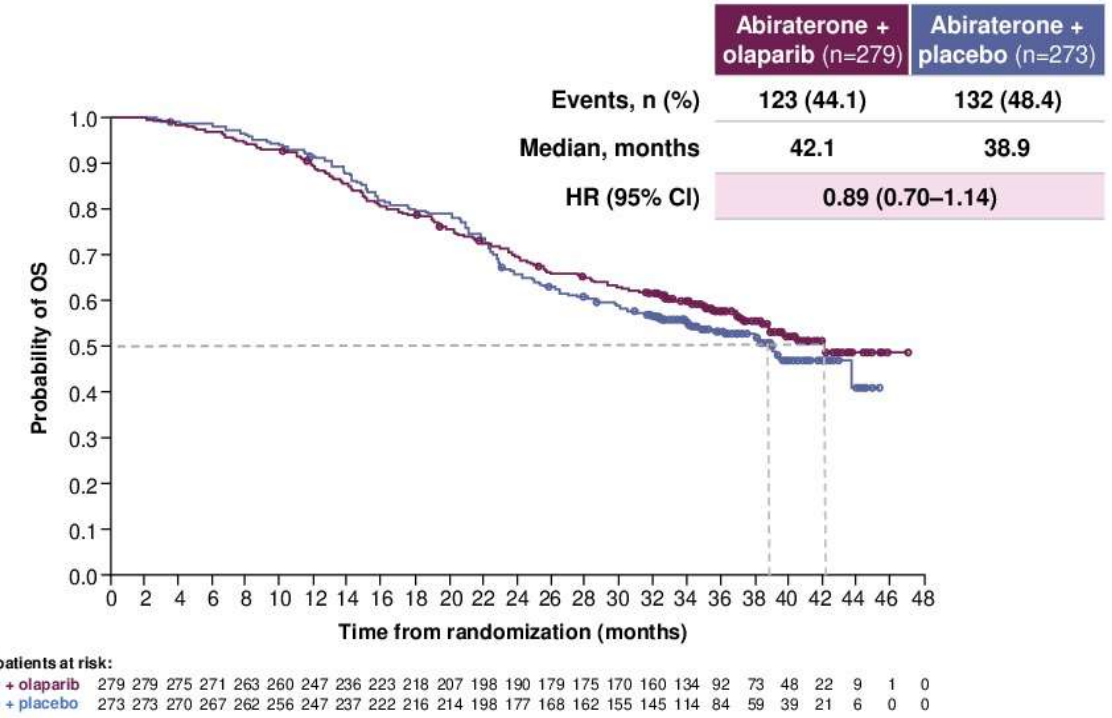
HRRm (28.4% of ITT population)



Number of patients at risk:

Abiraterone + olaparib	111	111	107	105	102	96	94	90	87	86	83	79	77	73	72	70	62	55	42	22	14	7	1	1	0
Abiraterone + placebo	115	113	109	107	105	105	99	92	86	82	80	77	70	66	57	53	51	40	32	22	12	4	1	0	0

Non-HRRm (69.3% of ITT population)



Number of patients at risk:

Abiraterone + olaparib	279	279	275	271	263	260	247	236	223	218	207	198	190	179	175	170	160	134	92	73	48	22	9	1	0
Abiraterone + placebo	273	273	270	267	262	256	247	237	222	216	214	198	177	168	162	155	145	114	84	59	39	21	6	0	0

DCO3: 12 October 2022.
The preplanned tumor tissue and plasma ctDNA testing was conducted after randomization and before primary analysis. Results from tumor tissue and plasma ctDNA were combined to determine patients HRRm status (see supplement for more details). 18 patients had unknown HRRm status.

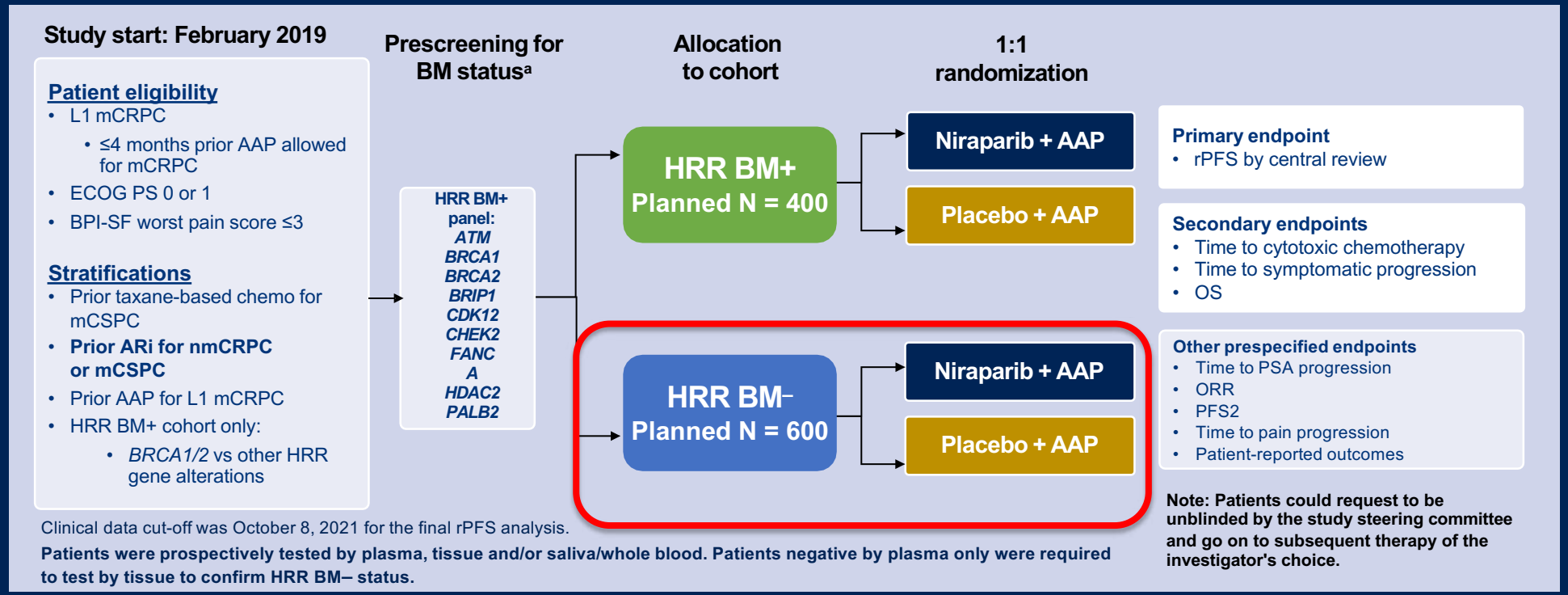
PROpel Trial: Approved by EMA Dec 21, 2022 mCRPC Olaparib and Abiraterone FDA May 13, 2023 approval for BRCA mutated pts only in mCRPC

FDA Conclusions

- Statistically significant **rPFS improvement in ITT population** in PROpel; **attributable to *BRCA*m.**
- As certainty regarding absence of tumor *BRCA*m increases, rPFS benefit appears to decrease.
- **Potential OS detriment** in patients **negative for *BRCA*m by both tumor and ctDNA assays**, comprising over half of the ITT population in PROpel (OS HR 1.06).

MAGNITUDE: 1st Line mCRPC Randomized, Double-Blind, Placebo-Controlled Study Niraparib + Abi and Pred vs PBO and Abi and Pred

Prospectively selected biomarker cohorts designed to test HRR BM+ and HRR BM–



Clinical data cut-off was October 8, 2021 for the final rPFS analysis.

Patients were prospectively tested by plasma, tissue and/or saliva/whole blood. Patients negative by plasma only were required to test by tissue to confirm HRR BM– status.

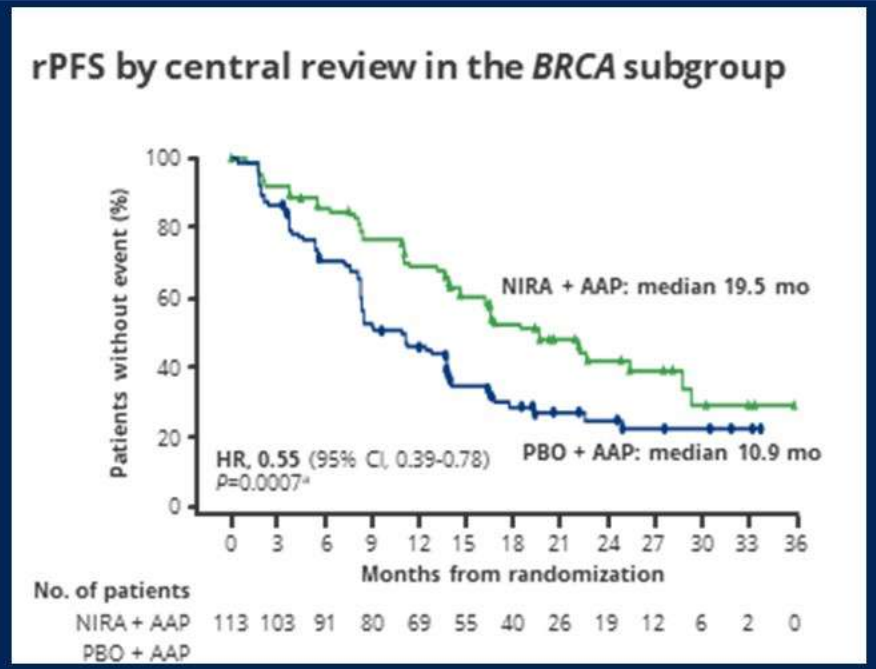
AAP, abiraterone acetate + prednisone/prednisolone; AR, androgen receptor; ARi, androgen receptor inhibitor; BM, biomarker; BPI-SF, Brief Pain Inventory–Short Form; ctDNA, circulating tumor deoxyribonucleic acid; ECOG PS, Eastern Cooperative Oncology Group performance status; HRR, homologous recombination repair; L1, first line; mCRPC, metastatic castration-resistant prostate cancer; mCSPC, metastatic castration-sensitive prostate cancer; nmCRPC, nonmetastatic castration-resistant prostate cancer; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; PFS2, progression-free survival on first subsequent therapy; PSA, prostate-specific antigen; rPFS, radiographic progression-free survival.

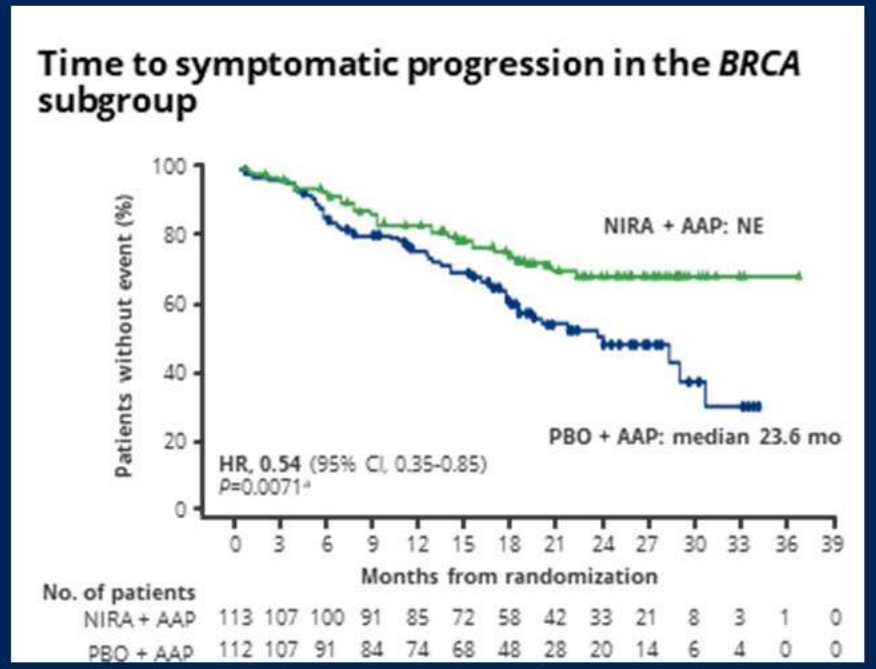
[a]Tissue and Plasma assays: FoundationOne tissue test (FoundationOne®CDx), Resolution Bioscience liquid test (ctDNA), AmoyDx blood and tissue assays, Invitae germline testing (blood/saliva), local lab biomarker test results demonstrating a pathogenic germline or somatic alteration listed in the study biomarker gene panel.

PRESENTED BY: Kim N. Chi, MD

MAGNITUDE BRCA Patients: NIRA + AAP improved rPFS and Time to Symptomatic Progression in the BRCA Subgroup

With additional 8 months of follow-up





- rPFS by central review demonstrated a consistent and clinically meaningful treatment effect favoring niraparib + AAP, with a median rPFS of 19.5 months at IA2 compared with 10.9 months for placebo + AAP
- **Investigator Assessed HR (95% CI) 0.46 (0.32,0.67)**
- A strong improvement in time to symptomatic progression (TSP) was observed in patients who received niraparib + AAP compared with placebo + AAP

NIRA+AAP reduced the risk of progression or death by 45% in pts with BRCA mutations, extending rPFS by >8 months

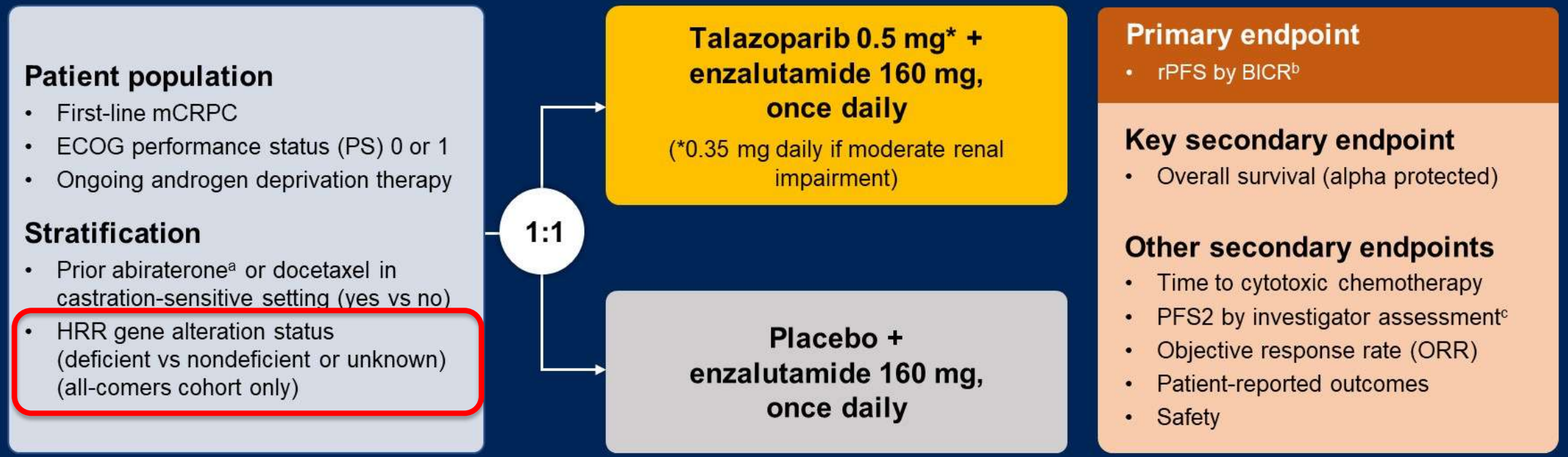
Results are descriptive. No formal statistical testing was performed. Consistent results were observed for rPFS assessed by investigator for both the BRCA subgroup and HRR+ population.

[a] Nominal P value.

AAP, abiraterone acetate with prednisone; HR, hazard ratio; HRR+, homologous recombination repair positive; NIRA, niraparib; PBO, placebo; rPFS, radiographic progression-free survival.

Placebo + AAP Niraparib + AAP

TALAPRO-2: A Randomized, Double-blind, Placebo-Controlled Study

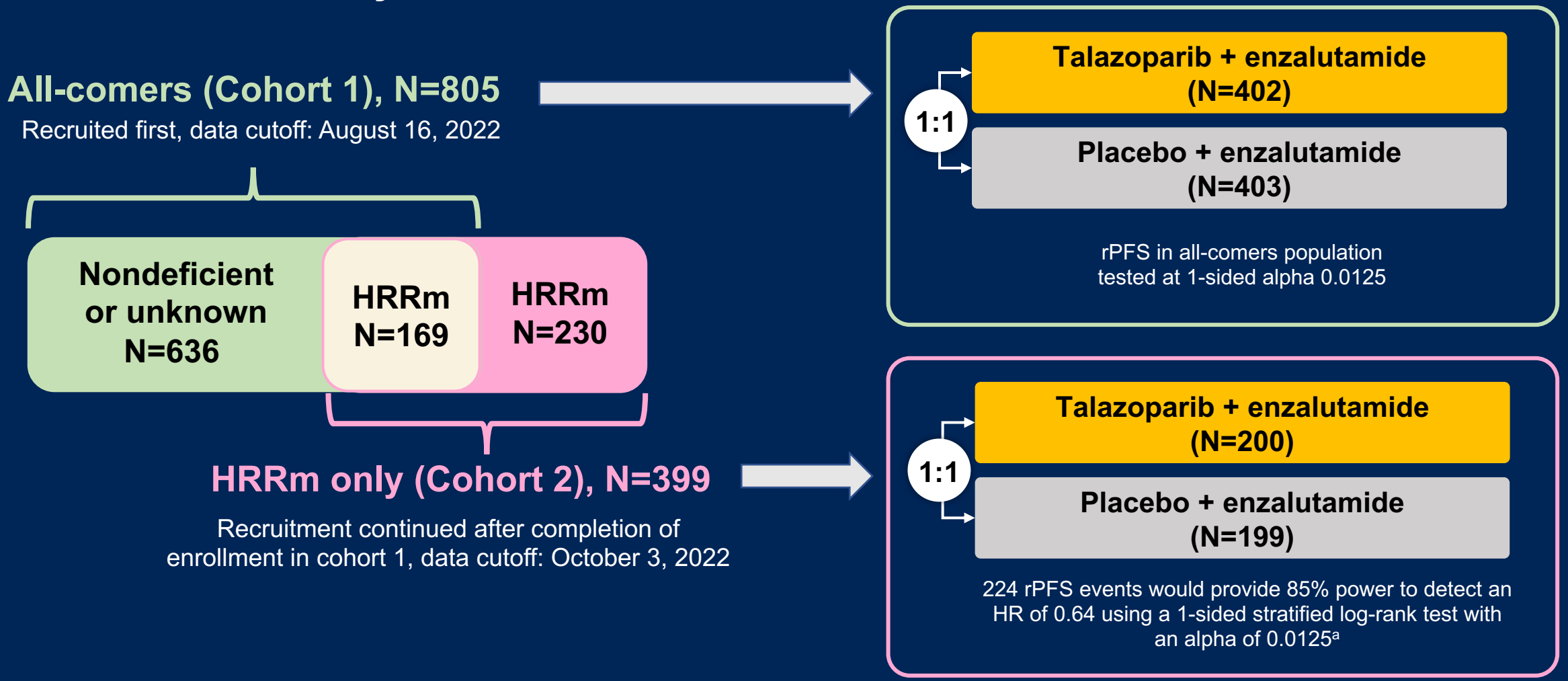


Samples prospectively assessed for HRR gene alterations *(BRCA1, BRCA2, PALB2, ATM, ATR, CHEK2, FANCA, RAD51C, NBN, MLH1, MRE11A, CDK12)* using FoundationOne®CDx and/or FoundationOne®Liquid CDx

BICR=blinded independent central review; rPFS=radiographic progression-free survival.
[a]One patient in each treatment arm received prior orteronel. [b]Per RECIST version 1.1 (soft tissue disease) and Prostate Cancer Clinical Trials Working Group 3 (bone disease). [c]Time from randomization to the date of documented progression on the first subsequent antineoplastic therapy or death from any cause, whichever occurred first.

Agarwal N et al, Lancet, 2023 Jul 22;402(10398):291-303.

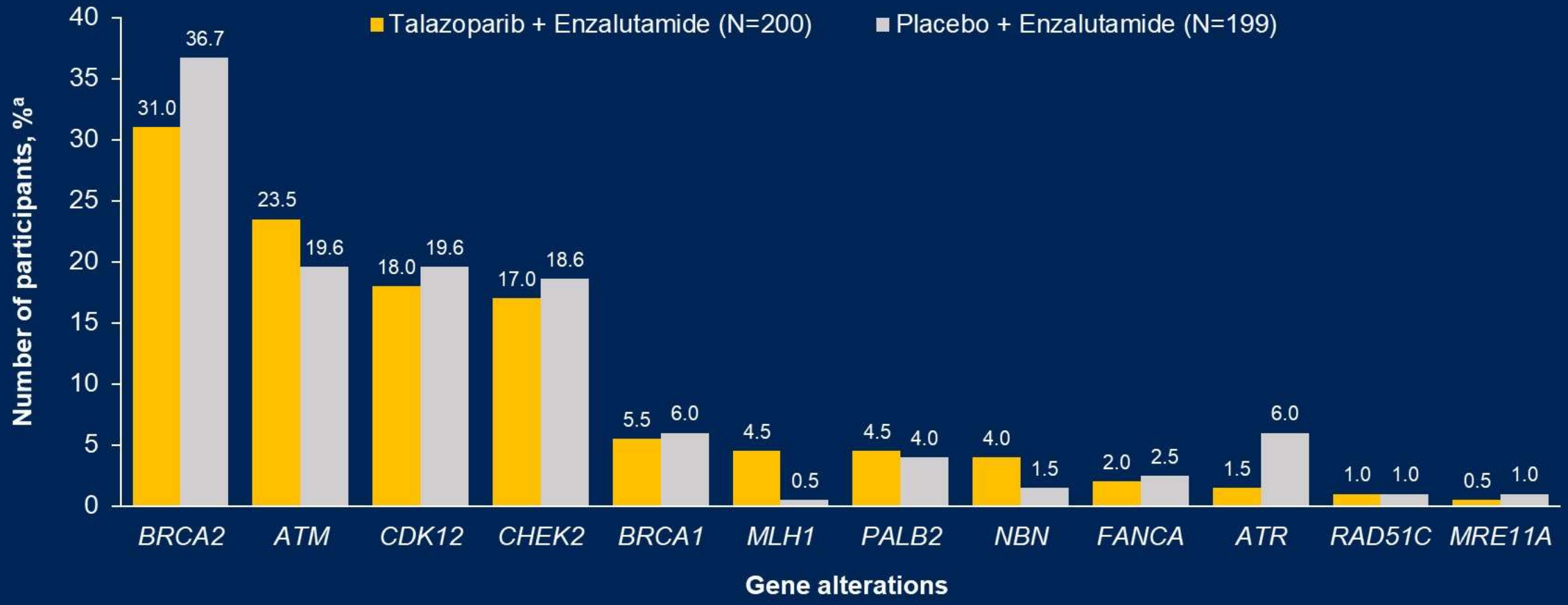
TALAPRO-2: Study Cohorts and Enrollment



[a]An interim analysis (IA) was planned with ~70% of the total required events. The HRRm cohort would be stopped for efficacy if the pre-specified efficacy boundary was crossed ($P \leq 0.003$). As the efficacy boundary was crossed at the IA rPFS, this became the final analysis. Survival and safety follow-up is continuing. All other endpoints are final.

TALAPRO-2 HRR-Deficient: Baseline HRR Gene Alterations

Representation of HRR gene alterations was consistent with previously published studies

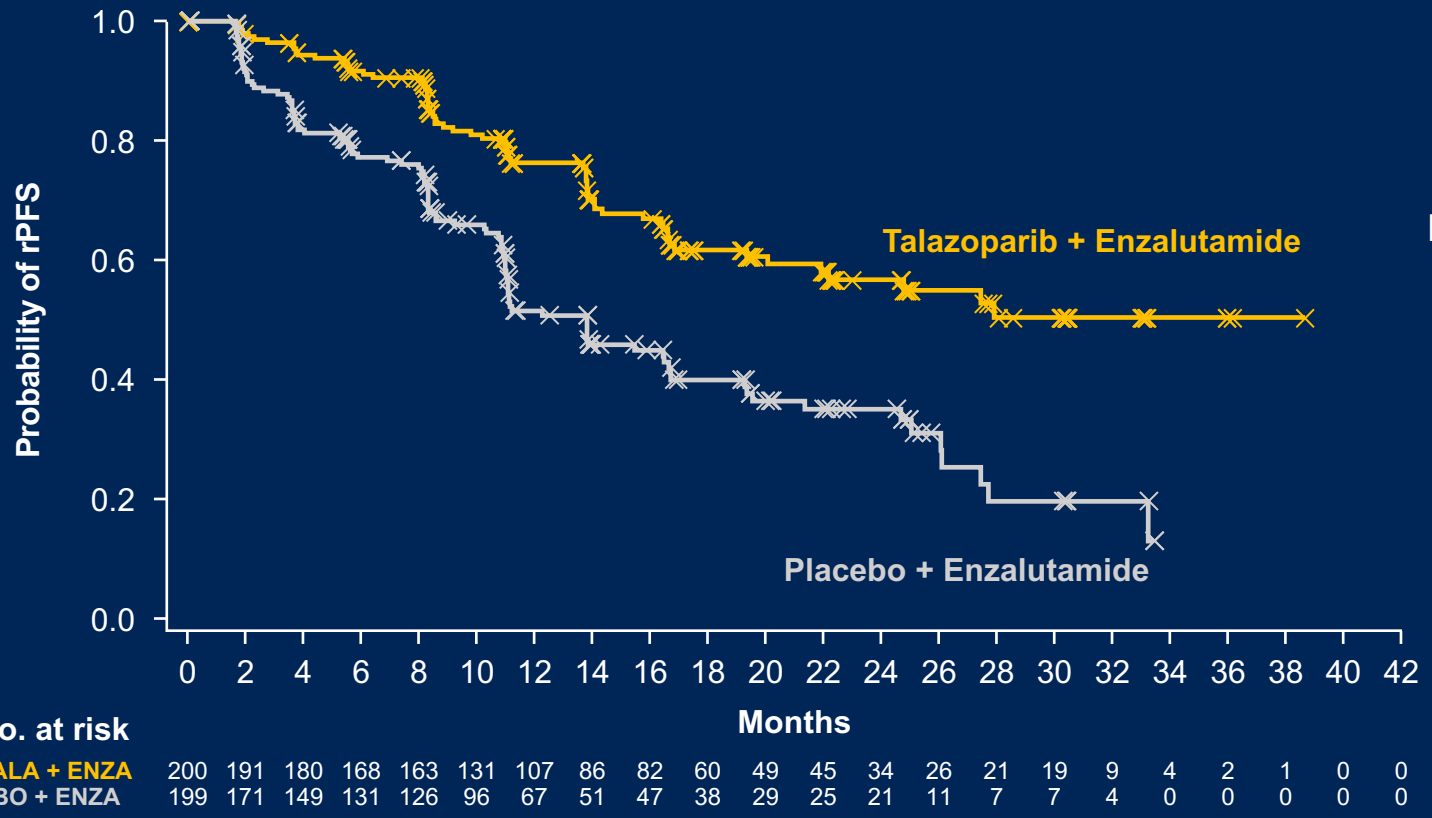


During the mid-point of the study (January-November 2021), recruitment of patients with *ATM* and/or *CDK12* alterations was paused to avoid over-representation.
[a]Number of participants with one or more alterations in corresponding gene. Three patients (1 in the talazoparib arm and 2 in the placebo arm) did not have HRR gene alterations, and 1 patient in the talazoparib arm was of unknown HRR gene alteration status.

Agarwal N et al. Lancet. 2023 Jul 22;402(10398):291-303

TALAPRO-2 HRR-Deficient Primary Endpoint: rPFS by BICR

Treatment with talazoparib plus enzalutamide resulted in a 55% reduced risk of progression or death



	TALA + ENZA (N=200)	PBO + ENZA (N=199)
Events, n	66	104
Median (95% CI), months	Not reached (NR) (21.9–NR)	13.8 (11.0–16.7)
HR (95% CI)	**0.45 (0.33–0.61); *P* < 0.0001**	

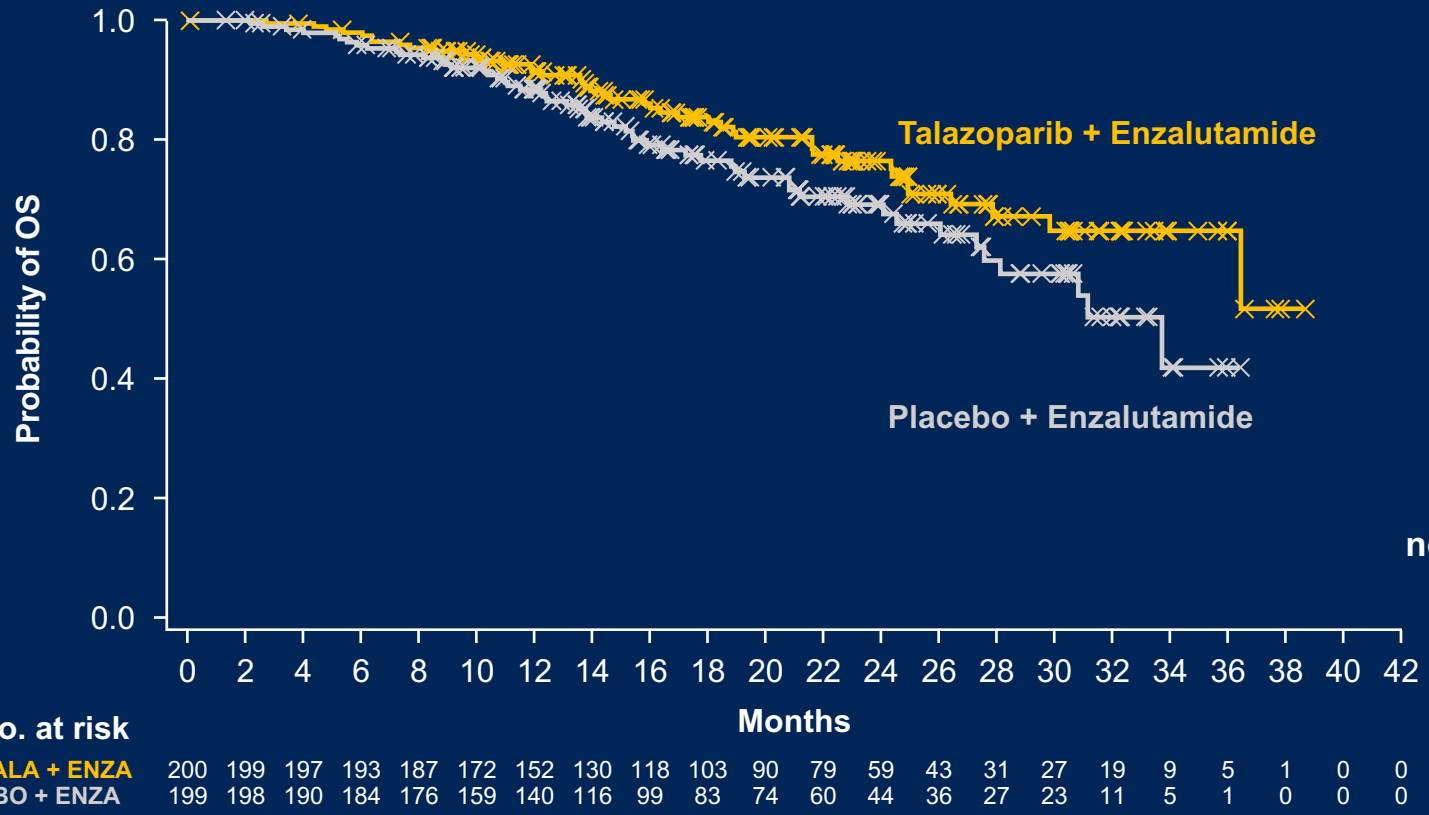
Median follow-up for rPFS was 17.5 and 16.8 months, respectively

A consistent treatment effect was seen for investigator-assessed rPFS: HR 0.48 (95% CI, 0.33–0.67); *P* < 0.0001

Stratified hazard ratios (HRs) and 2-sided *P* values are reported throughout this presentation unless otherwise stated.

TALAPRO-2 HRR-Deficient: Overall Survival (Interim Analysis)

Overall survival data are immature (24% maturity overall)



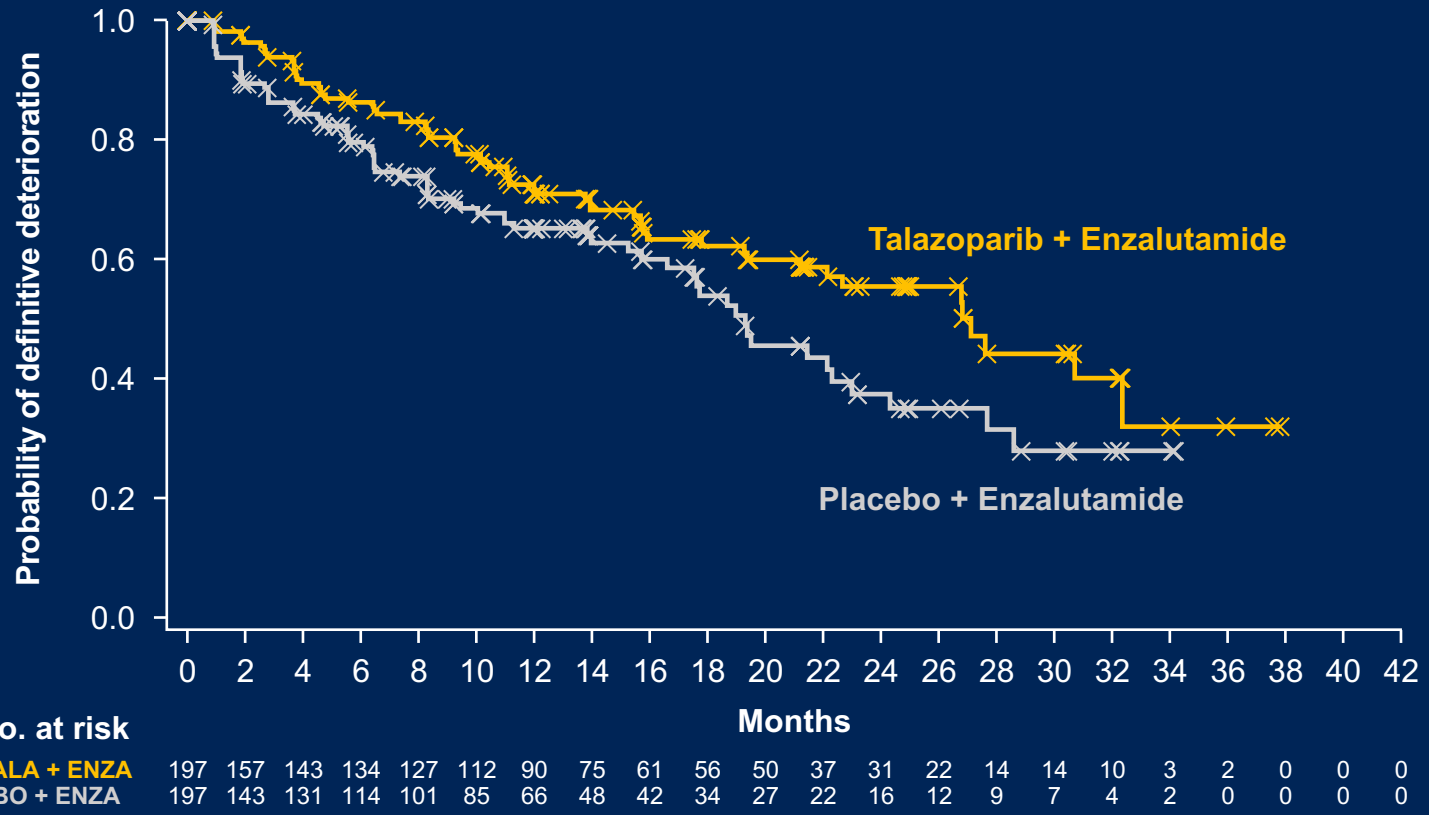
	TALA + ENZA (N=200)	PBO + ENZA (N=199)
Events, n	43	53
Median (95% CI), months	NR (36.4–NR)	33.7 (27.6–NR)
HR (95% CI)	HR 0.69 (95% CI, 0.46–1.03) *P* = 0.068	

***BRCA* alterations: HR 0.61 (95% CI, 0.31–1.23; *P* = 0.16)**
non-*BRCA* alterations: HR 0.66 (95% CI, 0.40–1.10; *P* = 0.11)

18 patients in the control arm and 3 patients in the talazoparib arm subsequently received olaparib

TALAPRO-2 HRR-Deficient: Patient-Reported Global Health Status

Talazoparib plus enzalutamide significantly prolonged time to definitive clinically meaningful deterioration in GHS/QoL[a]



	TALA + ENZA (N=197)	PBO + ENZA (N=197)
Events, n	64	71
Median (95% CI), months	27.1 (21.2–NR)	19.3 (16.6–23.0)
HR (95% CI)	HR 0.69 (95% CI, 0.49–0.97) *P* = 0.032	

EORTC QLQ-C30=European Organisation for Research and Treatment of Cancer cancer-specific global health questionnaire per EORTC QLQ-C30; GHS=global health status; QoL=quality of life.
[a]Definitive clinically meaningful deterioration defined as a ≥10-point decrease from baseline and no subsequent observations with <10-point decrease from baseline assessed by the EORTC QLQ-C30 (Gamper EM, et al. *BMC Cancer*. 2021;21:1083).

TALAPRO-2 HRR-Deficient: Conclusions

- In this large, randomized trial involving patients with mCRPC with HRR gene alterations, talazoparib plus enzalutamide resulted in a statistically significant and clinically meaningful improvement in the primary endpoint, rPFS by BICR, over placebo plus enzalutamide
  - rPFS benefit was greater for patients with *BRCA*m (HR 0.20; 95% CI, 0.11–0.36; $P < 0.0001$) versus non-*BRCA*m (HR 0.72; 95% CI, 0.49–1.07; $P = 0.10$)
  - Although OS data are immature, there was a favorable trend toward improved survival for patients with HRR gene alterations (HR 0.69; 95% CI, 0.46–1.03; $P = 0.068$)
- No new safety signals were identified – on-target anemia was the most common grade 3/4 AE
- Time to definitive clinically meaningful deterioration in GHS/QoL was significantly longer with talazoparib plus enzalutamide versus placebo plus enzalutamide

Talazoparib in combination with Enzalutamide is now approved for 1st line pts with mCRPC and HRR gene alterations by the FDA (June 20, 2023)

Agarwal N et al, Lancet, 2023 Jul 22;402(10398):291-303.

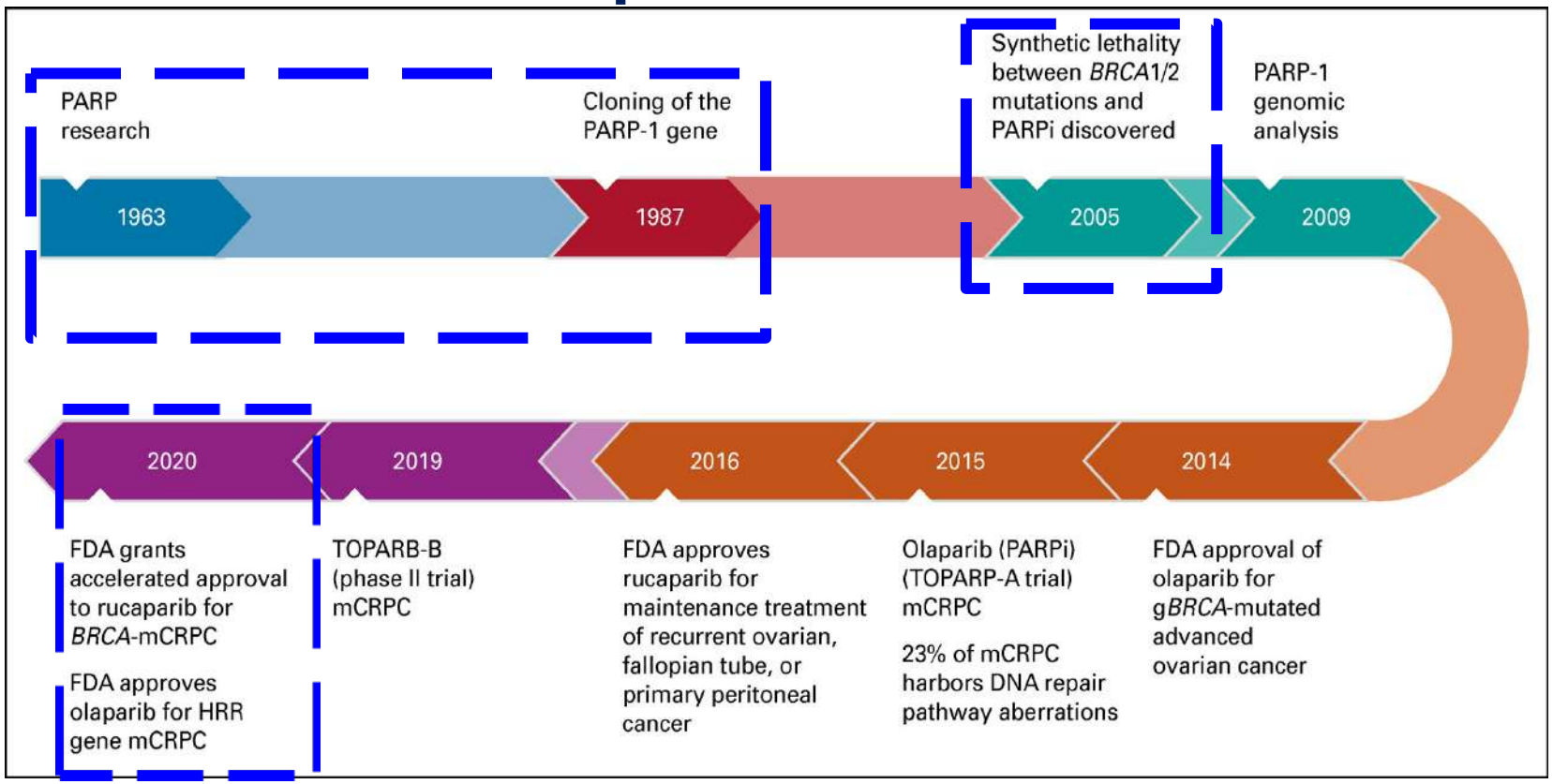
Timeline of PARPi approval for mCRPC illustrating PARP milestones and prostate cancer milestones

December 21, 2022 EMA grants approval for **Olaparib** and abiraterone and prednisone (or prednisolone) for **mCRPC**

May 13, 2023 FDA grants approval for **Olaparib** and abiraterone and prednisone (or prednisolone) for **BRCA-mutated mCRPC**

June 20, 2023 FDA grants approval of **Talazoparib** and enzalutamide for **HRR gene mutated mCRPC**

August 1, 2023 FDA grants approval for fixed-dose combination of **Niraparib** and abiraterone acetate for **BRCA-mutated mCRPC**



HRR, homologous recombination repair; mCRPC, metastatic castration-resistant prostate cancer; PARP, poly (ADP-ribose) polymerase; PARPi, poly (ADP-ribose) polymerase inhibition.

von Werdt A et al, JCO Precision Oncology 2021 51639-1649

Prostate-Specific Membrane Antigen

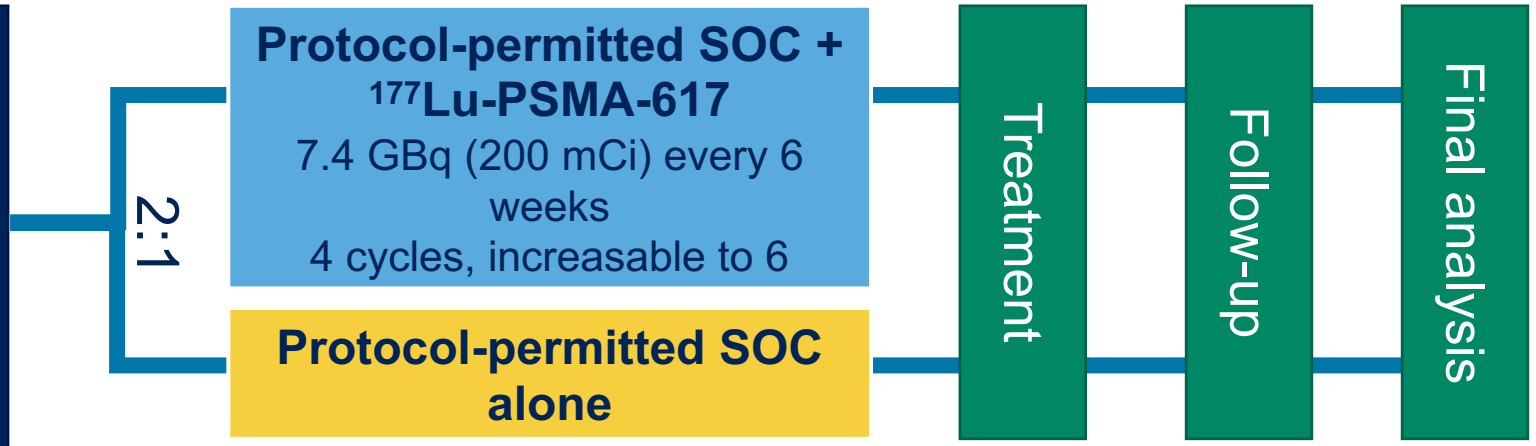
“PSMA is the single most well-established, prostate-restricted, cell membrane target known”

- Luminal expression proximal renal tubules, brush border small intestine, salivary and lacrimal glands (+ neovasculature of most solid tumors)
- Prognosis to PSMA directed RT correlates with PSMA expression intensity
- Heterogeneously expressed in prostate cancer
  - Intratumoral
  - across metastases in the same patient

Open-label study of protocol-permitted standard of care ± ^{177}Lu-PSMA-617 in adults with PSMA-positive mCRPC

Eligible patients

- Previous treatment with both
  - ≥ 1 androgen receptor pathway inhibitor
  - 1 or 2 taxane regimens
- Protocol-permitted standard of care (SOC) planned before randomization
  - Excluding chemotherapy immunotherapy, radium-223, investigational drugs
- ECOG performance status 0–2
- Life expectancy > 6 months
- PSMA-positive mCRPC on PET/CT with ^{68}Ga-PSMA-11

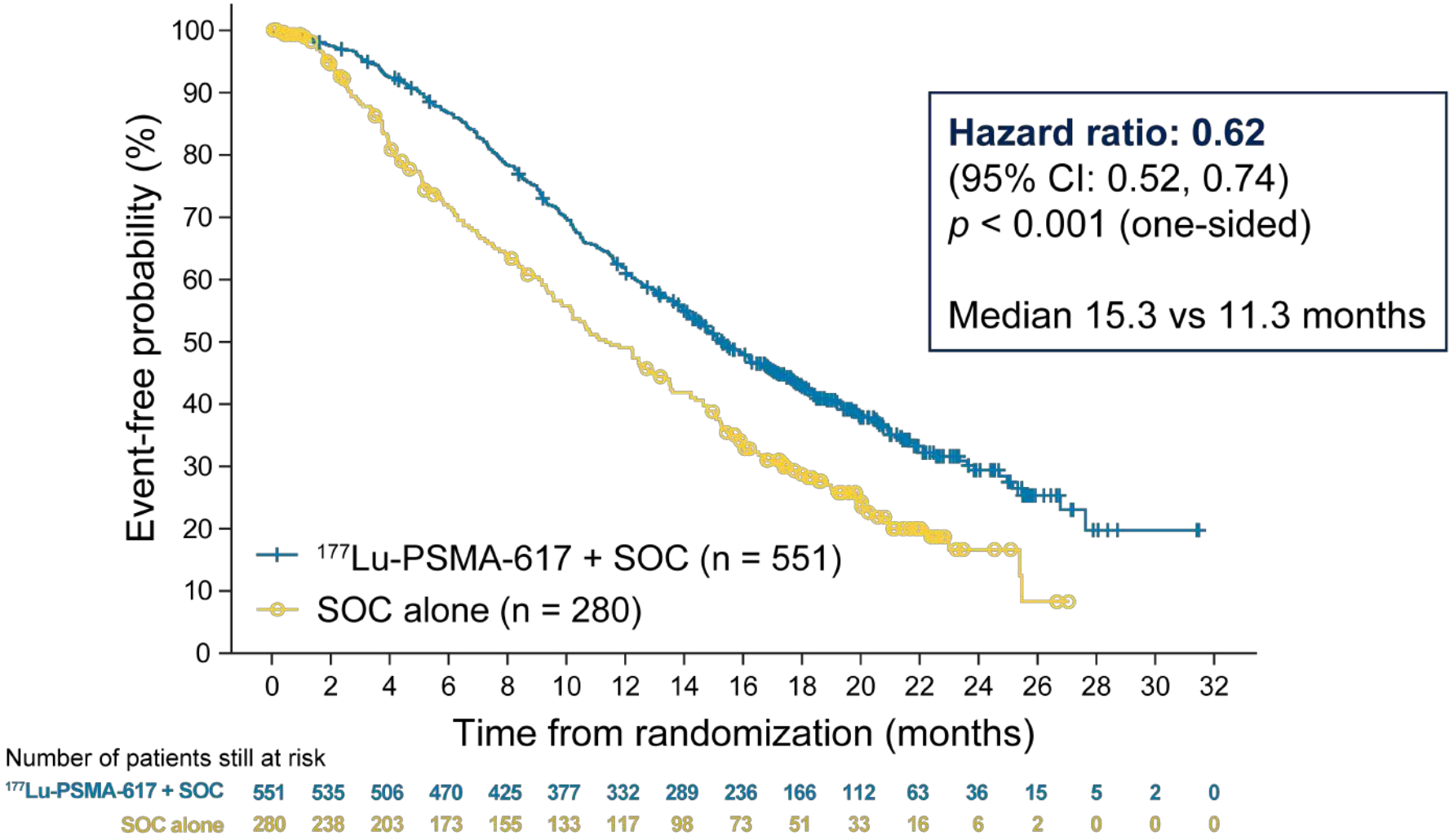


- Randomization stratified by
  - ECOG status (0–1 or 2)
  - LDH (high or low)
  - Liver metastases (yes or no)
  - Androgen receptor pathway inhibitors in SOC (yes or no)
- CT/MRI/bone scans
  - Every 8 weeks (treatment)
  - Every 12 weeks (follow-up)
  - Blinded independent central review

Primary endpoints: ^{177}Lu-PSMA-617 prolonged OS

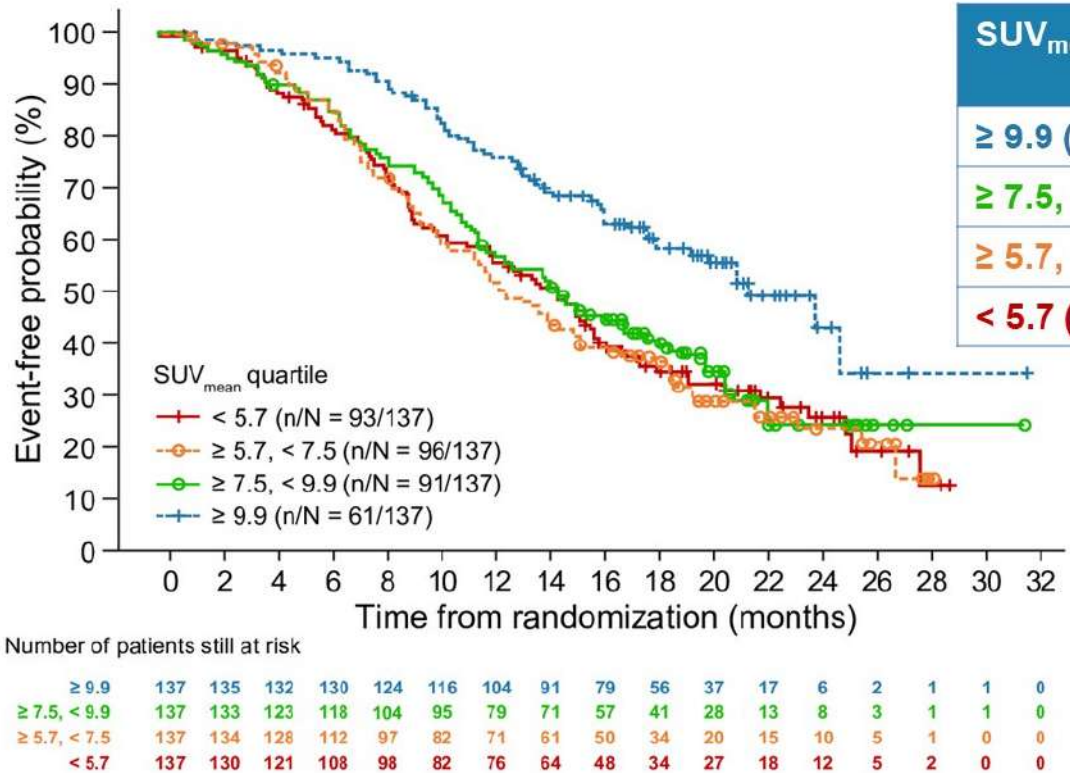
Primary analysis

All randomized patients
(N = 831)



OS by whole-body SUV_{mean} quartiles (FAS)

- **Higher whole-body SUV_{mean} was associated with improved OS**



SUV_{mean} quartile	Median OS (months)
≥ 9.9 (highest)	21.4
≥ 7.5, < 9.9	14.6
≥ 5.7, < 7.5	12.6
< 5.7 (lowest)	14.5

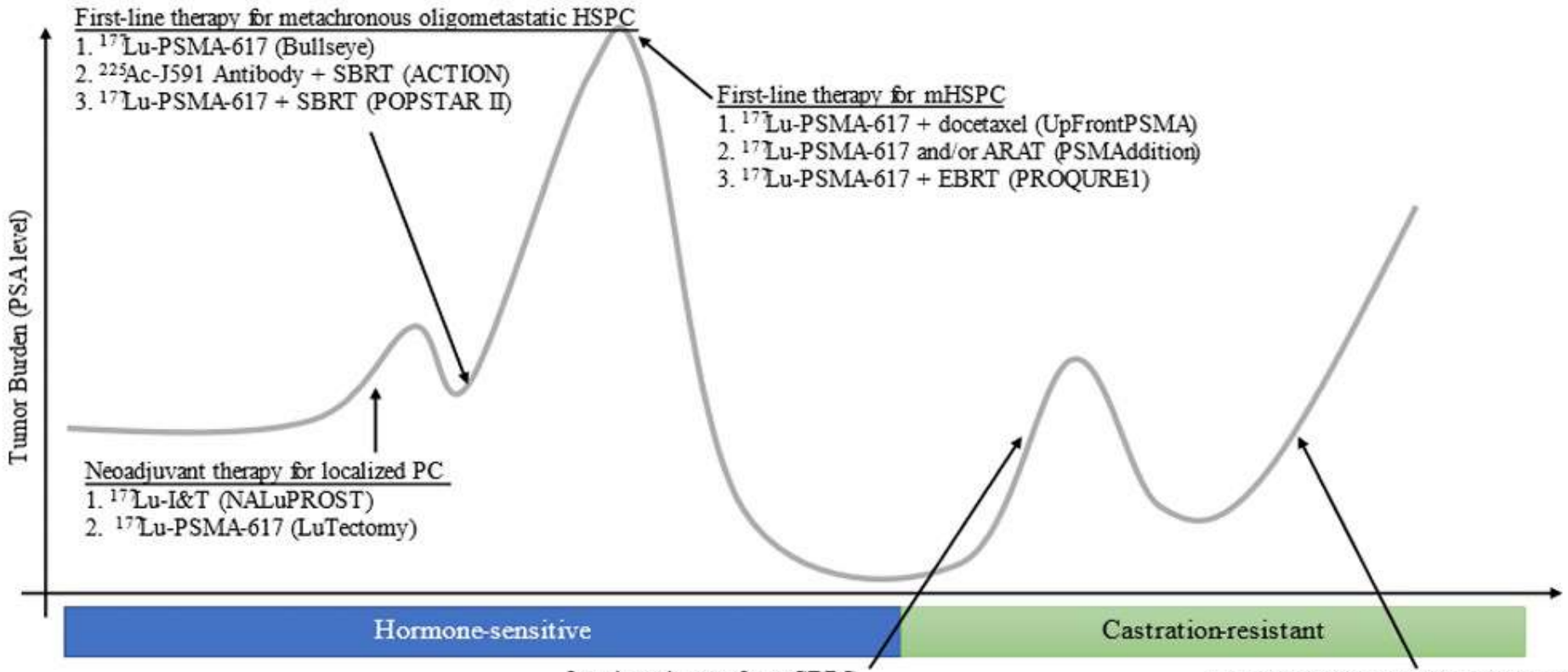
SUV_{mean}	OS HR [95% CI], *p* value
Univariate analysis	**0.92** [0.89, 0.95], < 0.001
Multivariate analysis	**0.88** [0.84, 0.91], < 0.001

CI, confidence interval; HR, hazard ratio; FAS, full-analysis set; OS, overall survival; SUV, standardized uptake value

Theranostics targeting PSMA

- ^{177}Lu-PSMA-617 and ^{177}Lu-PSMA I&T
- J591 PSMA labeled antibody (N. Bander at WCM)
- Isotopes
  - Actinium, lead, copper, terbium
- Combination therapies
  - ARSI, immunotherapy, PARP inhibitors, chemotherapy, radiation
- Prostate cancer states

PSMA Theranostic Trials



β-emitter therapy for mCRPC
1. ^{177}Lu-PSMA-617(LuPSMA, TheraP, VISION, LuCAB)
2. ^{177}Lu-J591
3. ^{177}Lu-PSMA-R2 (PROter)
4. ^{177}Lu-PSMA-617 + pembrolizumab (PRINCE)
5. ^{177}Lu-PSMA-617 + olaparib (LuPARP)
6. ^{177}Lu-PSMA-617 + Enzalutamide (ENZA-P)
7. ^{177}Lu-PSMA 617 + ipilimumab and nivolumab (ANZUP2001)
8. ^{177}Lu-PSMA 617 +abemaciclib (UPLIFT)
9. ^{177}Lu-EB-PSMA
10. ^{177}Lu-HTK03170

α-emitter (and/or β-emitter) therapy for mCRPC
1. ^{227}Th-BAY2315497 Antibody
2. ^{225}Ac-J591 Antibody
3. ^{225}Ac-PSMA-617
4. ^{225}Ac-J591 Antibody+ ^{177}Lu-PSMA-I&T
5. ^{225}Ac-J591 Antibody+ pembrolizumab
6. ^{161}Tb-PSMA-I&T
7. ^{212}Pb-NG001
8. ^{177}Lu-PSMA 617 +^{223}Ra (AlphaBet)

ARAT: androgen receptor axis-targeted therapy agent
PSA: prostate-specific antigen
PC: prostate cancer
HSPC: hormone-sensitive prostate cancer
mHSPC: metastatic hormone-sensitive prostate cancer
mCRPC: metastatic castration-resistant prostate cancer

Hoshi S et al, Curr Oncol. 2023 Aug; 30(8): 7286–7302

Precision Medicine for Prostate Cancer

- Genomic tests have the potential to increase therapeutic options for both localized and advanced prostate cancer patients
- Somatic testing is important given that approximately half of homologous recombination repair (HRR) mutations detected in prostate tumor tissue are germline while the rest are somatic.
- Germline and somatic testing is recommended
- Archived radical prostatectomy specimens are a resource for somatic tissue testing
- Parpi have gained momentum alone and in combination
- Psma Theranostics are a developing resource for pts with PC

Thank you for your attention

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for Precision Medicine