Panel Discussion

Atul Batra
Additional Professor
Medical Oncology
AIIMS, New Delhi

PANELISTS

Dr. Prahalad Elamarthi	Bengaluru	MO
Dr. Sudeep Das	Kolkata	MO
Dr. Niharika Alapati	Vizag	MO
Dr. Madan Maitre	Mumbai	RO
Dr. Varun Shukla	Chandigarh	NM
Dr. Arvind Suresh	Varanasi	NM
Dr. Archi Rungta	Mumbai	GC

mHSPC

ARANOTE Trial- Analysis by Volume

- Contemporary Comparator arm
- Doublet vs Triplet
- Doublet

Combination therapies in mHSPC

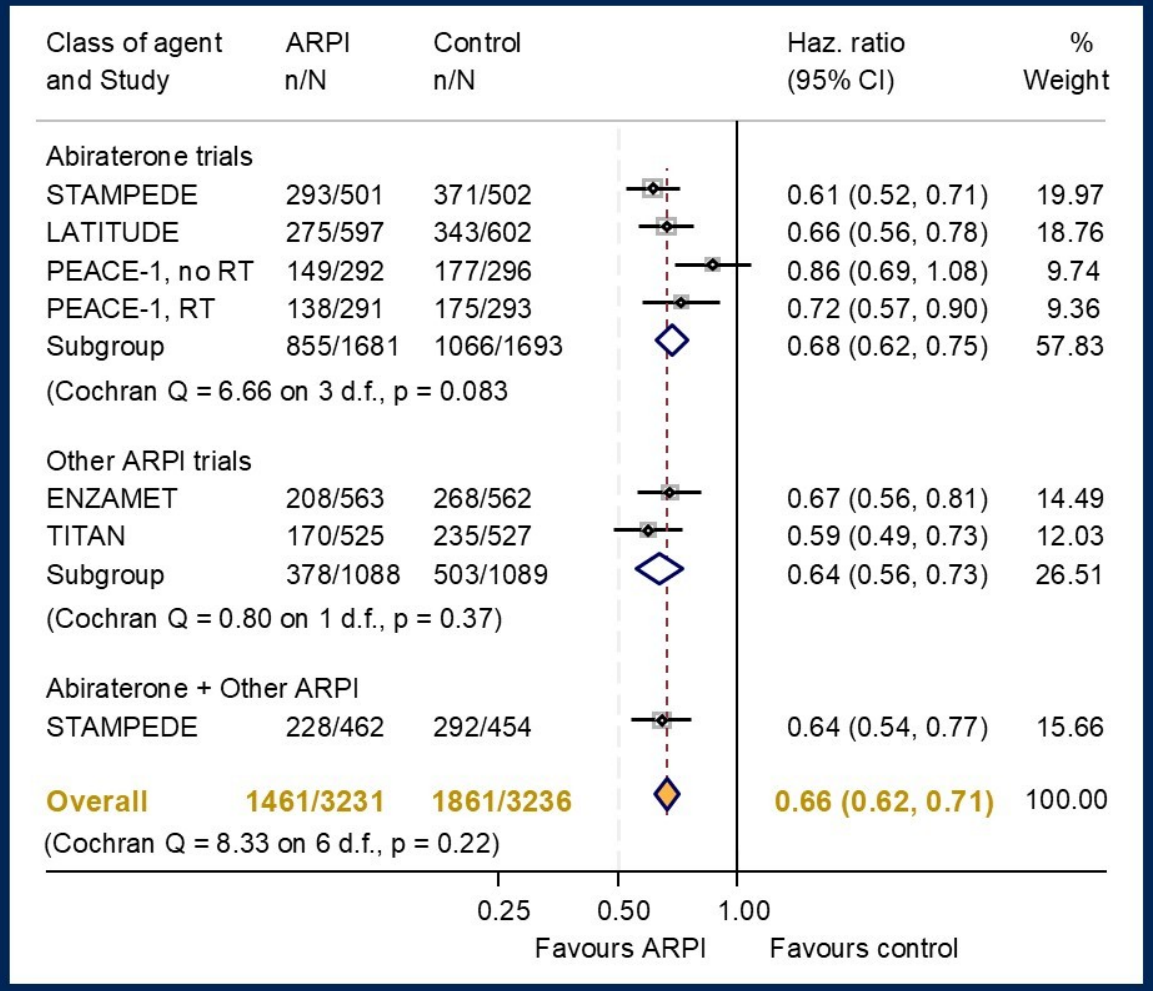
Therapy Combination	Trial Name	Hazard Ratio (HR) for OS	95% Confidence Interval
Docetaxel + ADT	CHAARTED	0.61	0.47–0.80
Abiraterone + Prednisone + ADT	LATITUDE	0.62	0.51–0.75
Enzalutamide + ADT	ARCHES	0.66	0.53–0.81
Apalutamide + ADT	TITAN	0.65	0.53–0.79
Darolutamide + ADT + Docetaxel	ARASENS	0.68	0.57–0.80
Darolutamide + ADT (without docetaxel)	ARANOTE	0.81	0.59–1.12

STOP CAP Meta analysis

- Selection of patients for ARPI

- How to choose patients
  - Age
  - BMI
  - Volume
  - Risk
  - Comorbid conditions
  - Metachronous vs Synchronous

Effects of ARPIs on OS by class of agent



- Clear benefit of ARPIs on OS
  - HR = 0.66 (CI 0.62 to 0.71)
  - 13% absolute improvement at 5 years
- Clear benefit of ARPIs on PFS
  - HR = 0.51 (CI 0.48 to 0.55)
  - 21% absolute improvement at 5 years
- No clear difference by class of agent
  - Based on 48% “amide” data

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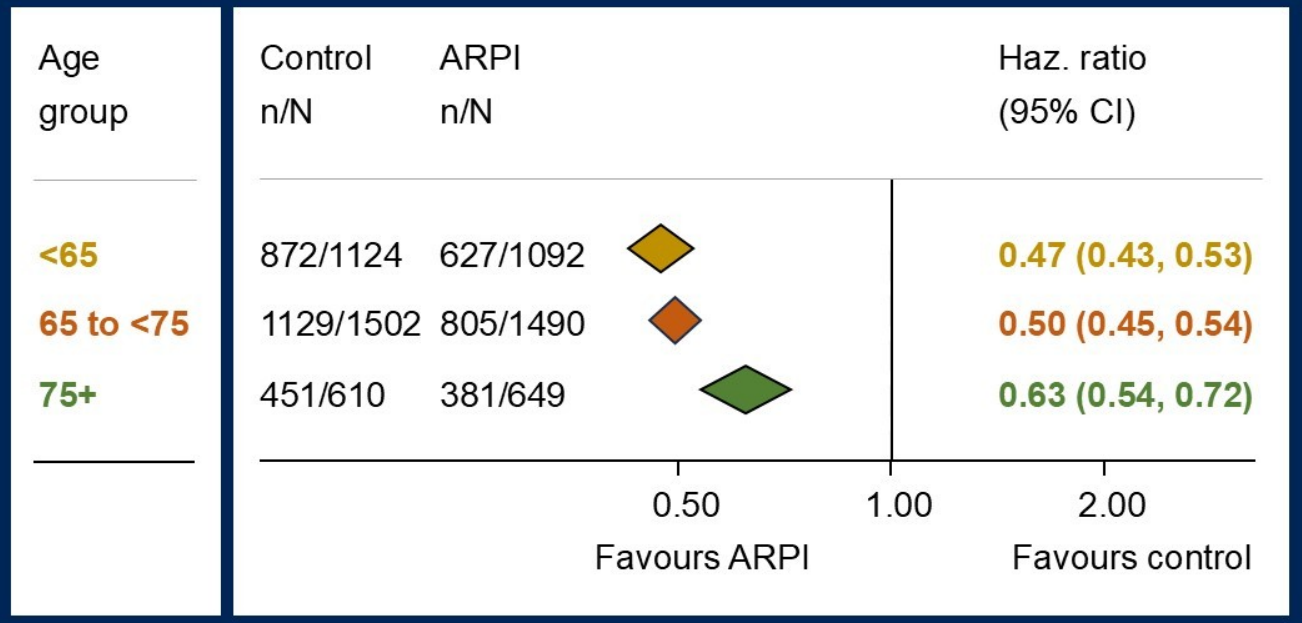
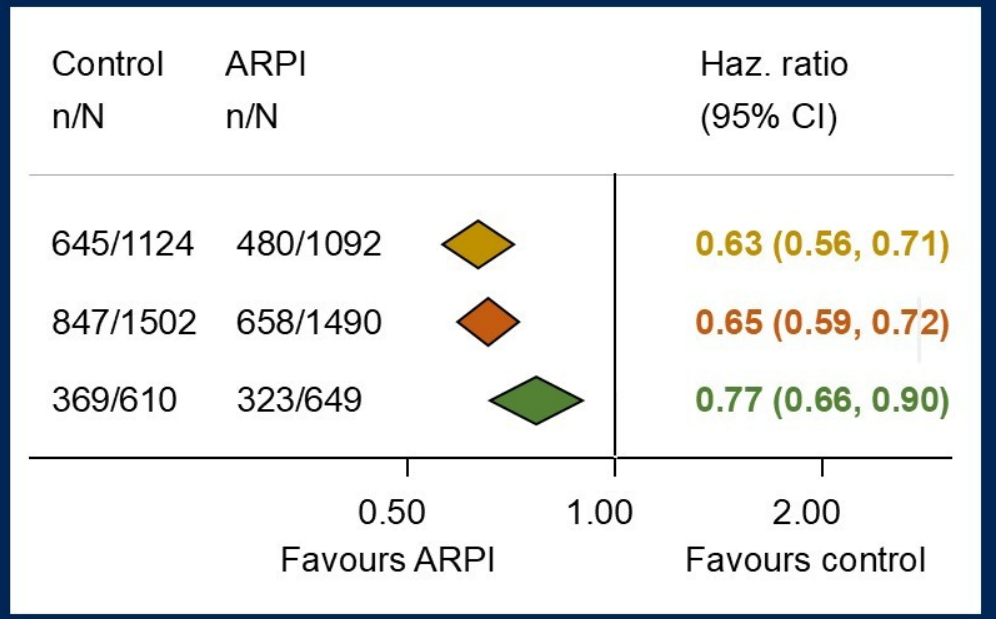
Effects of ARPIs by age group

PFS



OS



75+ vs <65:

Interaction HR=1.32, p=0.003
Heterogeneity p=0.055

Interaction HR=1.22, p=0.052
Heterogeneity p=0.16

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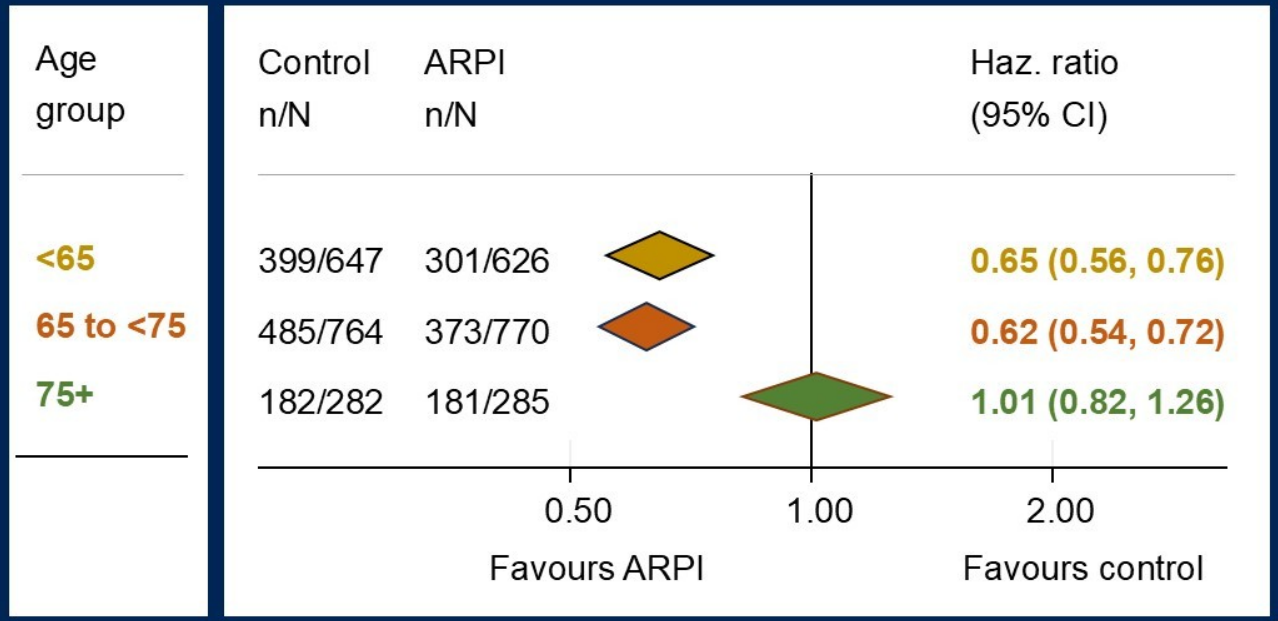
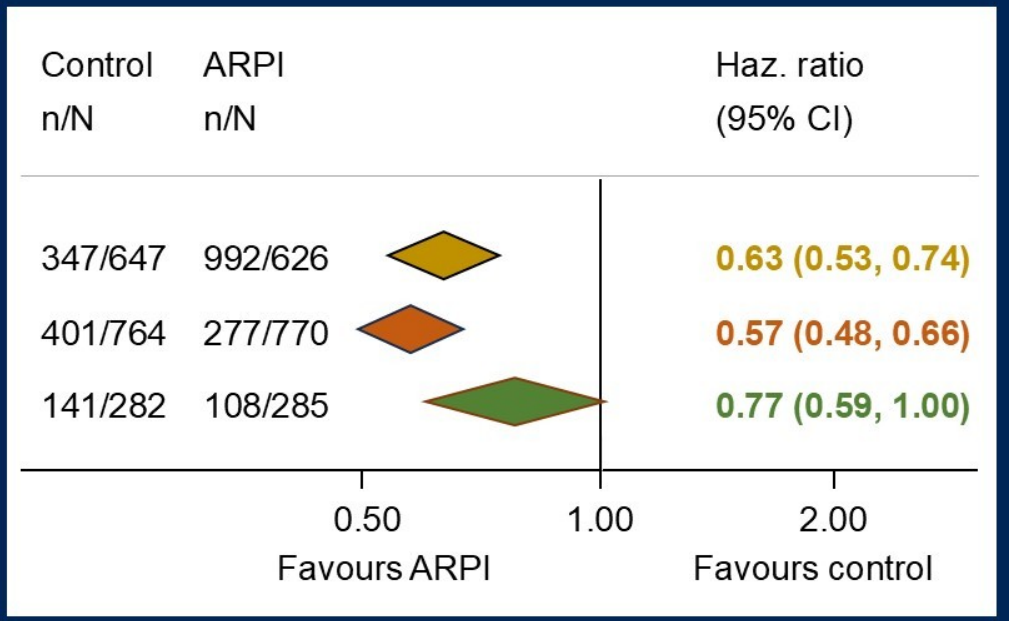
Effects of ARPIs by age group: abiraterone trials

OS



PCSS*



75+ vs <65: Interaction HR=1.56, p=0.001

Interaction HR=1.23, p=0.19

*PCSS=prostate cancer-specific survival

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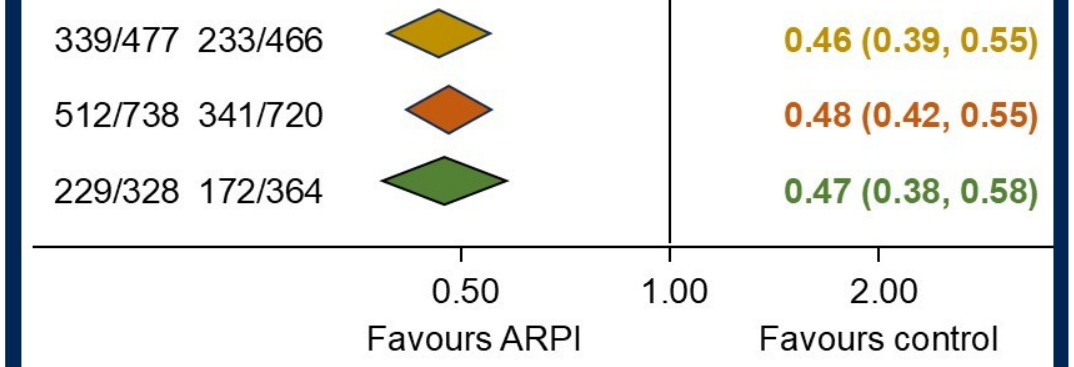
Effects of ARPIs by age subgroup: "amide" trials

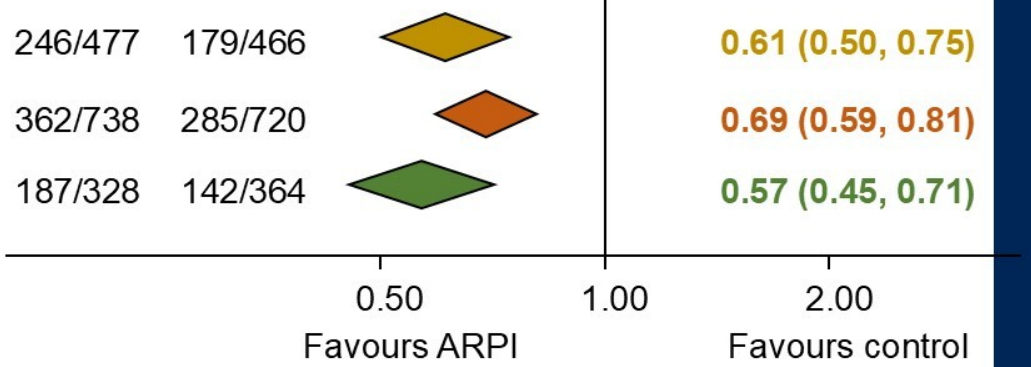
PFS

Age group	Control n/N	ARPI n/N	Haz. ratio (95% CI)
<65	339/477	233/466	0.46 (0.39, 0.55)
65 to <75	512/738	341/720	0.48 (0.42, 0.55)
75+	229/328	172/364	0.47 (0.38, 0.58)



OS

Control n/N	ARPI n/N	Haz. ratio (95% CI)
246/477	179/466	0.61 (0.50, 0.75)
362/738	285/720	0.69 (0.59, 0.81)
187/328	142/364	0.57 (0.45, 0.71)



75+ vs <65: Interaction HR=1.02, p=0.88 Interaction HR=0.93, p=0.61

Note: 48% available data at present

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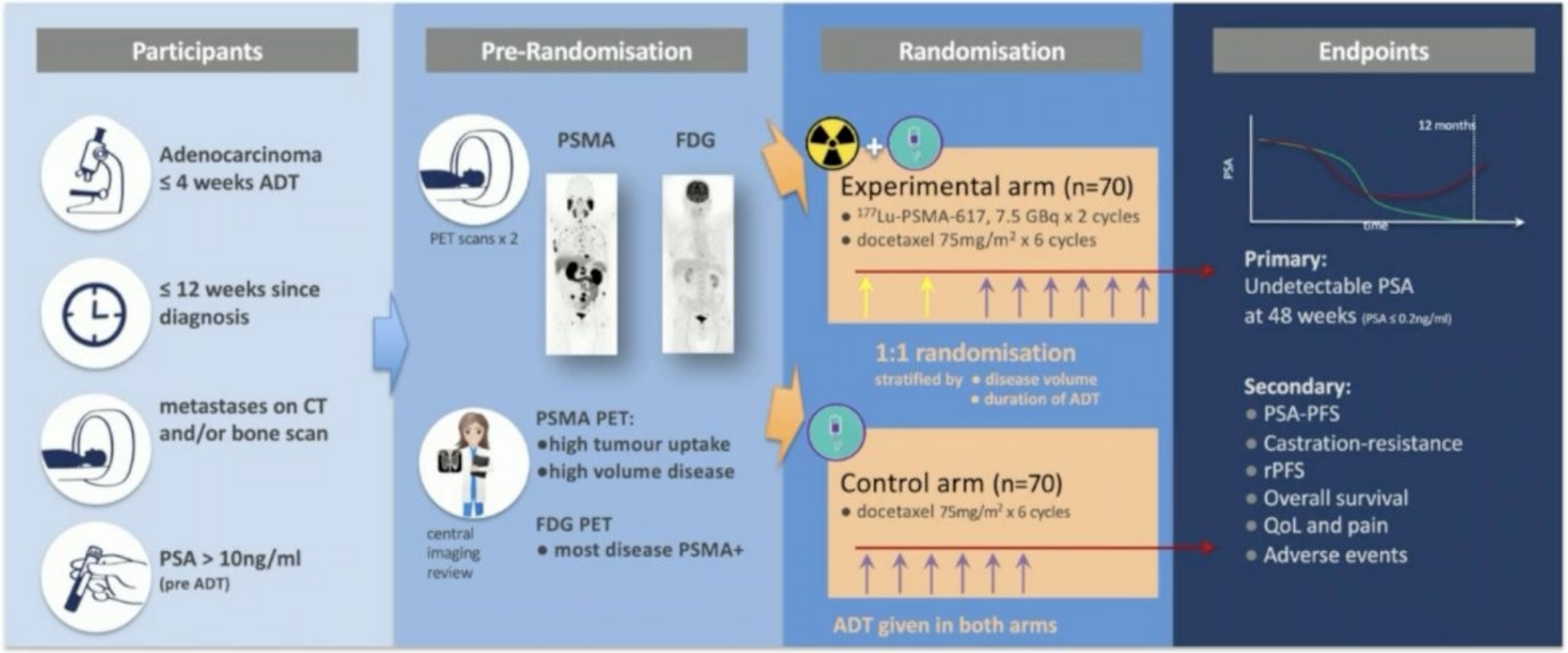
Choosing treatment for mHSPC

- ADT alone
- ADT plus ARPI
- ADT plus Docetaxel
- ADT plus Docetaxel Plus ARPI

- Germline: For all?
- What genes to be included?
- Somatic testing?

UpfrontPSMA



UpfrontPSMA

- Any candidate for this approach

Choosing treatment for mHSPC

- ADT alone
- ADT plus ARPI
- ADT plus Docetaxel
- ADT plus Docetaxel Plus ARPI
- ADT plus Docetaxel plus Lu-PSMA

Consolidation RT (PROLONG study)

- 4 subsets
  - Denovo
  - OligoPD
  - Oligorecurrent
  - Oligopersistent

- Single centre
- Upto 10 sites

Panelists

- Upto 3 or 5
- Prostate or all sites
- Or location- Low volume or Low risk
- When to give – 6 months?/ Upfront
- Response-based selection?

mCRPC

ASCO 2024: PLATIPARP: A Phase 2 Study of Induction Docetaxel and Carboplatin Followed by Maintenance Rucaparib in Treatment of Patients with mCRPC with Homologous Recombination DNA Repair Deficiency

mCRPC with HRR mutation

- PARPi
- PARPi plus ARPI
- Carboplatin f/b PARPi
- Doublet chemo x 4 cycles f/b PARPi

Significant message: Test for resistance

BRCA1/2/PALB2 only

Overall survival and quality of life with [^{177}Lu]Lu-PSMA-617 plus enzalutamide in metastatic castration-resistant prostate cancer (ENZA-p): secondary outcomes from an open-label, multicentre, randomised, phase 2 trial

ENZA-P

Louise Emmett, Shalini Subramaniam, Megan Crumbaker, Andrew Nguyen, Anthony M. Joshua, Andrew J. Weickhardt, Sze-Ting Lee, Siobhan Ng, Roslyn J. Francis, Jeffrey C. Goh, David A. Pattison, Thean Hsiang Tan, Ian D. Kirkwood, Shahneen Sandhu, Alison Yan Zhang, Michael S. Hofman, Hayley Thomas, Andrew J. Martin, Ian D. Davis* & Martin R. Stockler*

Clinicaltrials.gov NCT04419402

NHMRC Clinical Trials Centre

ANZUP Cancer Trials Group Limited

ASCO Genitourinary Cancers Symposium #GU25

PRESENTED BY: Prof Louise Emmett #ENZAp

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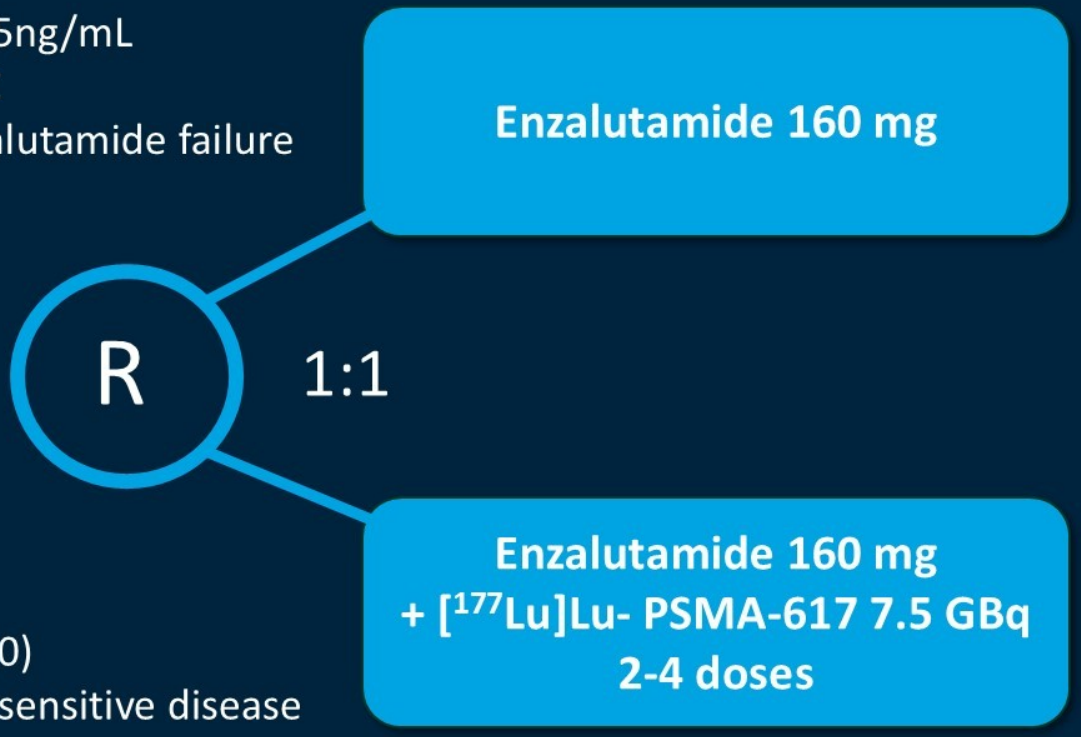
ENZA-p Schema

Eligibility

mCRPC with PSA rising and >5ng/mL
No chemotherapy for mCRPC
≥2 risk features for early enzalutamide failure
Positive ^{68}Ga PSMA PET/CT



Stratification

Study Site
Volume of disease (>20 vs ≤20)
Early docetaxel for hormone-sensitive disease
Prior treatment with abiraterone

Objectives

PSA-PFS (primary endpoint)
Overall survival
Health-related Quality of Life
Radiographic PFS
PSA response rate
Pain response and PFS
Clinical PFS
Adverse events
Health economic analyses
Translational/correlative

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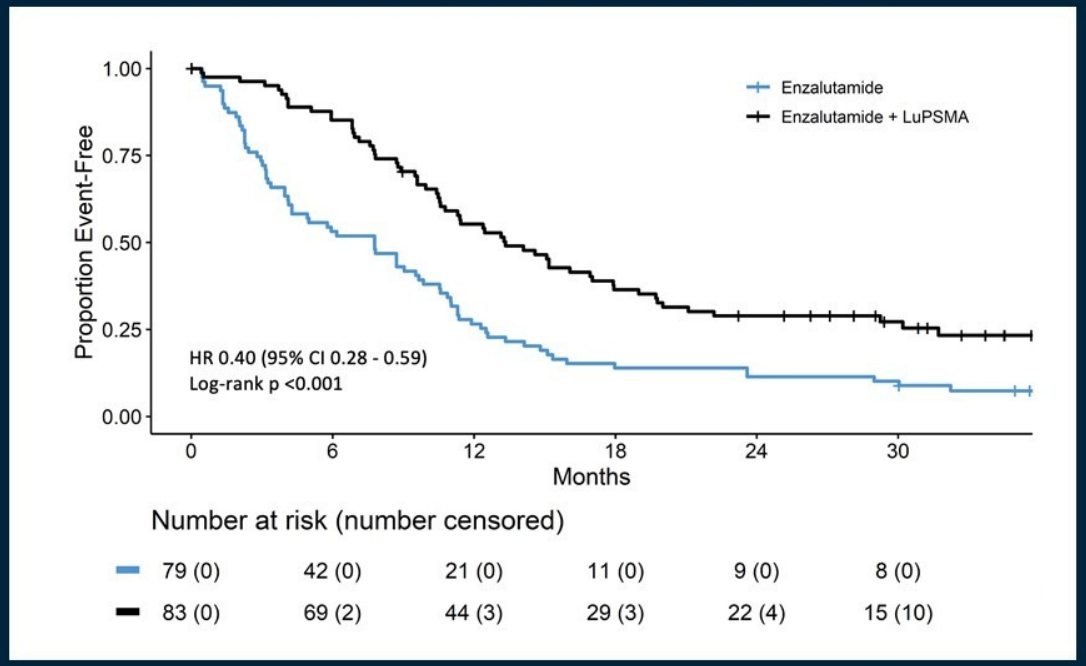
Progression Free Survival

PSA-PFS

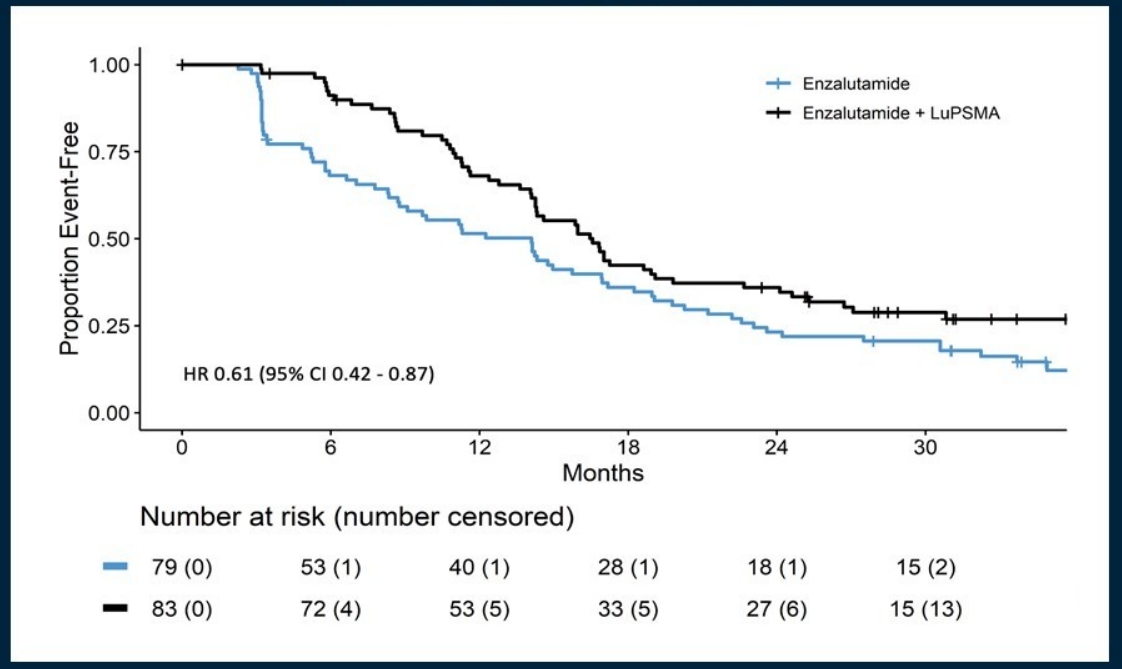
HR 0.40 (95%CI 0.28-0.59) p=0.000001



PSA-PFS	Participants	Events	Censored	Median Months
Enzalutamide	79	73	6	7.8
Enzalutamide+[^{177}Lu]LuPSMA617	83	60	23	13

R-PFS

HR 0.61 (95% CI 0.42-0.87)



R-PFS	Participants	Events	Censored	Median Months
Enzalutamide	79	69	10	14
Enzalutamide+[^{177}Lu]LuPSMA617	83	56	27	17

Lancet Oncol. 2024 May;25(5):563-571

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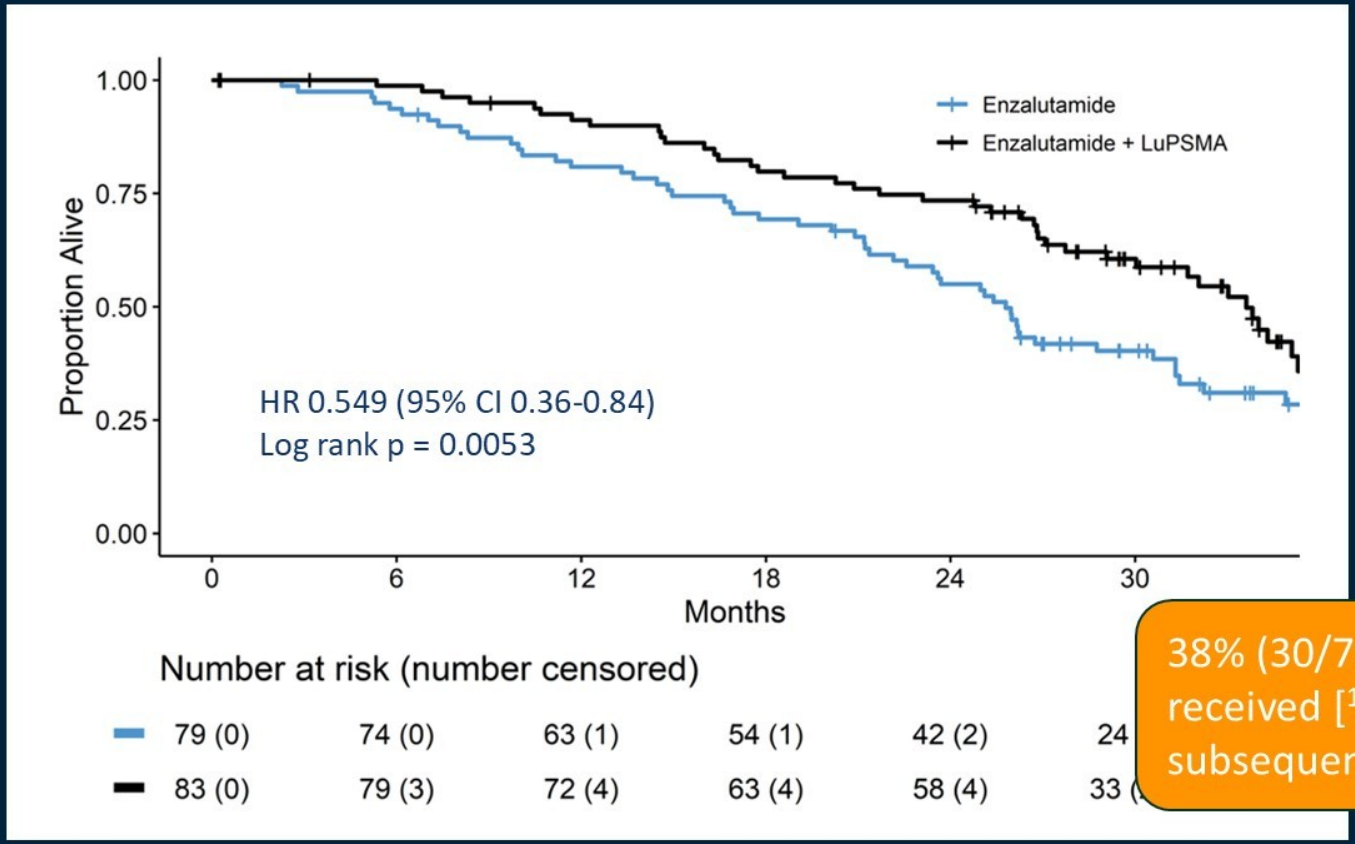
Overall Survival



38% (30/79) on enzalutamide-alone received [^{177}Lu]Lu-PSMA 617 as subsequent treatment off protocol

Overall Survival	Participants	Events	Censored	Median Months
Enzalutamide	79	53	26	26 (C195% 23-31)
Enzalutamide + Lu-PSMA 617	83	43	40	34 (CI95% 30-37)

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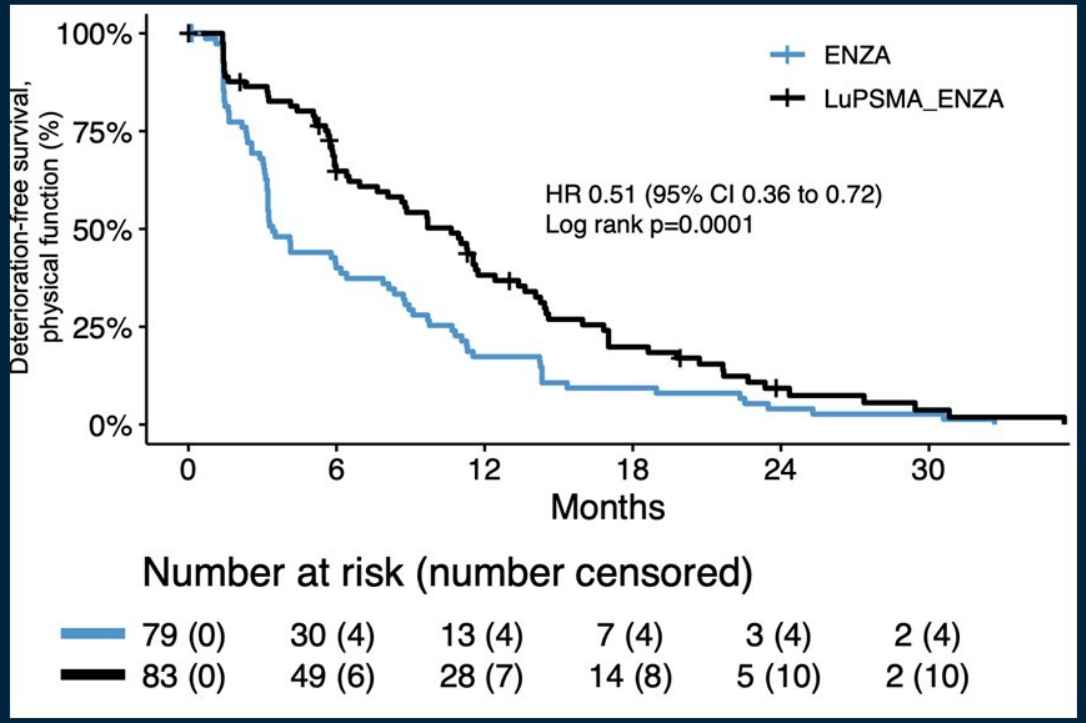
Deterioration-Free Survival

Physical Function

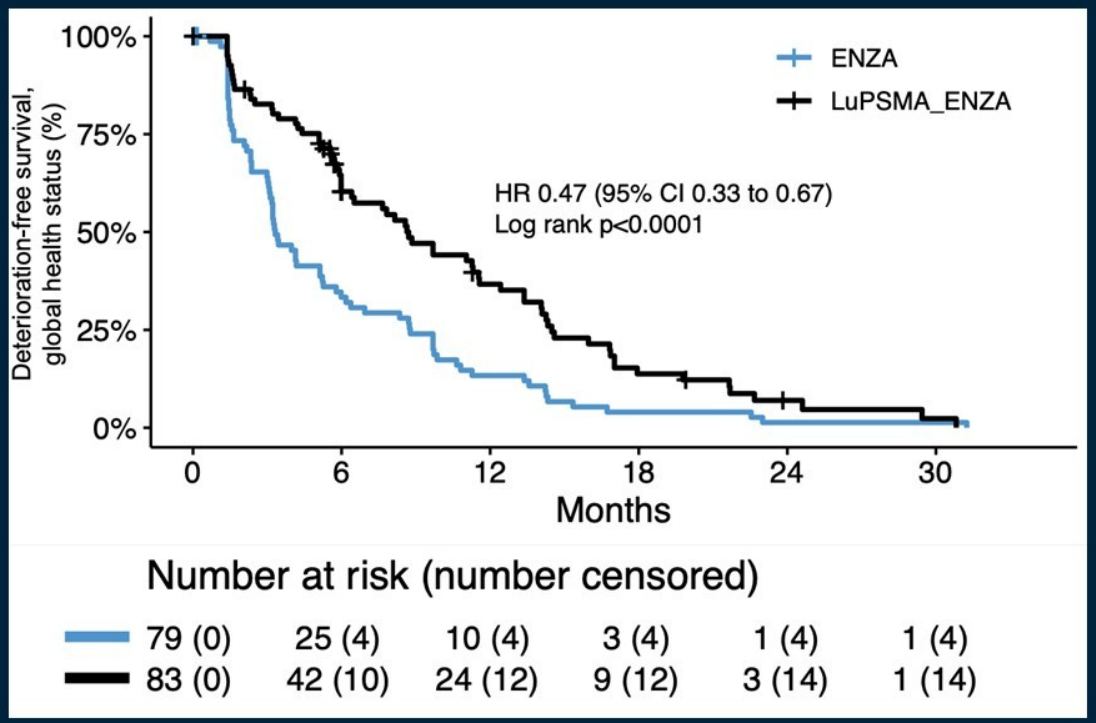
HR 0.51 (95%CI 0.36-0.72)



Physical Function	Participants	Median Months
Enzalutamide	79	3.4 (3.2-7.9)
Enzalutamide + Lu-PSMA 617	83	10.6 (7.7-12.4)

Overall Health Status

HR 0.47 (95%CI 0.33-0.67)



Overall Health Status	Participants	Median Months
Enzalutamide	79	3.3 (3.1-5.3)
Enzalutamide + Lu-PSMA 617	83	8.7 (6.4-11.6)

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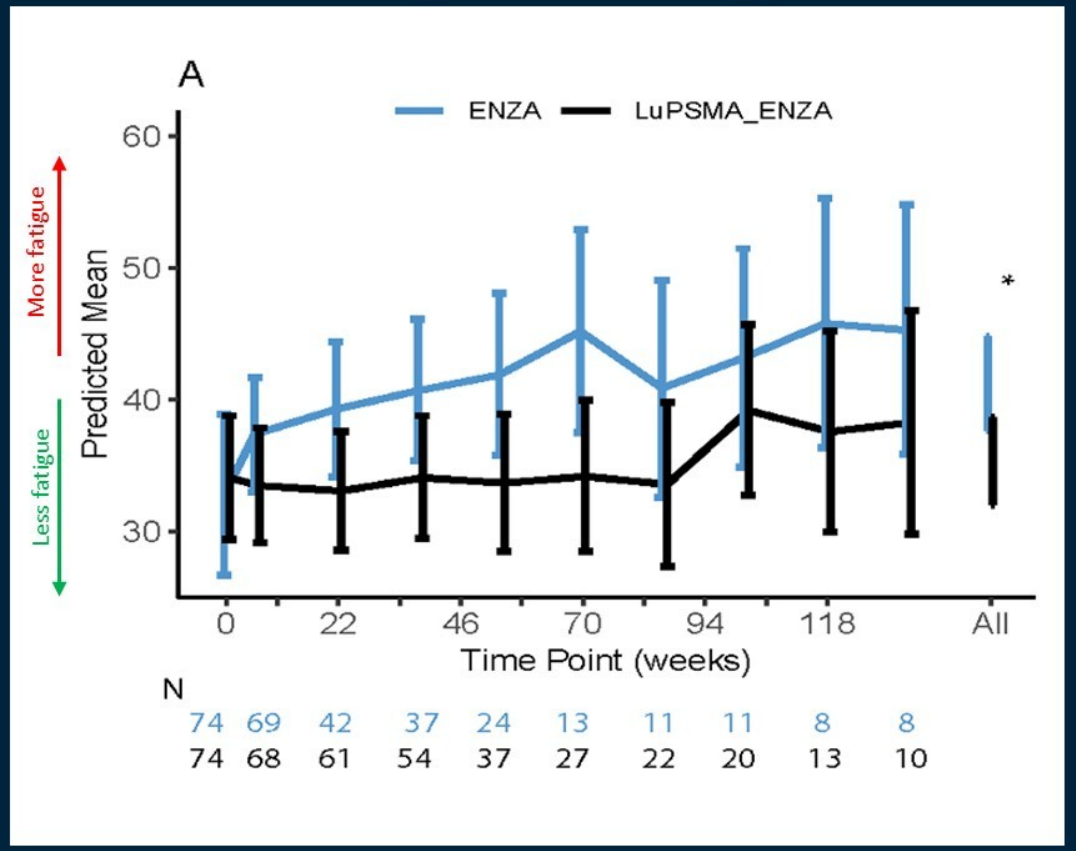
Health-Related Quality of Life

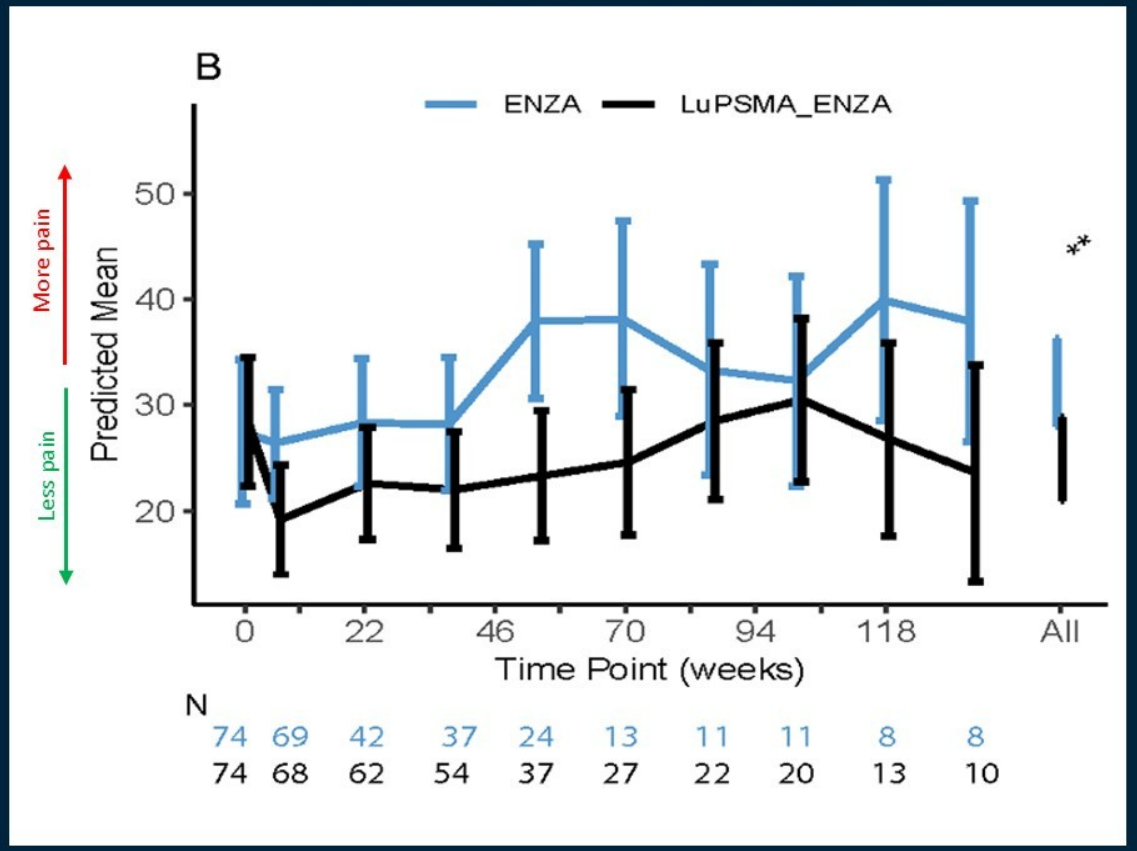
Fatigue

Difference 5.9, 95%CI 1.1 to 11; p=0.02



Pain

Difference 7.3, 95%CI 1.6 to 13; p=0.01



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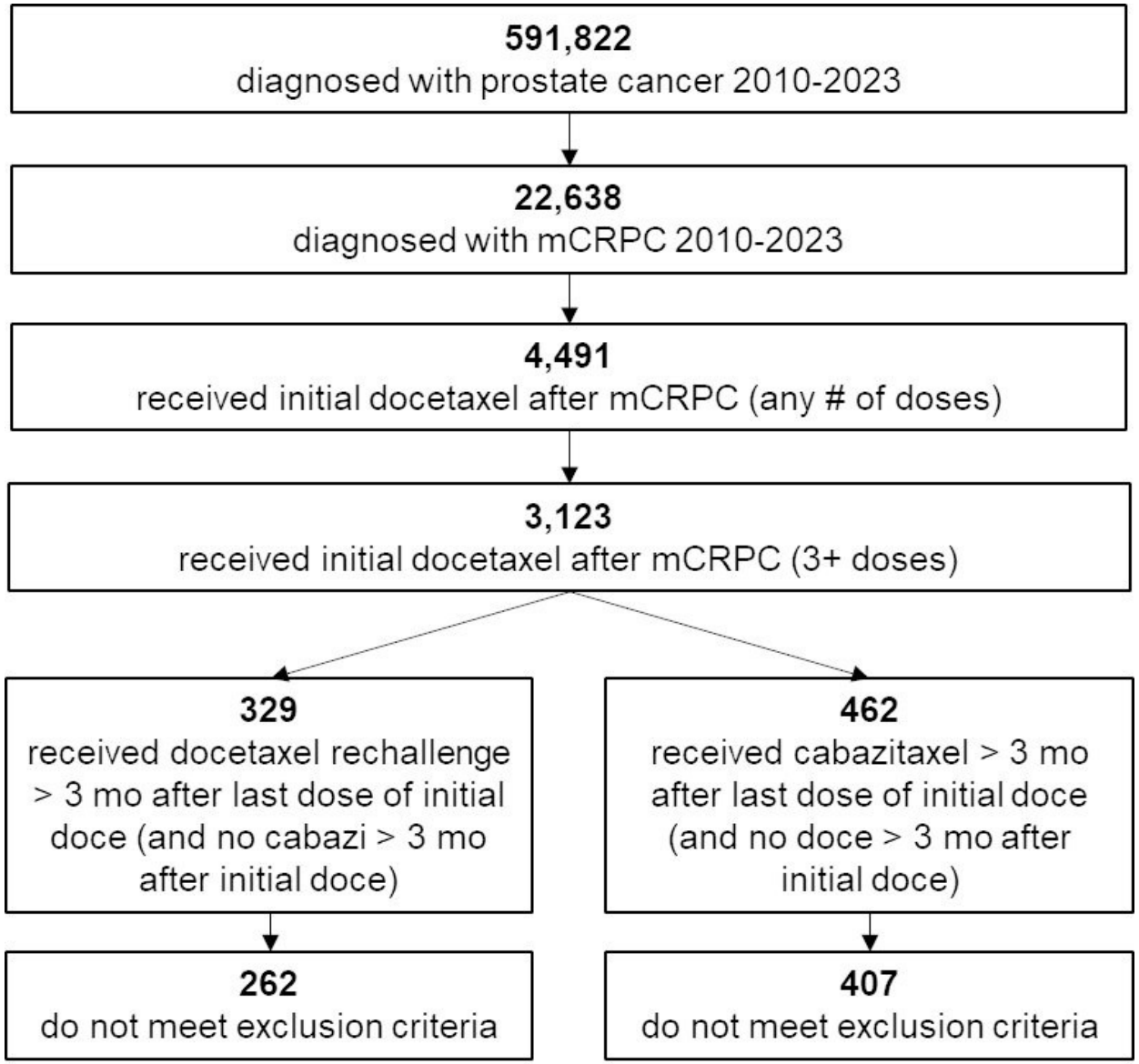
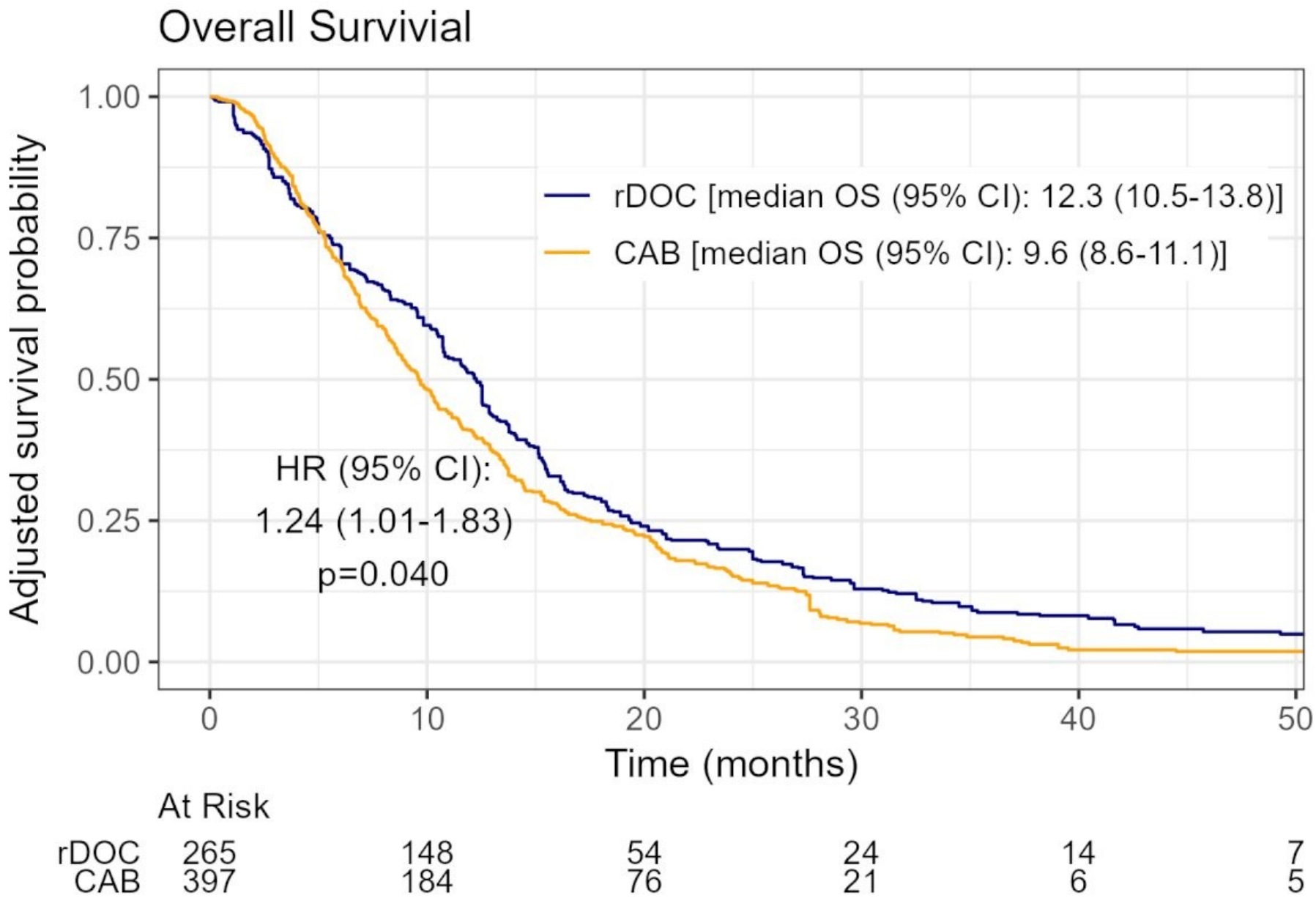
Cabazitaxel vs Docetaxel rechallenge




Overall Survivial
Adjusted survival probability
1.00
0.75
0.50
0.25
0.00
rDOC [median OS (95% CI): 12.3 (10.5-13.8)]
CAB [median OS (95% CI): 9.6 (8.6-11.1)]
HR (95% CI):
1.24 (1.01-1.83)
p=0.040
0
10
20
30
40
50
Time (months)
At Risk
rDOC 265 148 54 24 14 7
CAB 397 184 76 21 6 5

Inference

- Whom to rechallenge vs Cabazitaxel?

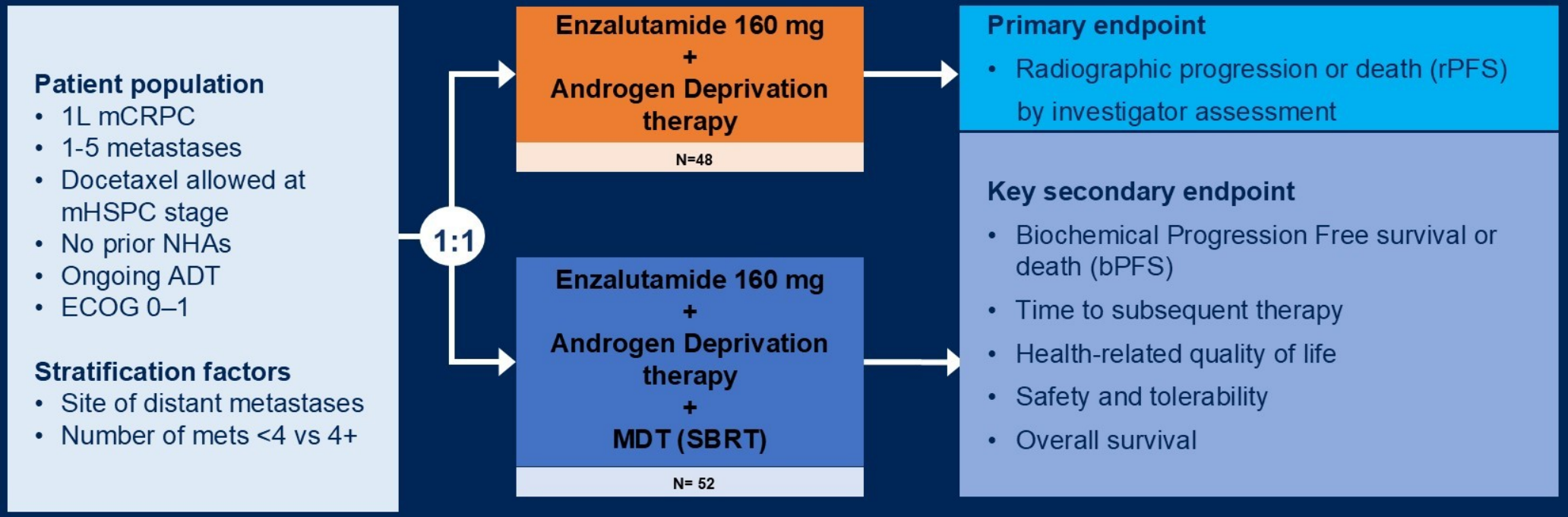
- Docetaxel sensitive vs resistant
  - 12 months
  - 18 months
  - 24 months

Panelists

- Patient received triplet in mHSPC and 12 months later has mCRPC

- Options
  - Cabazitaxel
  - Docetaxel rechallenge
  - LuPSMA therapy
  - LuPSMA plus Enzalutamide
  - ARPI

PCS-9 Study Design



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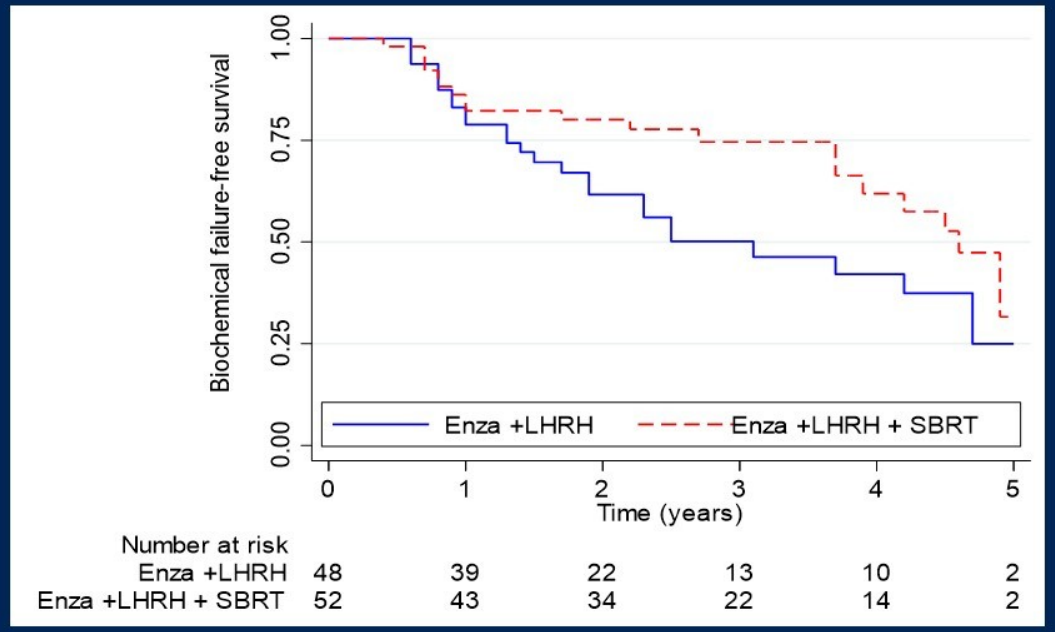
PCS-9 secondary endpoint of interest: bPFS

42% risk reduction of biochemical progression or death with SBRT



	Enza + ADT (n=48)	Enza + ADT + SBRT (n=52)
Events, n (%)	27 (59)	20 (40)
Median bPFS (years)	4.6	3.1
HR (95% CI)	0.58 (0.32–1.03); *P*=0.065	

Pre-specified 2-sided alpha: 0.05

Median bPFS improvement of 1.5 YEARS favors SBRT + Enzalutamide + ADT

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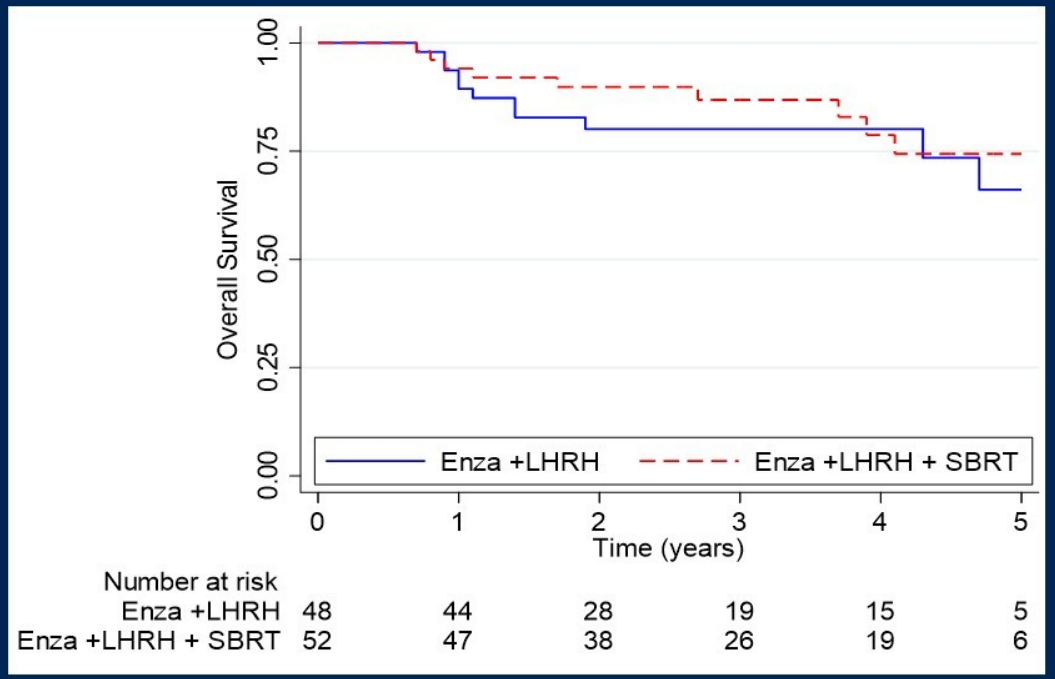
PCS-9 secondary endpoint of interest: Overall Survival

29% risk reduction of death with SBRT



	Enza + ADT (n=48)	Enza + ADT + SBRT (n=52)
Events, n (%)	13 (27)	11(21)
Median OS (years)	NR	NR
HR (95% CI)	0.71 (0.31–1.59); *P*=0.407	

Pre-specified 2-sided alpha: 0.05

Although not statistically significant 29% risk risk reduction of death favors SBRT + Enzalutamide + ADT

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GROUQ-PCS 9

- HR: 0.50 (95% CI: 0.28–0.88), p = 0.017
- 4.6 vs 2.3 years
- Will you start (or have you already started) SBRT in OM-CRPC?

Adjunct therapies

Denosumab dosing interval

- 4 weeks vs 6 weeks ?? Retrospective
- Zoledronate dosing intervals
- 12 weeks

A Prospective Trial of a Structured Exercise Program to Lessen Fatigue in Patients with Advanced Prostate Cancer (aPC) Undergoing Androgen Deprivation Therapy (ADT)

Exercise prescription

- Decreases fatigue
- Needs supervision
- Adherence

Thank you!