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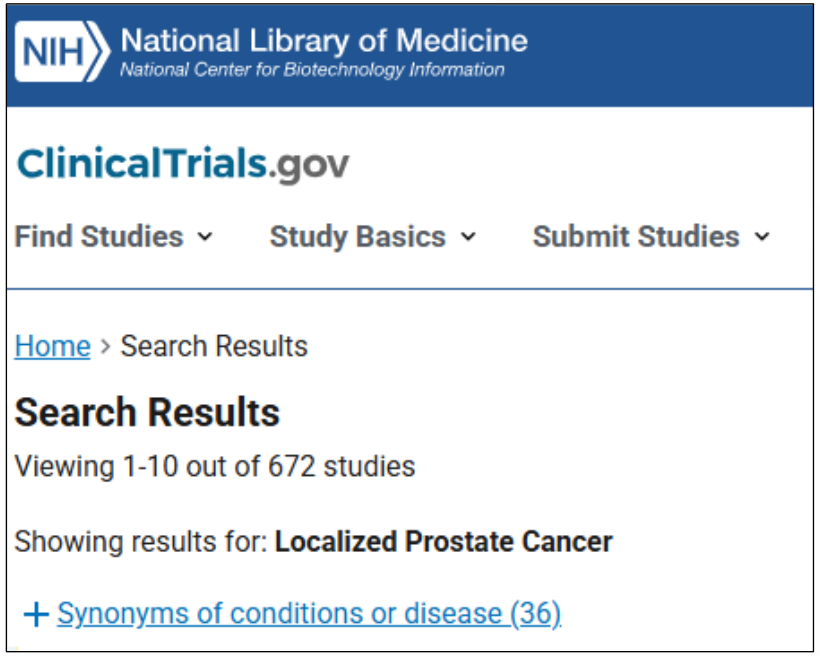
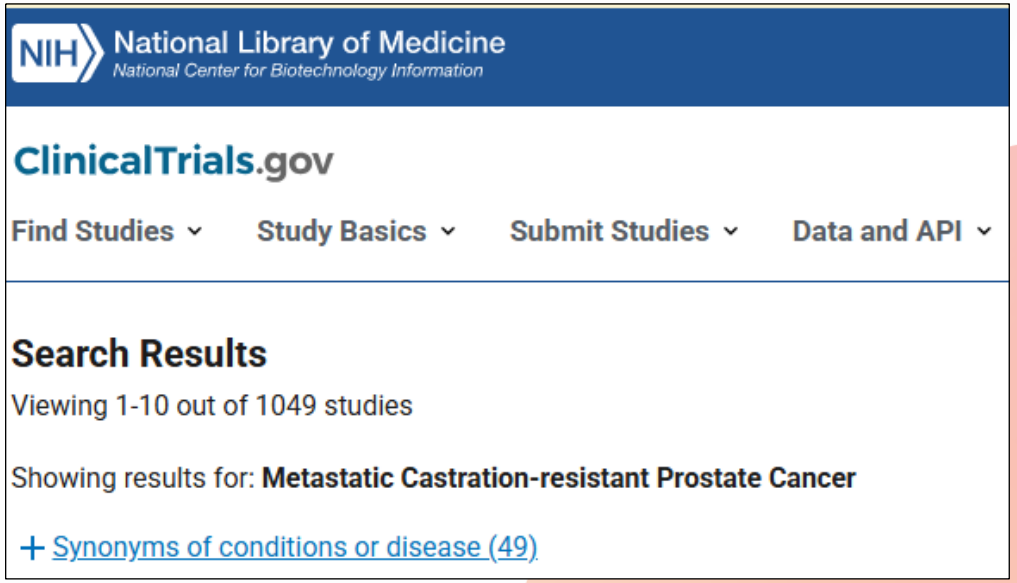
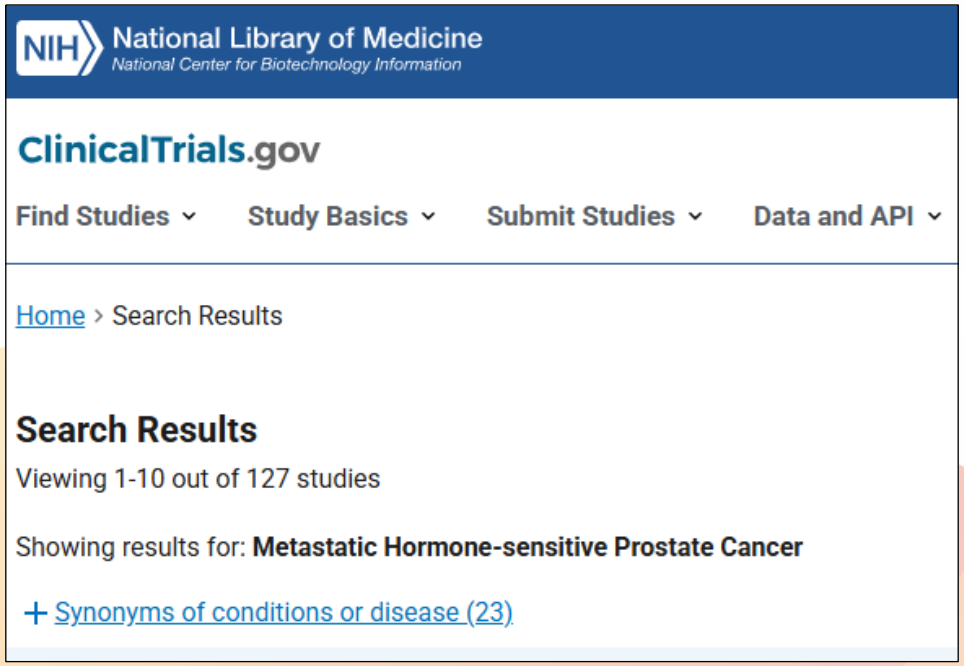
New clinical trials in Prostate Cancer

Alejo Rodriguez-Vida MD PhD

Hospital del Mar Barcelona







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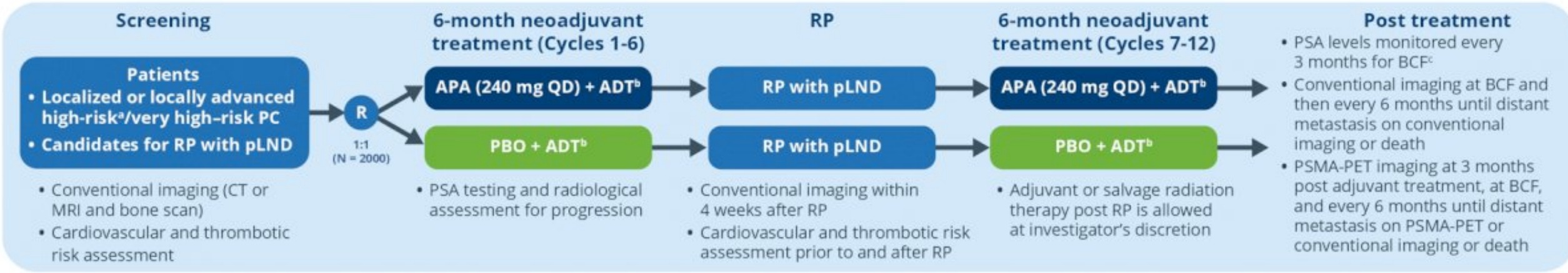
Localized Disease

PROTEUS

A Randomized, Double-Blind, Placebo-Controlled, Phase 3 Trial of **Apalutamide** plus ADT Versus Placebo plus ADT Prior to **Radical Prostatectomy** in Patients with Localized or Locally Advanced High-Risk Prostate Cancer

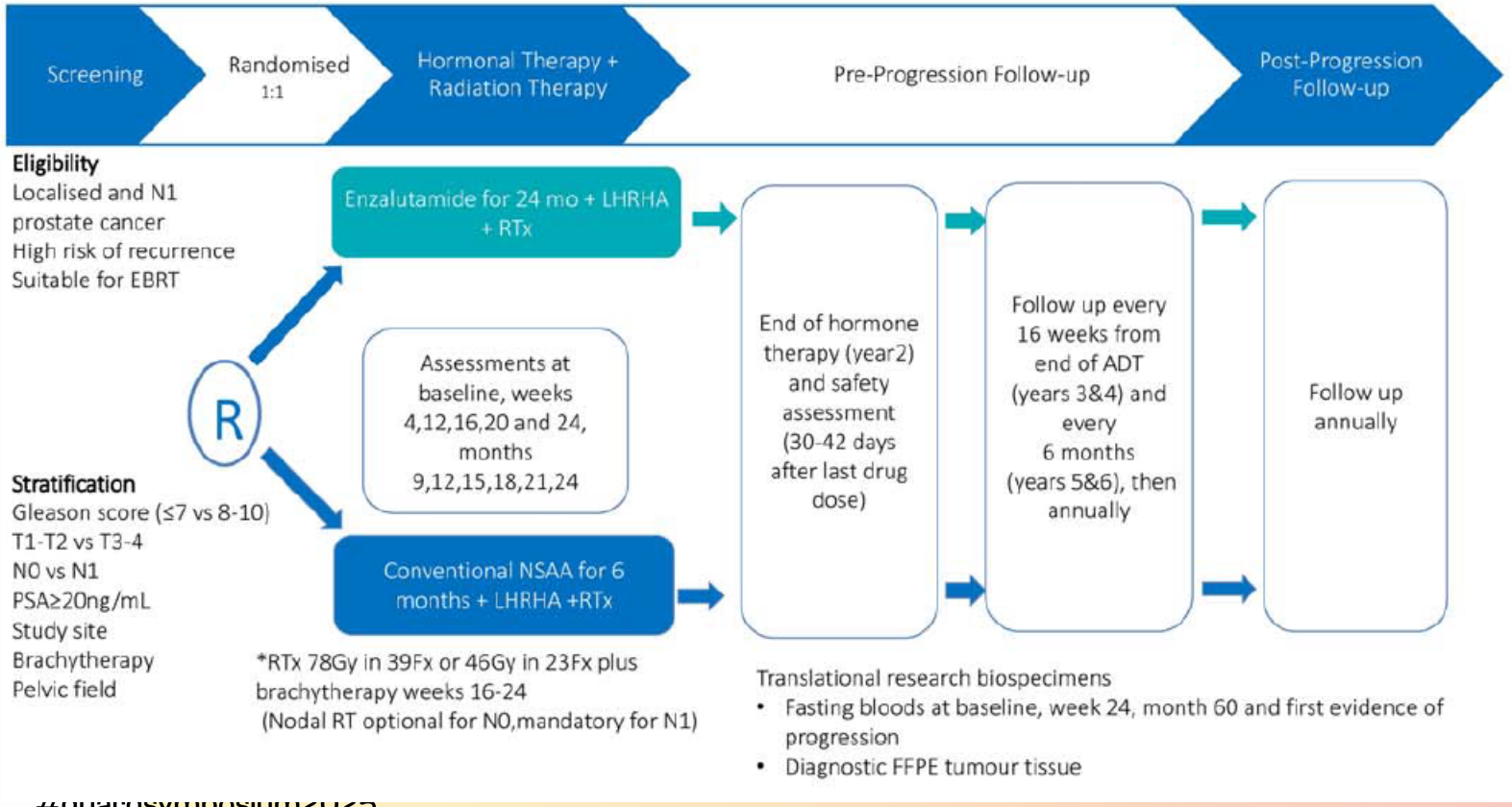


- The primary endpoints are pCR rate and MFS.
- In addition to MFS based on conventional imaging, MFS based on PSMA PET or conventional imaging will be assessed as a separate endpoint

NCT03767244

ENZARAD

Phase 3 Study of **Enzalutamide** Added to ADT in High-Risk or node positive Localized or Locally Advanced Prostate Cancer Prior to **Radical Radiotherapy**



Specific Objectives (Endpoints)

Primary objective (endpoint):

Overall survival (death from any cause)

Secondary objectives (endpoints):

1) Cause specific survival (prostate cancer, and other causes)
2) PSA progression-free survival (Phoenix criteria)
3) Clinical progression free survival
4) Time to subsequent hormonal therapy (restarting ADT)
5)Time to castration-resistant disease (PCWG2 criteria)
6) Metastasis-free survival
7) Adverse events (CTCAE v4.03)
8) Health-related quality of life (EORTC QLQC-30 & PR-25, EQ-5D-5L)
9) Health outcomes relative to costs (incremental cost effectiveness ratio)

Tertiary and correlative objectives (endpoint) :

To identify biomarkers that are prognostic or predictive of response to treatment, safety and resistance to study treatment (association of biomarkers with clinical outcomes).

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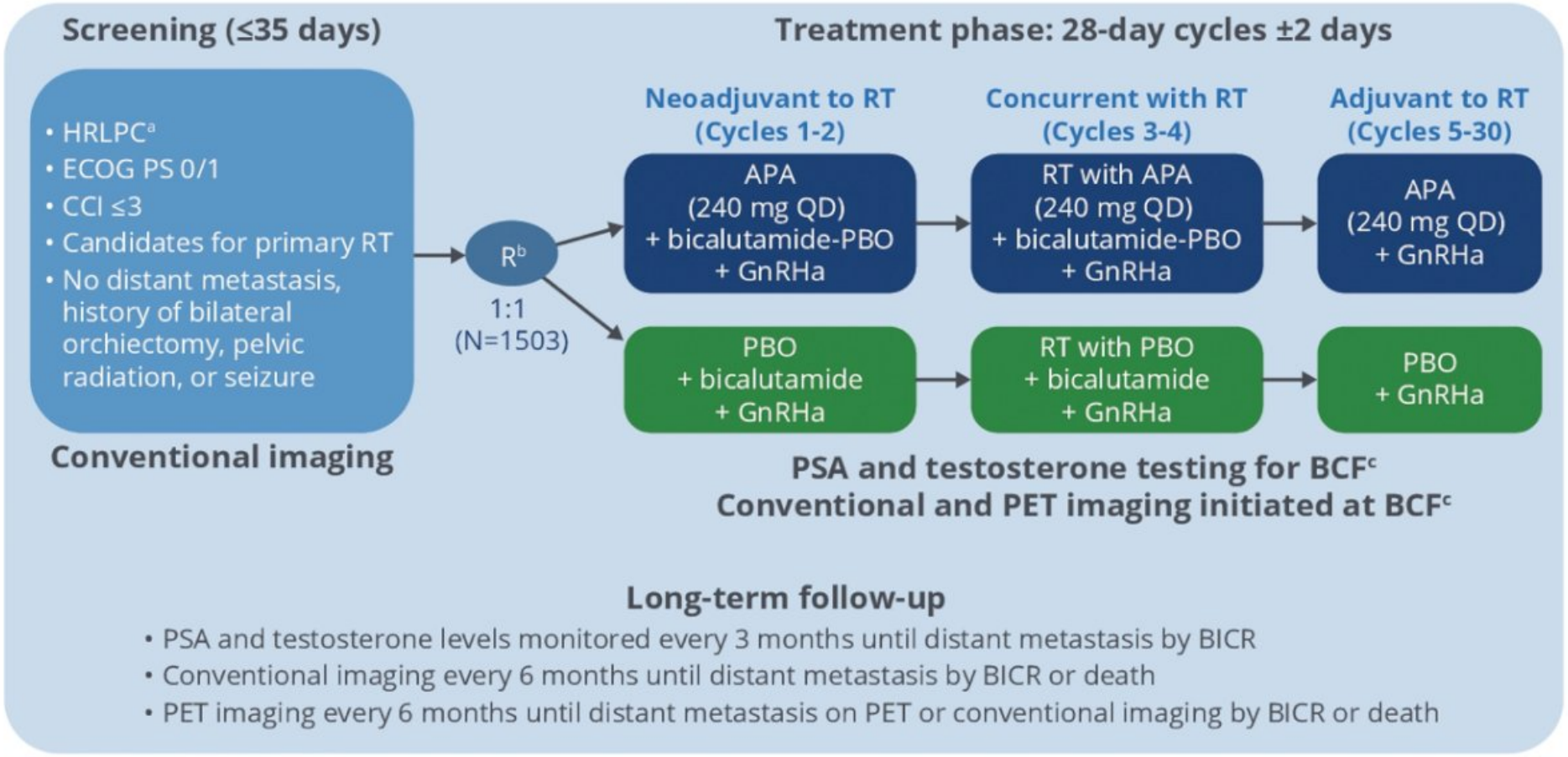
NCT02446444

ATLAS

Phase 3 Double-Blind, Placebo-Controlled Study of **Apalutamide** Added to ADT in High-Risk Localized or Locally Advanced Prostate Cancer Prior to **Radical Radiotherapy**



- Primary endpoint: **MFS**
- Imaging: the protocol has been amended to include PET imaging (PSMA, fluciclovine, or choline)

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NCT02531516

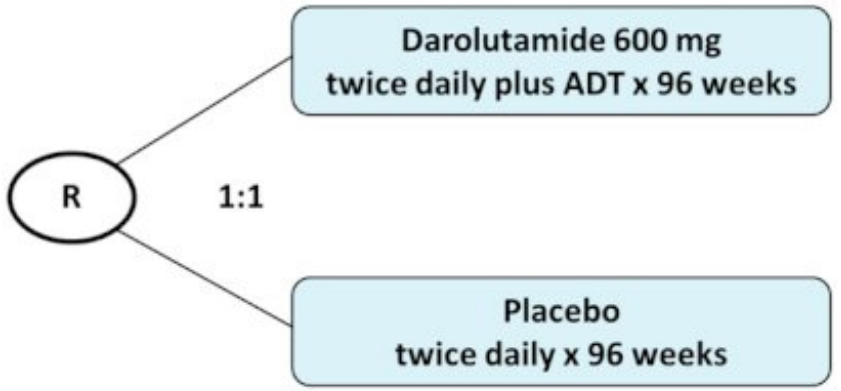
DASL-HiCaP

All participants are also treated concurrently with an LHRHA for 96 weeks post randomization, plus RT starting at week 8-24 post randomization.

Eligibility

- Very high risk localized prostate cancer to be treated with definitive radiation, or

  Very high risk features + PSA persistence/rise within 12 months following radical prostatectomy (RP) to be treated with post RP radiation
- Suitable for EBRT with or without brachytherapy
- CT/MRI and bone scan negative for distant metastases (allow pelvic LN)



Endpoints

Primary
- Metastasis-free survival

Secondary
- Overall survival
- Prostate cancer-specific survival
- PSA-progression free survival
- Time to subsequent hormonal therapy
- Time to castration-resistance
- Frequency and severity of adverse events
- Health-related quality of life
- Fear of cancer recurrence

Exploratory
- Incremental cost-effectiveness
- Prognostic/predictive biomarkers

Statistical analysis

1100 participants:
- 3 years accrual + at least 4 years of additional follow up (until 130 events recorded)
- 80% power to detect: 40% reduction in the hazard for metastasis or death
  - assuming MFS rate at 5 years: 85% in the control group; 90.7% darolutamide group, allowing for interim analysis and missing data

Stratification

1. Previous radical prostatectomy (yes or no)
2. Planned docetaxel use (yes or no)
3. Clinical or pathological pelvic LN involvement (yes or no)

- Early treatment with up to 6 cycles of docetaxel completed at least 4 weeks prior to RT is permitted.
- The primary endpoint is **metastasis-free survival**

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NCT04136353.

PEACE-2

A randomized phase III, factorial design, of **neoadjuvant cabazitaxel** prior to **radical radiotherapy** in patients with localized prostate cancer and high-risk features of relapse), in a 2 by 2 factorial trial.

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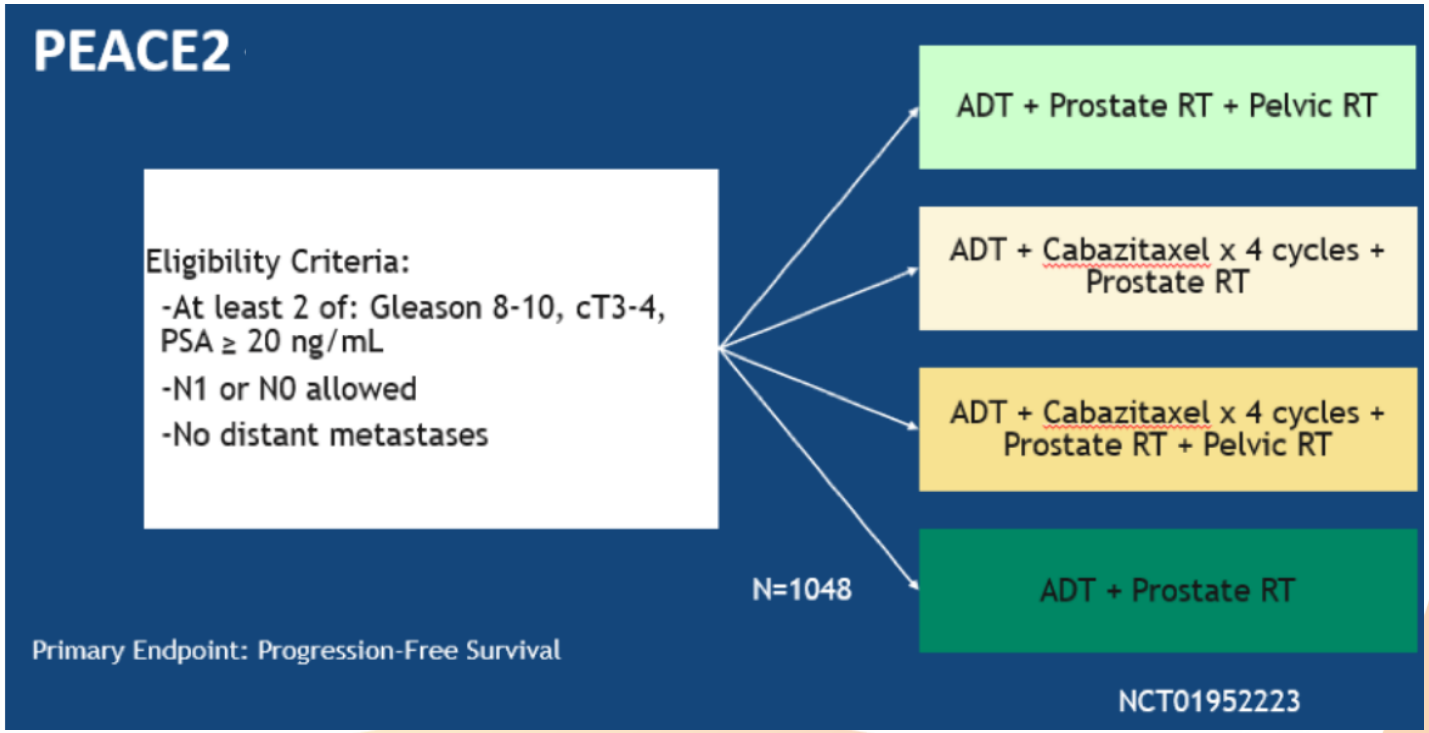


Primary endpoint: **clinical progression-free survival (composite PSA and radiological)**

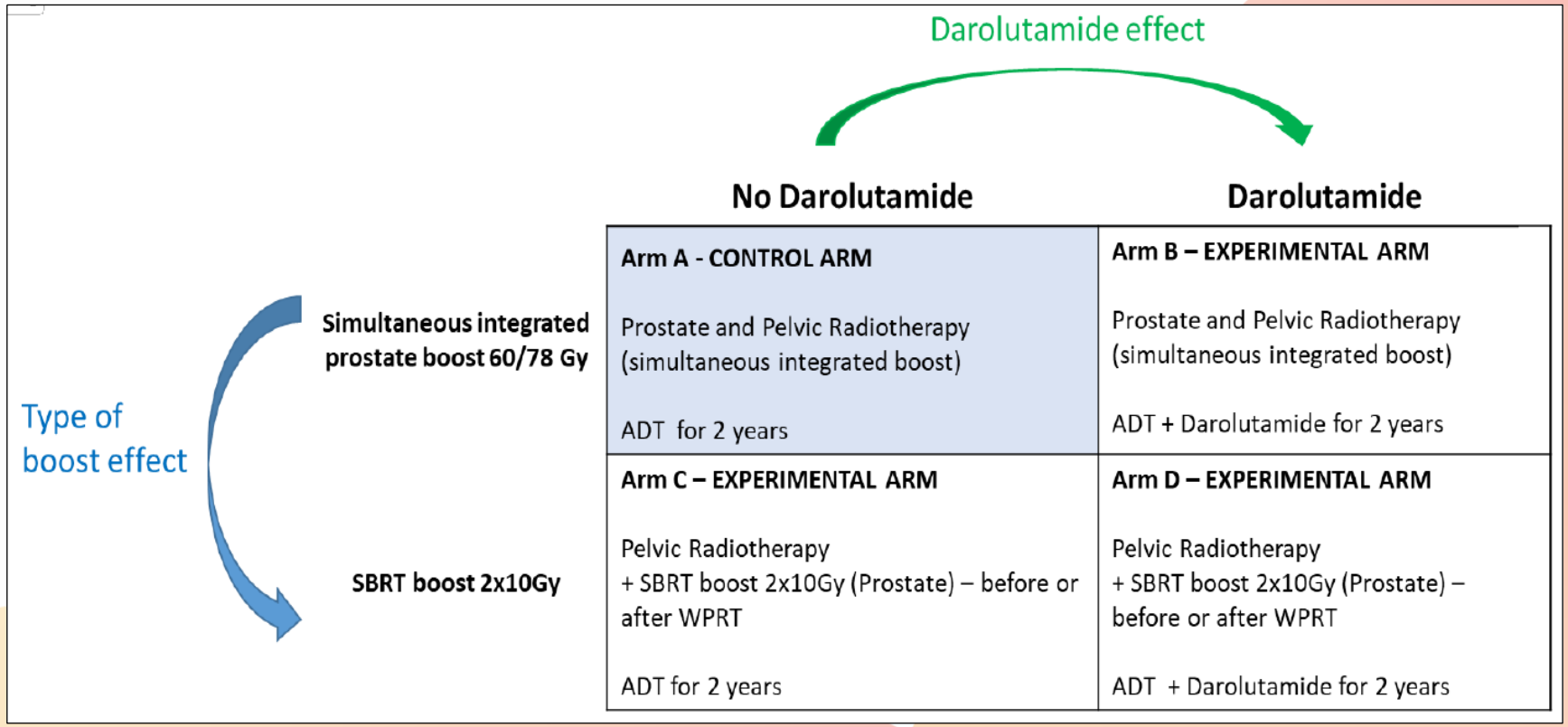
PEACE-7

Randomised, open-label phase III study of **darolutamide** and stereotactic dose escalated **prostate radical radiotherapy** in patients with localised prostate cancer and high-risk features using a factorial (2x2) design

At least 2 poor risk criteria:
- T3-4 disease
- Gleason score of 8 or greater
- PSA≥40 ng/ml

Primary objective:
- MFS

Secondary objectives:
- Biochemical PFS
- Time to local relapse
- Overall survival (OS)



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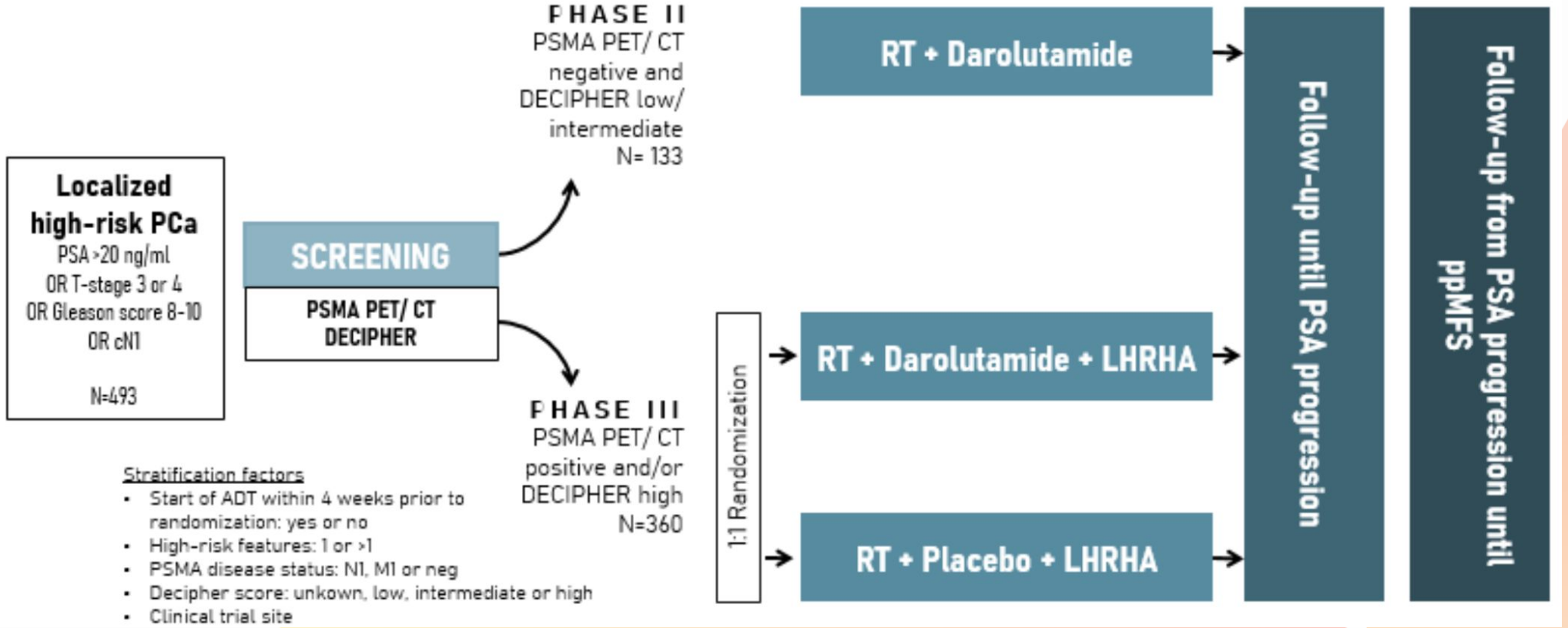
NCT06625970

THUNDER

Cancer Research Antwerp

Treatment of High-Risk Prostate Cancer Guided by **Novel Diagnostic Radio- and Molecular Tracers**: A Two-part Phase 2/ 3 Trial prior to **radical radiotherapy**



Primary objective:
- MFS by PET-PSMA

Secondary objectives:
- Biochemical PFS
- Overall survival (OS)

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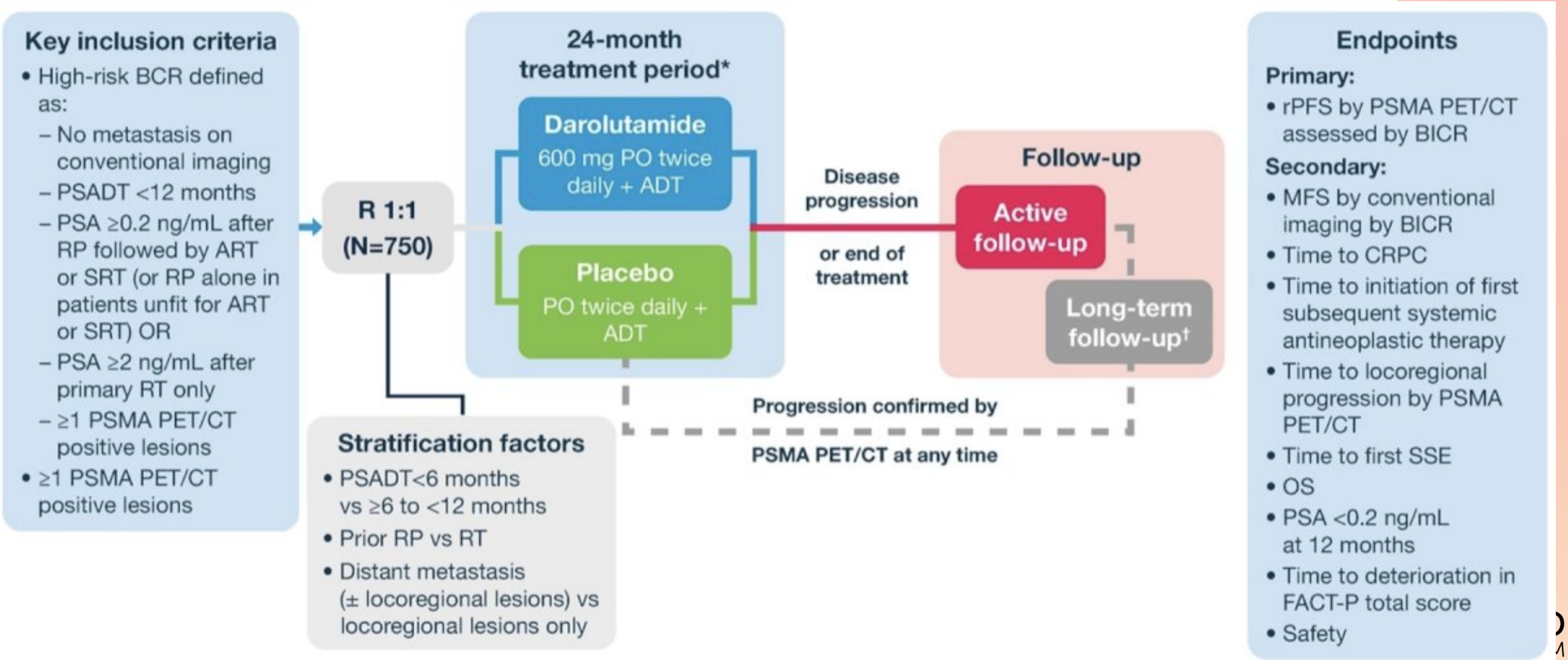
NCT06282588

High-Risk Biochemical Recurrence

ARASTEP

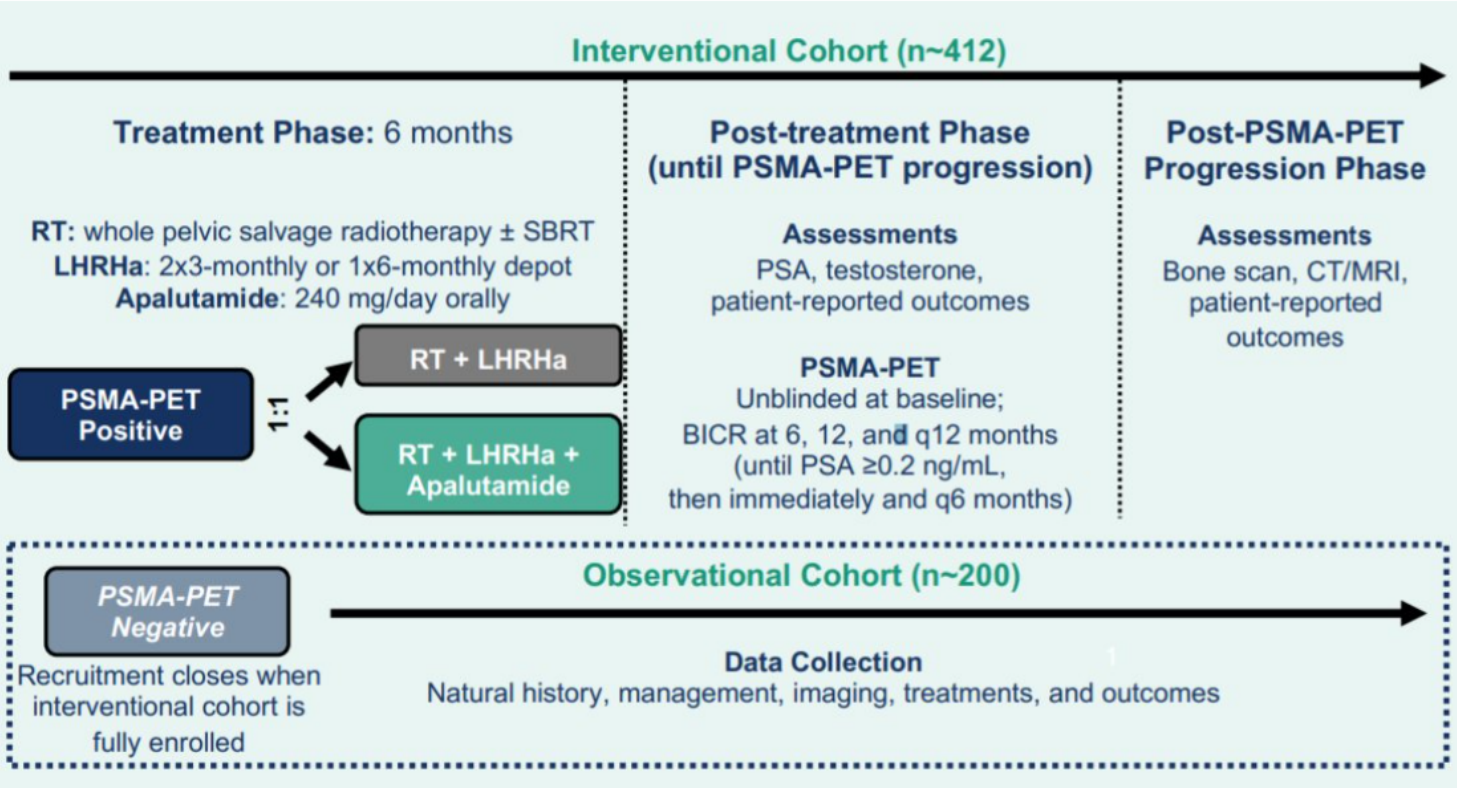
Phase 3, randomized, double-blind, placebo-controlled study assessing **darolutamide + ADT** in patients with high-risk biochemical recurrence of prostate cancer with **PSMA-PET-Positive lesion**.



NCT05794906

PRIMORDIUM

A Randomized, Phase 3 trial of Adding **Apalutamide** to salvage **Radiotherapy** in High-Risk biochemical recurrence with **PSMA-PET-Positive** Hormone-Sensitive Prostate Cancer



Primary study endpoint:
rPFS by PET-PSMA

Secondary endpoints:
- OS
- Patient-reported outcomes
- PSA progression
- Safety
- MFS by conventional imaging

- Patients with ≥1 locoregional lesion on PSMA-PET and high-risk biochemical recurrence (defined as either PSA doubling time ≤12 months or pathologic Gleason score ≥8) after radical prostatectomy.
- Salvage RT includes whole pelvic salvage radiotherapy, with stereotactic body radiation therapy for ≤3 PSMA-avid distant metastases at sites where it is a standard approach.

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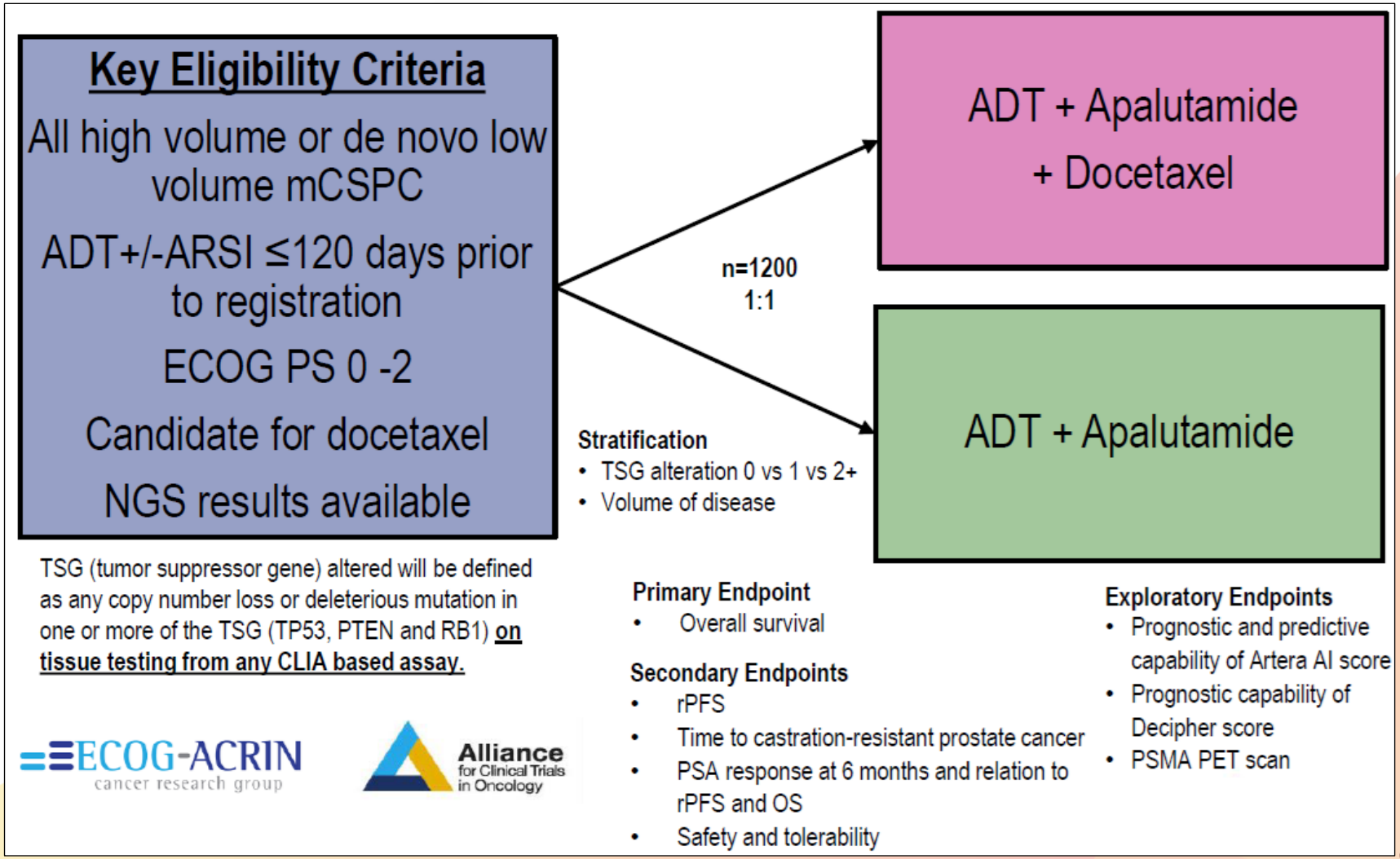
NCT04557059

Metastatic HSPC

ASPIRE



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NCT06931340

START-MET: SbrT Androgen Receptor Thera METastatic HS Prostate Cancer

Meets following criteria

Inclusion criteria

- **Castration sensitive → Local prior treatment allowed**
- **ECOG PS 0 or 1**
- **Distant metastatic disease by ≤ 3 lesions based on CT and Bone Scan and ≤ 5 lesions based on Coline or PSMA PET/TC**

***Stratification factors*:**

- **Prior local treatment**
- **New Imaging technique (Coline vs PSMA PET/TC)**

Exclusion criteria

- **Metastases in previously irradiated areas**
- **Prior docetaxel or second generation hormonal treatments**
- **Tumor stage T4**

N = 266

Randomization 1:1

STANDARD OF CARE + SBRT (all metastatic lesions)

ADT+ RT to the primary tumor (previously not treated) + Second generation hormonal treatment

STANDARD OF CARE

ADT+ RT to the primary tumor (previously not treated) + Second generation hormonal treatment

ENDPOINTS

Primary endpoint:
- **rPFS**

Key Secondary endpoints:
- **Overall survival**
- **Time to cytotoxic chemotherapy**
- **Time to PSA progression**
- **Time to pain progression**
- **Time to castration resistance**
- **Time to skeletal-related event**
- **Quality of life and safety profile**

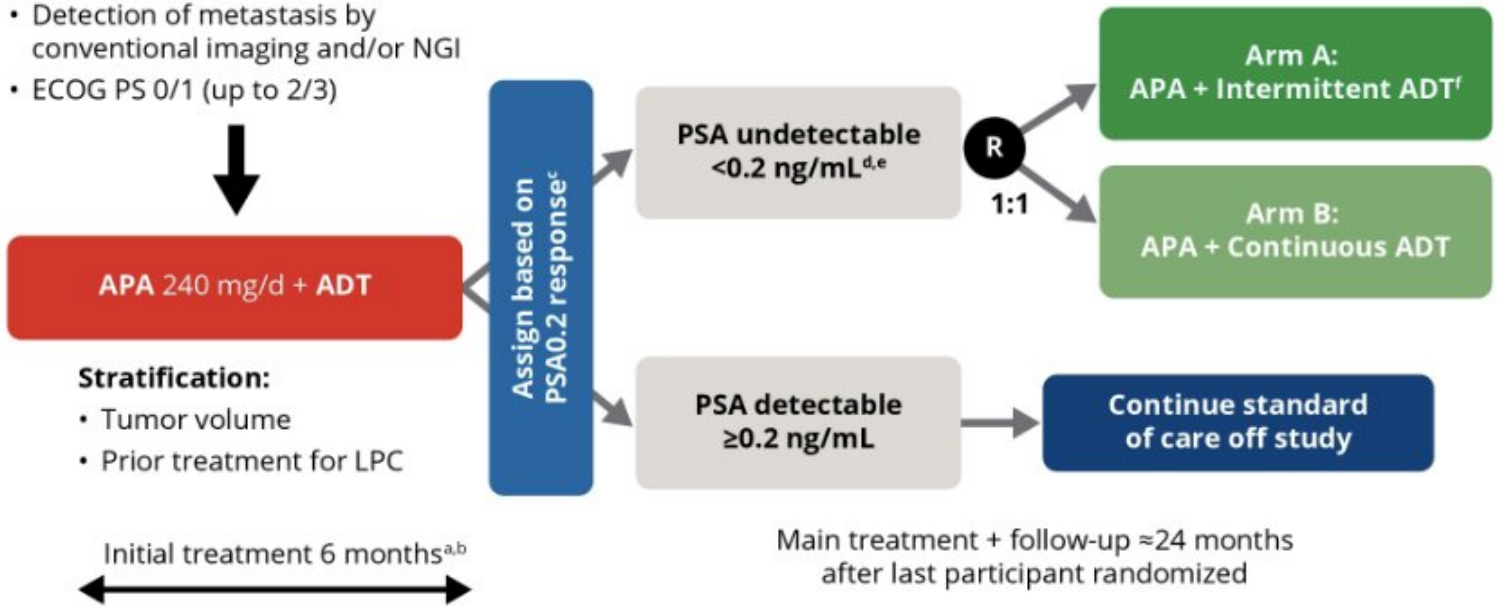
Exploratory endpoints:
- **Biomarkers assessment**
- **Local control**
- **Second progression free survival (PFS2)**
- **Time to symptomatic progression**

(ADT+ Abi/Apa/Enza/Daro)

PIs: Conde-Moreno, López-Campos, Gómez-Iturriaga.

LIBERTAS

FIGURE 1: LIBERTAS study design



[a]Participants receive APA 240 mg/d + ADT during the initial 6-month treatment phase.
[b]The choice of the GnRHa (agonist or antagonist) will be at the discretion of the investigator.
[c]PSA0.2 response refers to whether PSA is <0.2 or ≥0.2 ng/mL.
[d]Participants with confirmed PSA <0.2 ng/mL at the end of the initial 6-month treatment phase enter the main treatment phase and are randomized 1:1 to APA (240 mg/d) + intermittent ADT or APA + continuous ADT.
[e]Participants with PSA <0.2 ng/mL undergoing gender-affirming care will be evaluated as a separate cohort. These participants will not be randomized for the main treatment phase and will be treated similarly to Arm A participants.
[f]ADT can be restarted in the APA + intermittent ADT group for participants with new or worsening cancer symptoms, PSA increase to >10 ng/mL (or return to baseline level when PSA was <10 ng/mL before start of ADT), or PSA doubling time <6 months.
[g]Conventional imaging (CT/MRI and ^{99m}Tc bone scans) will be used for the assessment of the primary and secondary end points.
[h]Findings from digital health tools measure sleep, activity and neurocognitive function, and PROs, including physical and mental wellbeing.

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NCT05884398

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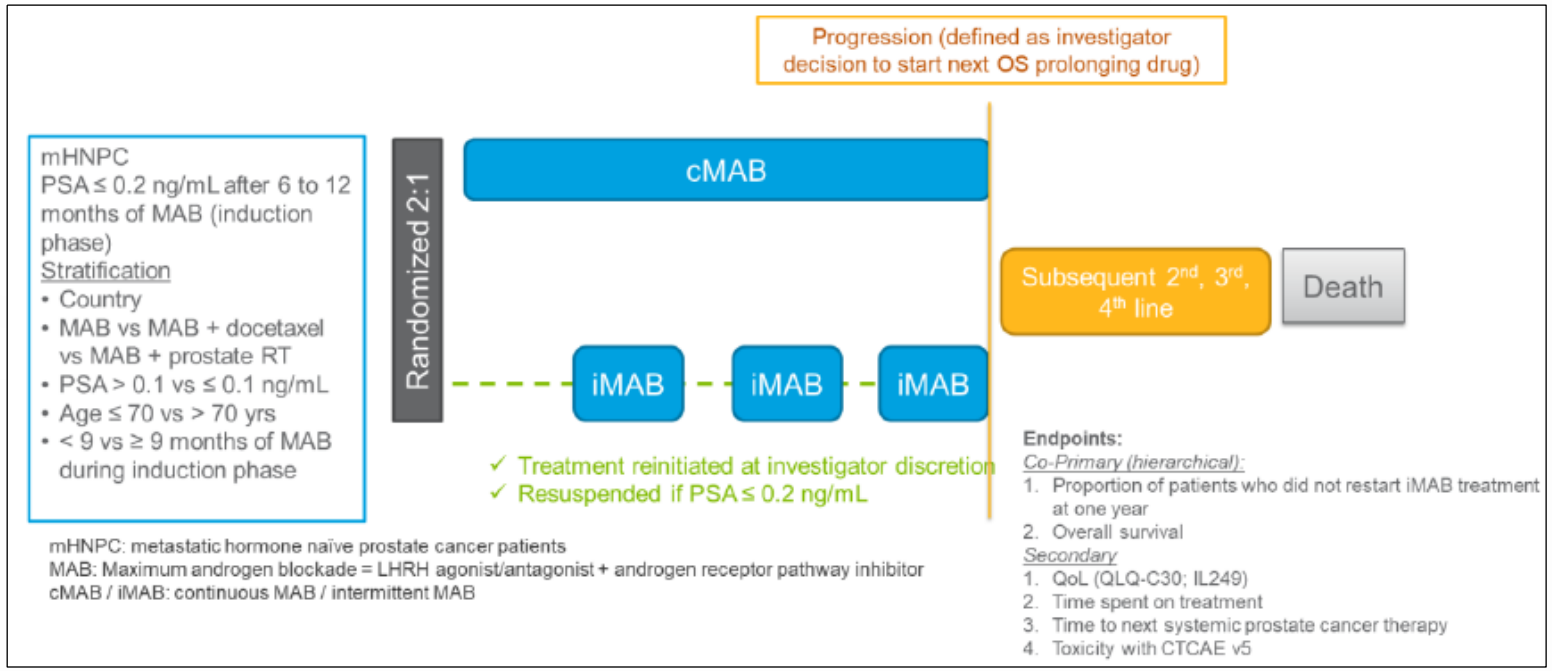


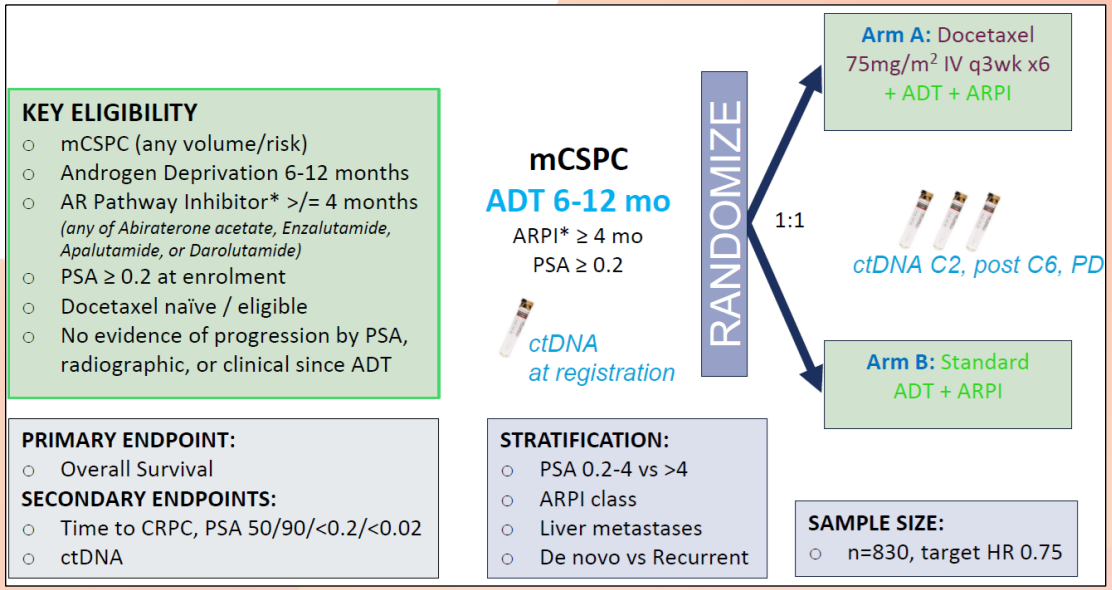
NCT05974774

EORTC

EORTC DE-ESCALATE

Canadian Cancer Trials Group
A national program of the Canadian Cancer Society

TRIPLE SWITCH



NCT06592924

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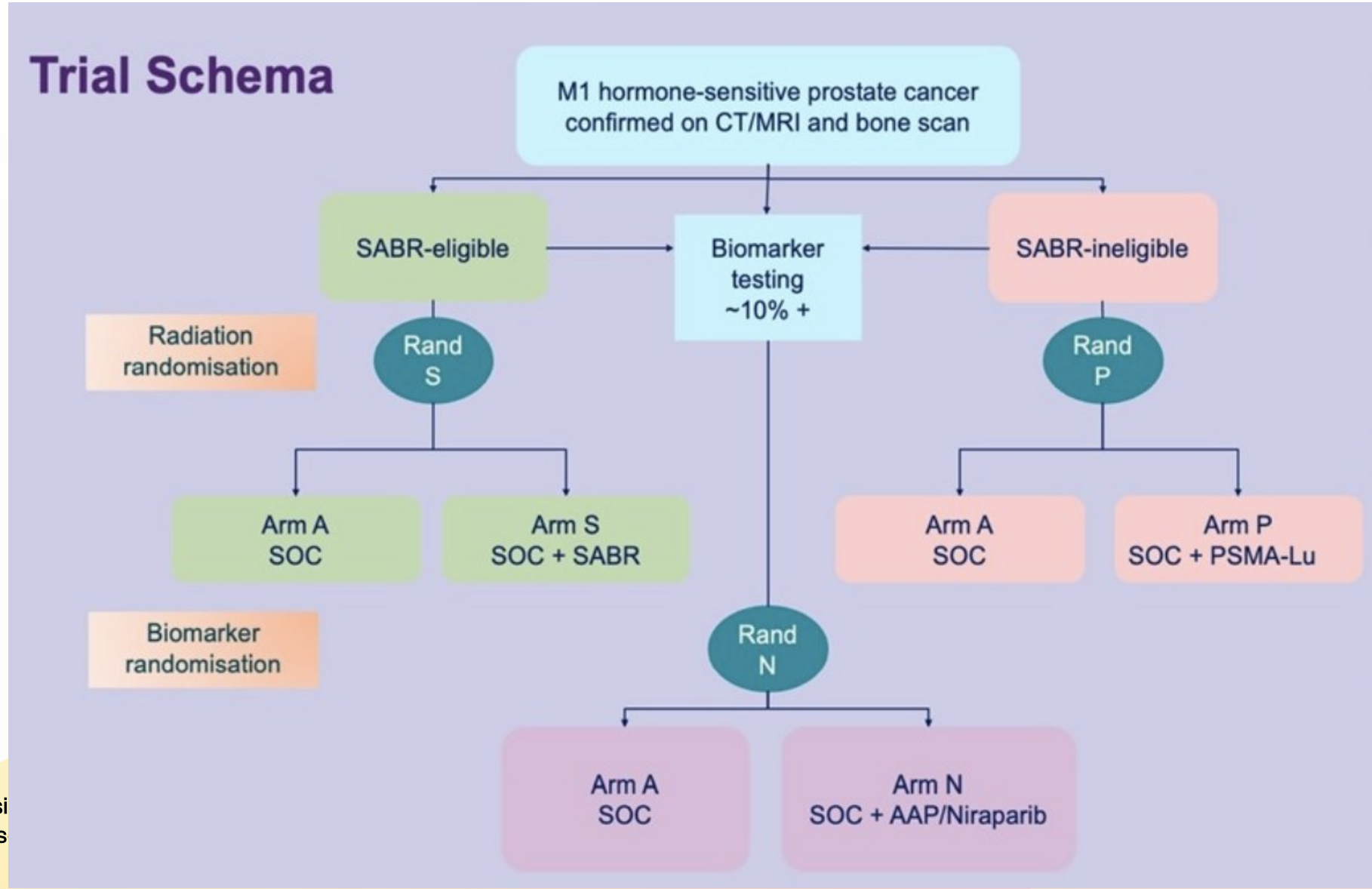
STAMPEDE-2

MRC Clinical Trials Unit

UCL



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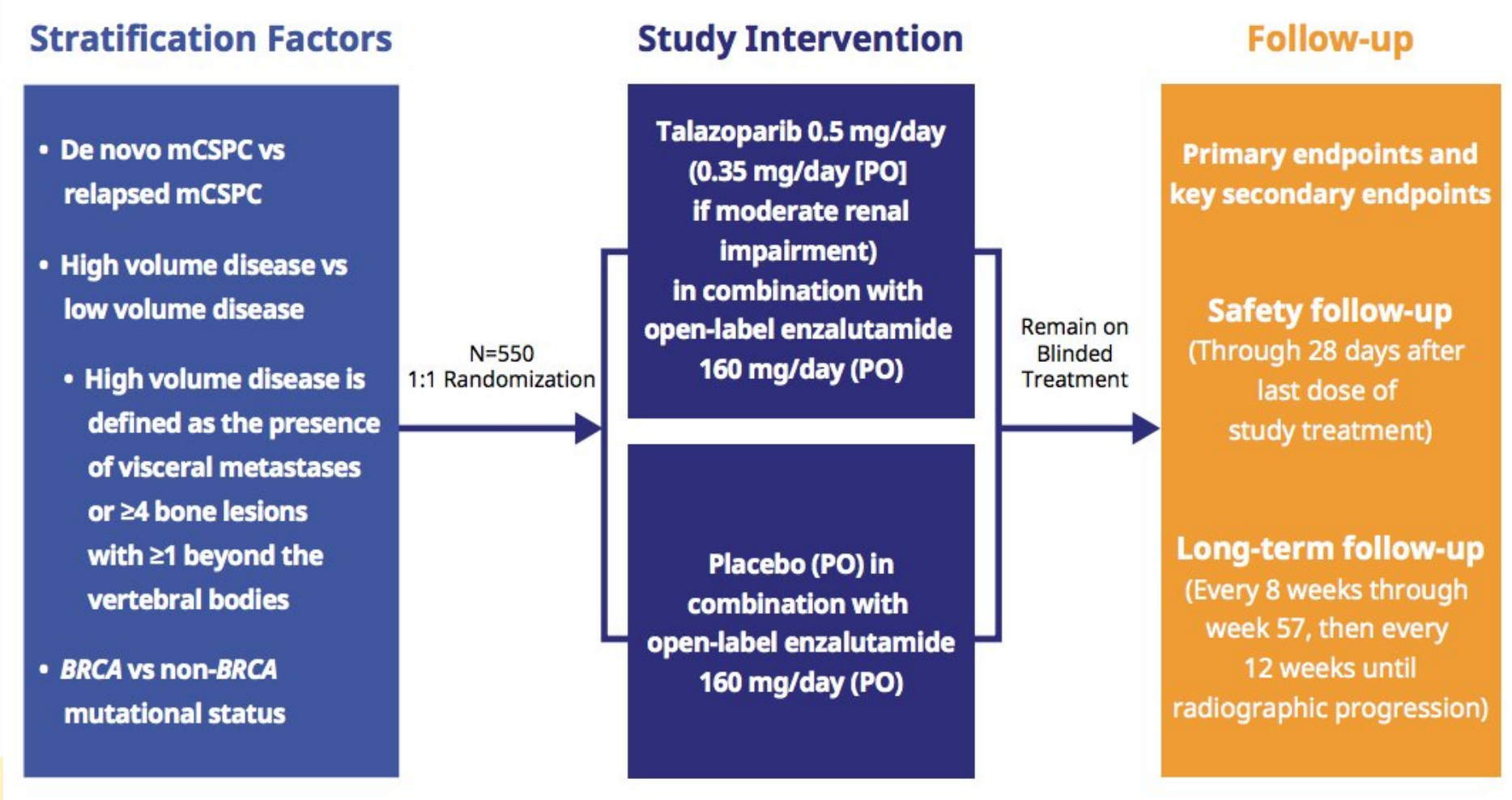
NCT06320067

TALAPRO-3



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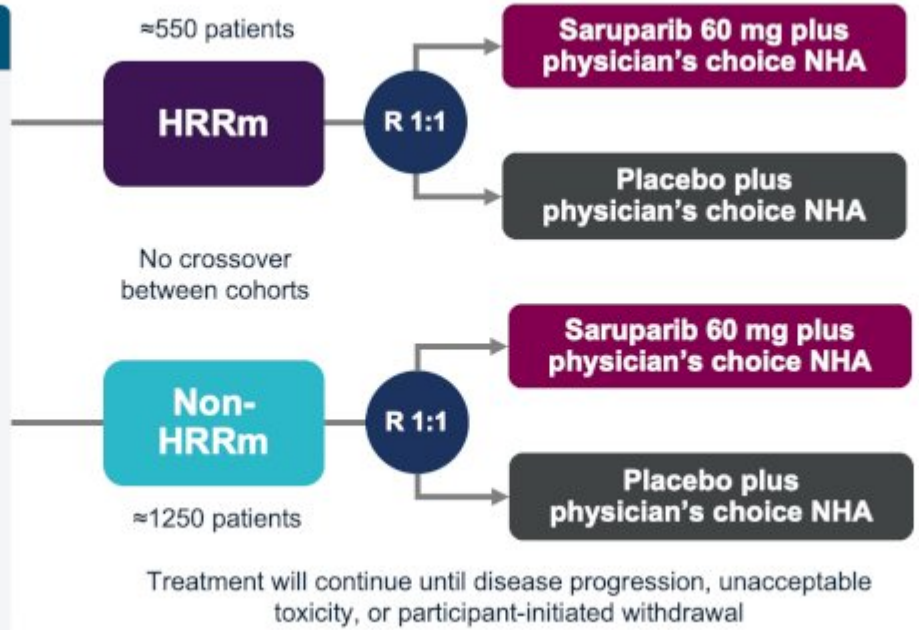
NCT04821622

EvoPAR-Prostate01

All comer trial (stratifying for HRRm and non-HRRm): **EvoPAR-Prostate01**
Double blind, placebo controlled, Ph3 study of AZD5305 (Saruparib) in combination with physician's choice ARPI in mCSPC patients **with and without** HRRm

Eligibility criteria

- Aged ≥18 years
- Histologically confirmed mCSPC (*de novo* or recurrent low- or high-volume disease)
- ECOG PS 0–1
- Prospectively defined HRRm status*
- Must be receiving ADT throughout the study or have undergone bilateral orchiectomy, and must be suitable for treatment with NHAs
- No prior treatment with PARP inhibitors, CT, or NHAs in the metastatic setting†
- No suspected or prior history of myelodysplastic syndrome/acute myeloid leukemia



Select endpoints

HRRm cohort	Non-HRRm cohort
• rPFS	• rPFS
• OS	• OS

Statistical analyses

rPFS and OS will be tested for each cohort separately using a stratified log-rank test

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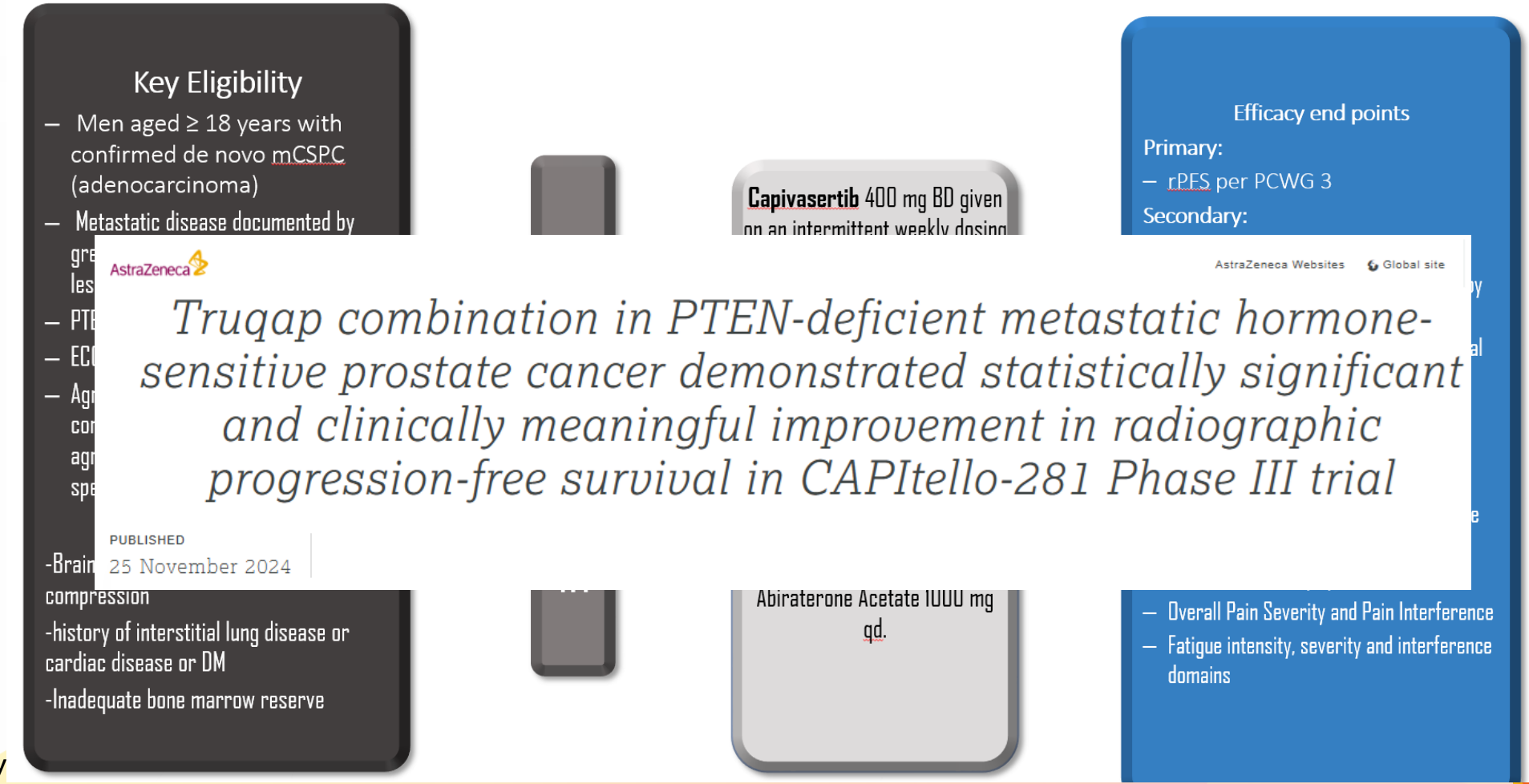
NCT06120491

CAPItello-281

A phase 3 study of **capivasertib and abiraterone** versus placebo and abiraterone in patients with **PTEN deficient** mHSPC



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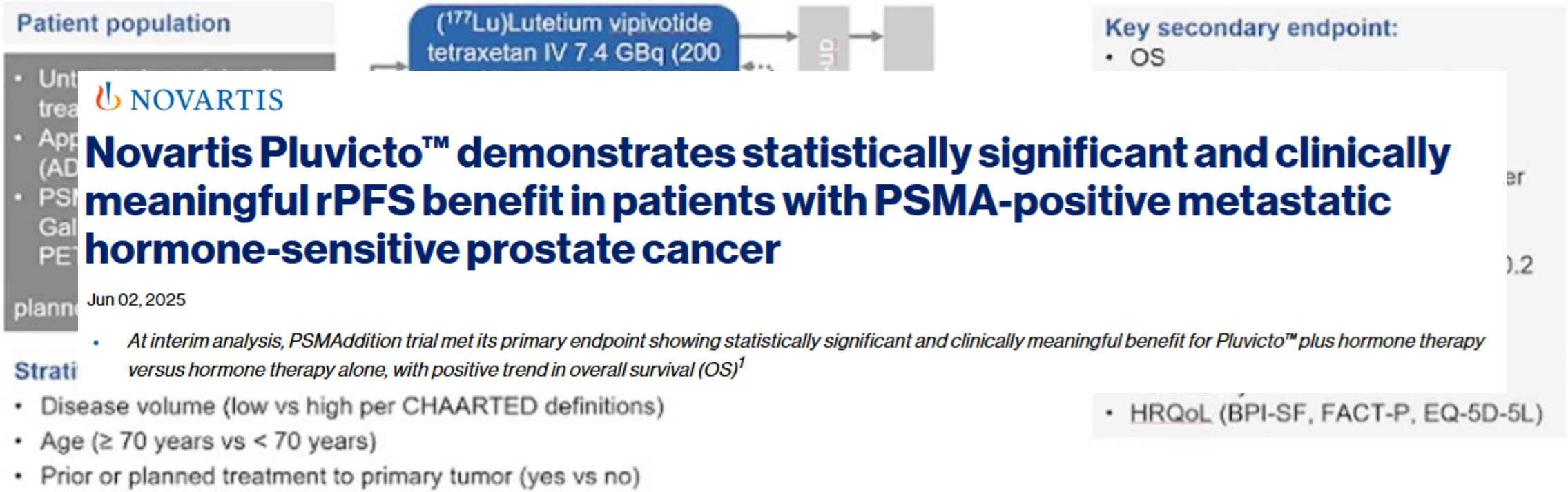
NCT04493853

PSMAddition

Prospective Open-label, Randomized, Phase III Study Comparing **177Lu-PSMA-617** in Combination With SoC, Versus SoC Alone, in Adult Male Patients With PET-PSMA positive mHSPC



*SoC= ADT + ARPi

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NCT04720157

MEVPRO-3

Randomized, open-label, phase III trial of **mevrometostat** in **mHSPC** patients.

Key inclusion/exclusion criteria:

- mCSPC documented by bone scan (bone disease) or metastatic lesions on CT/MRI (soft tissue)
- No prior EZH2i
- No prior docetaxel
- Prior treatment allowed with up to 3 months of ADT and 1 course of palliative surgery or radiation to treat symptoms of metastastic disease

N = 1000

Stratification factors:

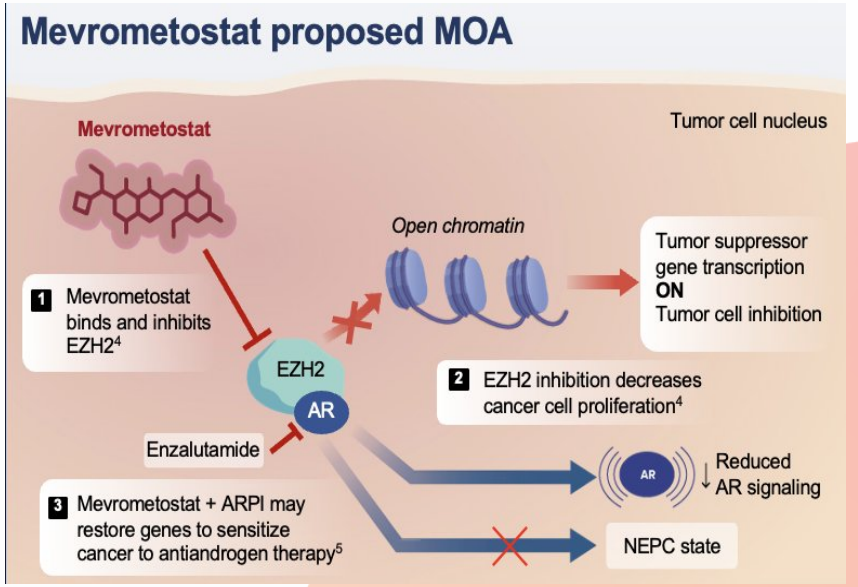
- Disease volume (low vs high)
- De-novo vs relapsed

RANDOMIZATION

Arm A
Mevrometostat 875 mg BID
+
Enzalutamide 160 mg QD

1:1

Arm B
Placebo
+
Enzalutamide 160 mg QD



Primary Endpoint

- rPFS by BICR

Secondary Endpoints

- OS (alpha-protected)
- ORR
- DOR
- PSA response 50%
- Time to PSA progression
- Time to initiation of antineoplastic therapy
- Time to first symptomatic skeletal event
- Time to CRPC
- PROs
- Safety, PK, and ctDNA

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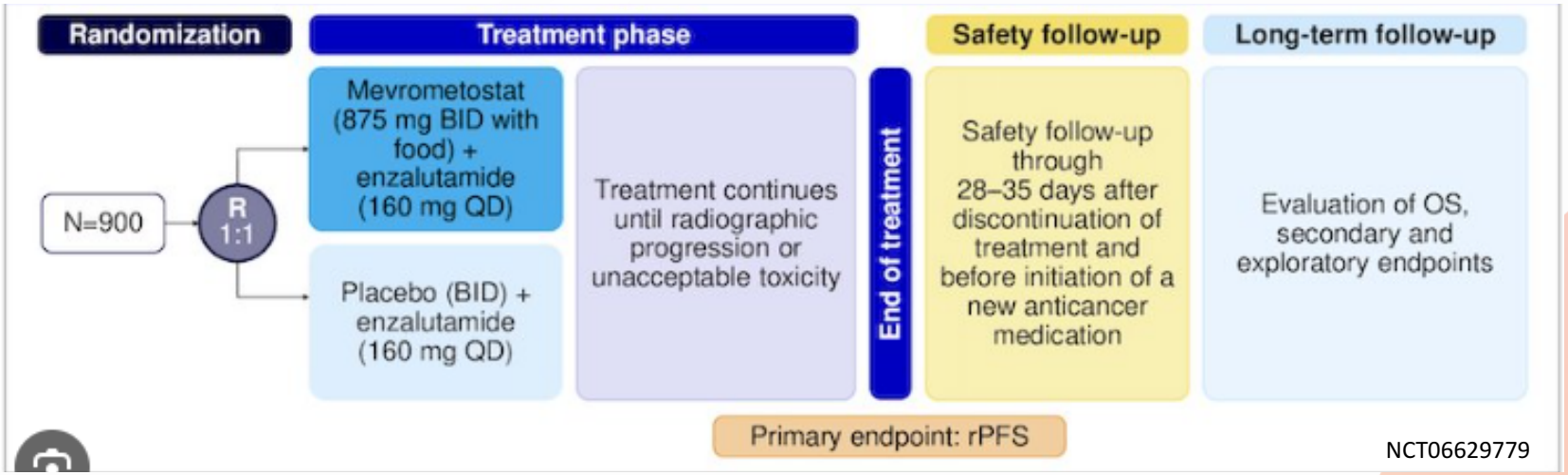
EU CT Number: 2024-519369-24-00

Metastatic CRPC

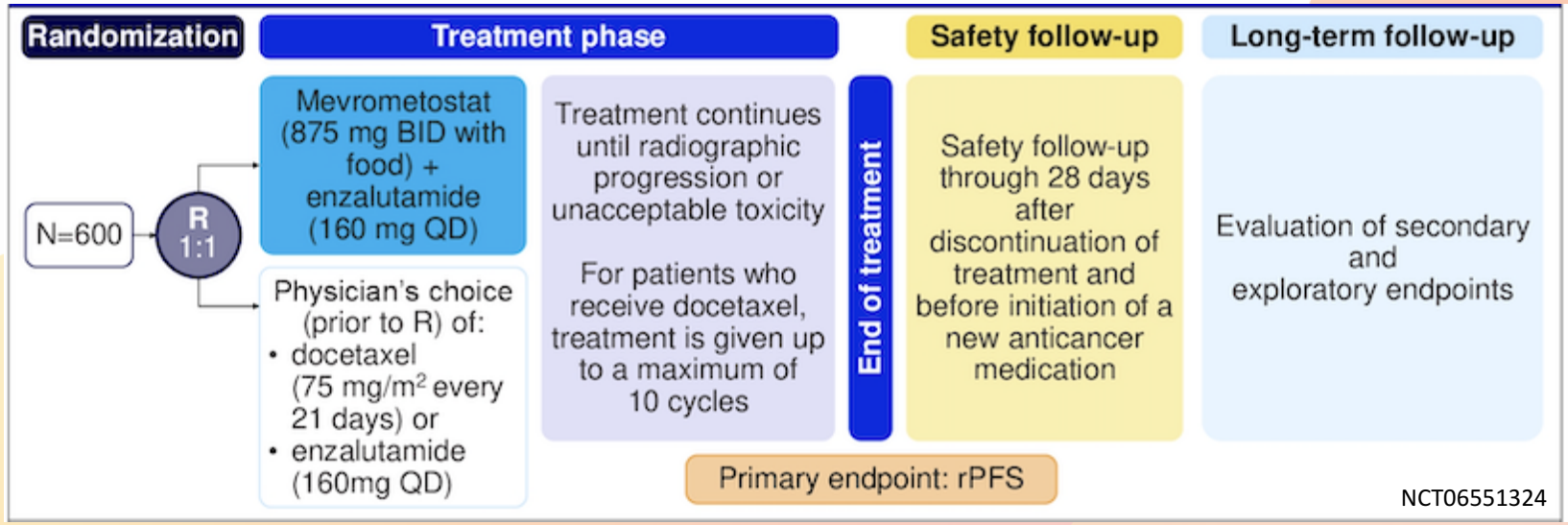
MEVPRO-2

Randomized, open-label, phase III trial in **mCRPC** patients who are **ARPI naive**.



MEVPRO-1

Randomized, open-label, phase III trial in **mCRPC** patients who were **previously treated with abiraterone** for ≥12 weeks.



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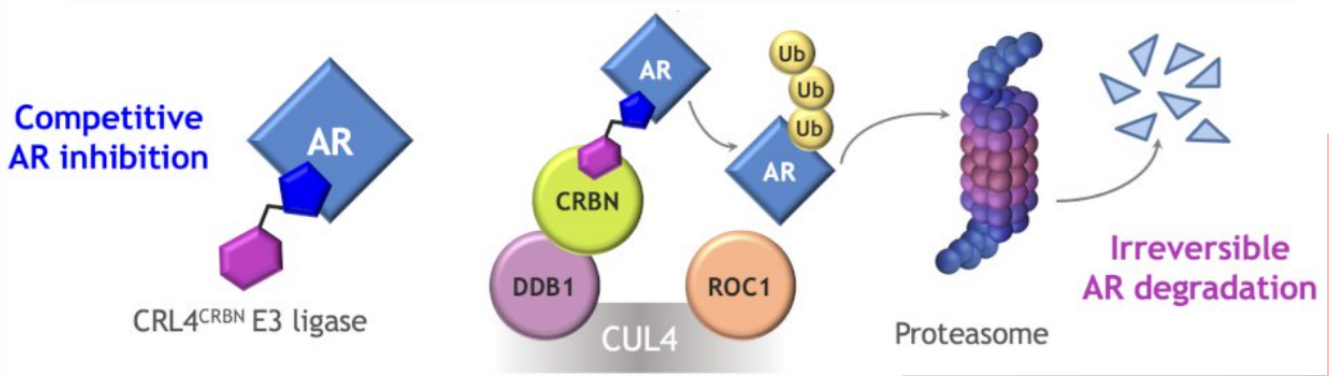
RECHARGE

A phase 3 trial of the androgen receptor ligand-directed degrader **(PROTAC), BMS-986365**, versus investigator's choice in patients with mCRPC (CA071-1000).



Key inclusion criteria

Progressive mCRPC

No more than 1 previous ARPI

No prior chemotherapy for mCRPC setting (docetaxel permitted for mCSPC if >12 months since completion).

ECOG PS of 0–1

Asymptomatic or mildly symptomatic from prostate cancer No liver metastases

N=960

R

BMS-986365

400 or 300 mg BID Q28D

Stratified by prior type of ARPI and investigator's choice (2nd ARPI vs docetaxel).

Investigator's choice:

Enzalutamide 160 mg or abiraterone 1000 mg or docetaxel 75 mg/m2

Primary endpoint

rPFS by BICR using RECIST 1.1 (soft tissue) and PCWG3 (bone) criteria.

Main secondary endpoints

OS

Safety

Overall response rate

PSA response rates (PSA30 and PSA50)

ePROs

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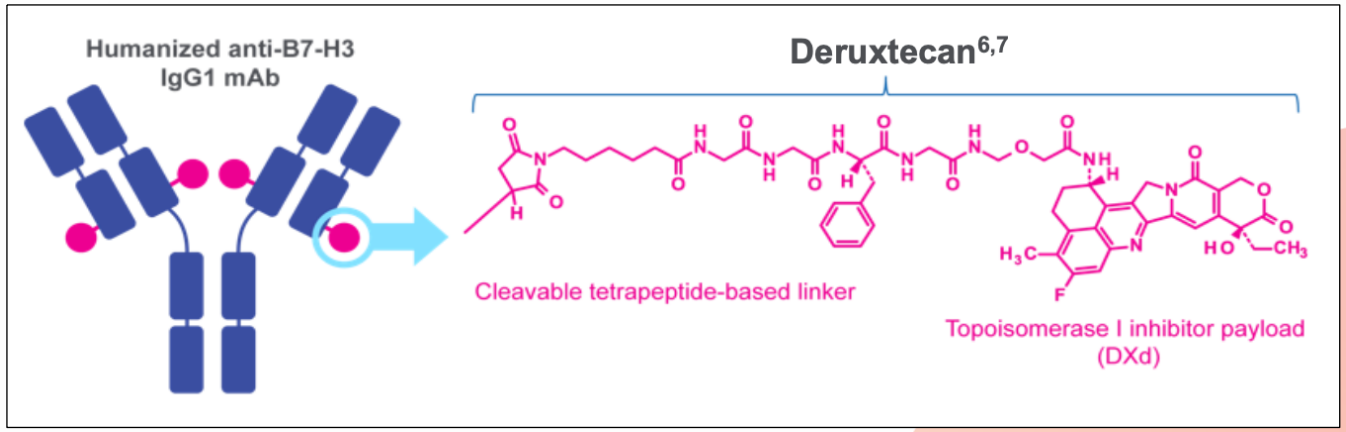
NCT06764485

IDeate-Prostate01

Phase 3, Open-label Study of **Ifinatamab Deruxtecan** Versus Docetaxel in Participants With mCRPC



Key inclusion criteria

- Progressive mCRPC
- Prior treatment with 1 or 2 ARPI and progressed during or after at least 8 weeks of treatment
- No prior chemotherapy for mCRPC setting
- ECOG PS of 0–1

R

Ifinatamab deruxtecan

12mg/kg IV q3W

Until progression

Docetaxel 75 mg/m2

x10 cycles

Primary endpoint

OS

rPFS

Main secondary endpoints

Safety

Overall response rate

PSA response rates (PSA30 and PSA50)

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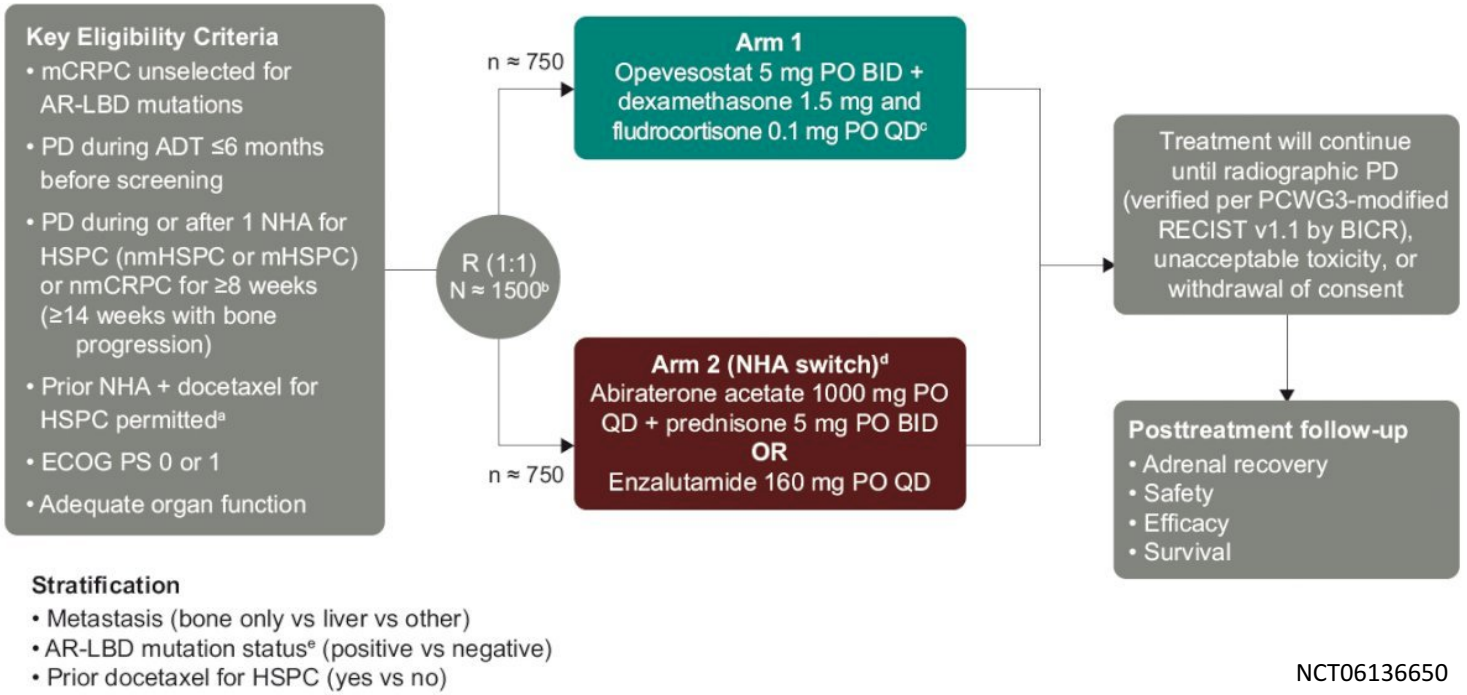
NCT06925737

OMAHA-004

PostARSI



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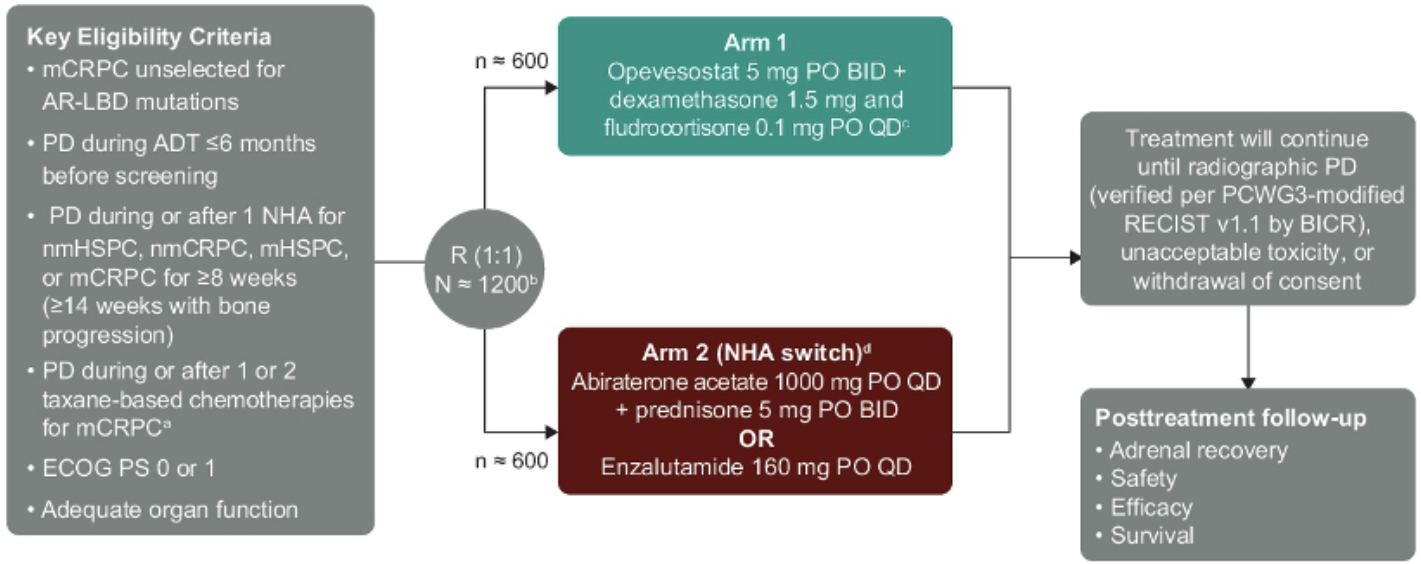
OMAHA-003

PostARSI and taxane for mCRPC



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ECLIPSE

Open-Label, Randomized Phase 3 Trial Comparing the Safety and Efficacy of **177Lu-PSMA-I&T** Versus Hormone Therapy in Patients With Metastatic Castration-Resistant Prostate Cancer

Key inclusion criteria

Progressive mCRPC

ECOG PS of 0 to 1.

PSMA-positive disease a
PSMA PET/CT scan

Prior treatments with 1 /

No prior taxane chemotl
CRPC, or prior 177Lu-
targeted therapy, no
223

N=400

Urology Times

ECLIPSE trial: 177Lu-PSMA-I&T extends rPFS vs hormone therapy in mCRPC

Key Takeaways

- Lu-PSMA-I&T significantly extended rPFS in PSMA-positive mCRPC patients compared to hormone therapy in the ECLIPSE trial.
- The trial enrolled over 400 patients globally, with primary and secondary endpoints including rPFS, overall survival, and quality-of-life measures.

The phase 3 ECLIPSE trial (NCT05204927) has met its primary end point, showing that ^{177}Lu-PSMA-I&T (lutetium (^{177}Lu) zadavotide guraxetan) significantly extended the median radiographic progression-free survival (rPFS) vs hormone therapy in patients with prostate-specific membrane antigen (PSMA)-positive metastatic-castration resistant prostate cancer (mCRPC), Curium announced in a news release.[1]

Primary endpoint

secondary endpoints

onse rate

se rates

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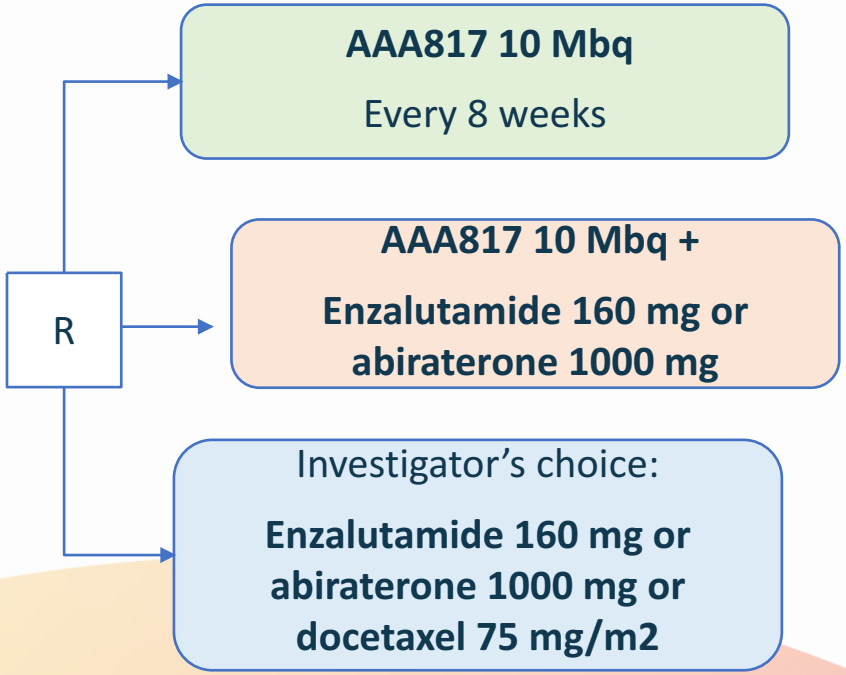
NCT05204927

AcTFIRST

Phase III, Open-label, Randomized Study of **AAA817 (225Ac-PSMA-617) plus ARPI** vs Standard of Care in PSMA Positive Metastatic Castration-resistant Prostate Cancer **NOT previously** treated with 177Lu-PSMA Targeted Therapy

Key inclusion criteria

- Progressive mCRPC
- ECOG PS of 0 to 2.
- PSMA-positive disease as assessed by PSMA PET/CT scan
- Prior treatments with only 1 ARPI (and must be the last ttm).
- No prior taxane chemotherapy for CRPC, or prior 177Lu-PSMA targeted therapy.



Primary endpoint

rPFS

Main secondary endpoints

OS

rPFS by PET-PSMA

Safety

Overall response rate

PSA response rates

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NCT06855277

PSMAcTION

A Phase II/III, Open-label, Randomized Study of **AAA817 (225Ac-PSMA-617)** vs Standard of Care in PSMA Positive Metastatic Castration-resistant Prostate Cancer **Who Progressed on or After** 177Lu-PSMA Targeted Therapy

Key inclusion criteria

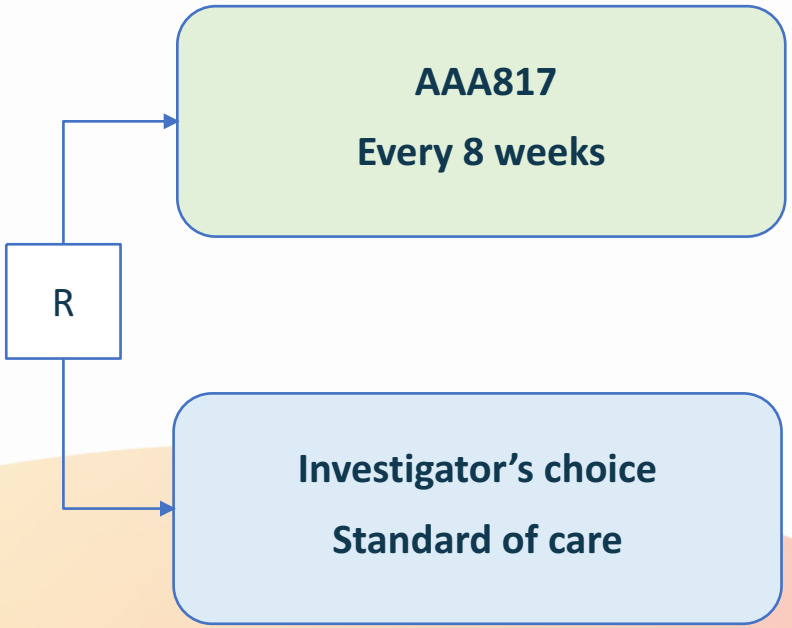
Progressive mCRPC

ECOG PS of 0 to 2.

PSMA-positive disease as assessed by PSMA PET/CT scan

Prior treatments with an ARPI, taxane chemotherapy, and progressed on or after 177Lu-PSMA targeted therapy.

≥ 1 metastatic lesion that is present on screening/baseline CT, MRI, or bone scan imaging obtained ≤ 28 days prior to randomization



Primary endpoint

rPFS

Main secondary endpoints

OS

Safety

Overall response rate

PSA response rates

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NCT06780670

DORA

An open-label, randomized phase 3 study of **docetaxel** versus **docetaxel in combination with radium-223** in patients with mCRPC

Key inclusion criteria

Patients with progressive mCRPC

Prior ARPI therapy

No prior chemotherapy for mCRPC

≥2 bone lesions

No visceral metastases with ≥3 lung and/or liver metastases or individual lesions ≥2 cm

N=738

R

Docetaxel
(60 mg/m^2 q3w, 10 cycles)
+
Radium-223
(55 kBq/kg q6w x 6 injections)

Docetaxel
(75 mg/m^2 q3w, 10 cycles)

Primary endpoint

OS

Main secondary endpoints

rPFS

SSE-FS

Time to total ALP progression

On-treatment alterations in quality of life as assessed by FACT-P, BPI, and BFI measures

NCT03574571

CAPItello-280

Phase 3 study of **capivasertib and docetaxel** versus placebo and docetaxel in PTEN-**UNSELECTED** patients with mCRPC

- Patients ≥1 bone lesion
- Previous months
- No prior
- ECOG PS 0-1

Actual enrolment=1035

AstraZeneca

AstraZeneca Websites | Global site

Update on CAPItello-280 Phase III trial of Truqap in metastatic castration-resistant prostate cancer

PUBLISHED
29 April 2025

AstraZeneca is discontinuing the CAPItello-280 Phase III trial evaluating the efficacy and safety of *Truqap* (capivasertib) in combination with docetaxel and androgen-deprivation therapy (ADT) compared to docetaxel and ADT with placebo in patients with metastatic castration-resistant prostate cancer (mCRPC).

This decision is based on the recommendation of the Independent Data Monitoring Committee (IDMC) following their review of data from a pre-specified interim analysis, which concluded that the *Truqap* combination was unlikely to meet the dual primary endpoints of radiographic progression-free survival (rPFS) and overall survival (OS) versus the comparator arm upon trial completion. The safety profile for *Truqap* was consistent with previous trials.

+

Docetaxel

(75 mg/m^2 for 6–10 cycles)

- Safety and tolerability

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NCT05348577

RADIANT Trial

Phase 3/4, randomized, open-label, multicenter efficacy and safety study of **radium-223 vs ARPi** in patients with bone-dominant mCRPC progressing on/after 1 line of ARPi

Key inclusion criteria

Patients progressing on/after abiraterone or enzalutamide for metastatic PC (mHSPC or mCRPC)

One line of chemotherapy mandatory unless ineligible or unwilling

≥2 bone metastases

Symptomatic based on BPI-SF

No visceral disease

LN <3 cm

N=696

R

2nd switch ARPi

(abiraterone or enzalutamide, depending on prior ARPi)

Stratified by ALP, prior chemotherapy, prior ARPi

Radium-223

at 55 kBq/kg x 6 cycles

Primary endpoint

OS

Main secondary endpoints

rPFS

Time to pain progression

Time to first SSE

AEs

Incidence of fractures

Time to deterioration of FACT-P total score

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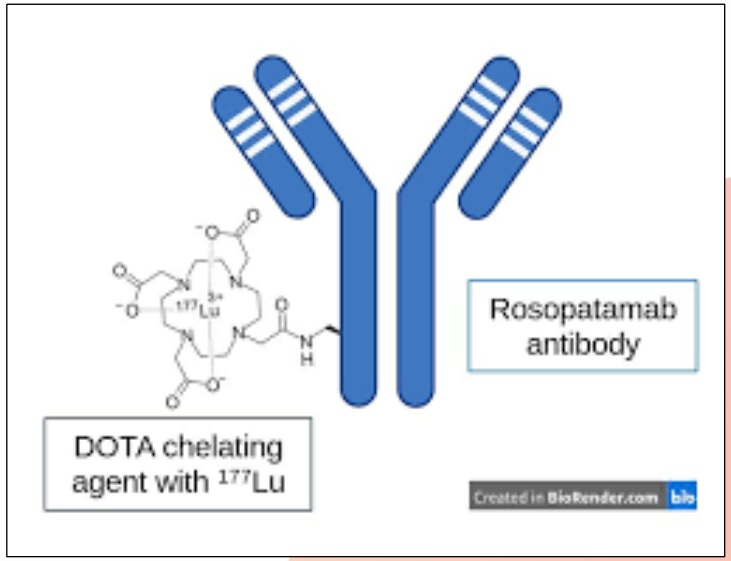
NCT04597125

ProstAct

Phase 3 study of ^{177}**Lu-DOTA-rosopatamab** (PSMA-targeted radio-ADC) and enzalutamide, abiraterone or docetaxel in patients with mCRPC



Key inclusion criteria

- Progressive mCRPC
- Prior ARPI for ≥12 weeks
- Prior line of taxane therapy or ineligible
- PSMA positive lesion
- Adequate organ function
- ECOG PS 0-2

Estimated enrolment=392

R 1:1

^{177}Lu-DOTA-rosopatamab
(320 mg orally BID[a])
+
Enzalutamide or abiraterone or docetaxel

Enzalutamide or abiraterone or docetaxel

Primary endpoint

- rPFS

Main secondary endpoints

- OS
- Tumour ORR
- Time to first SSE
- PFS
- Safety and tolerability

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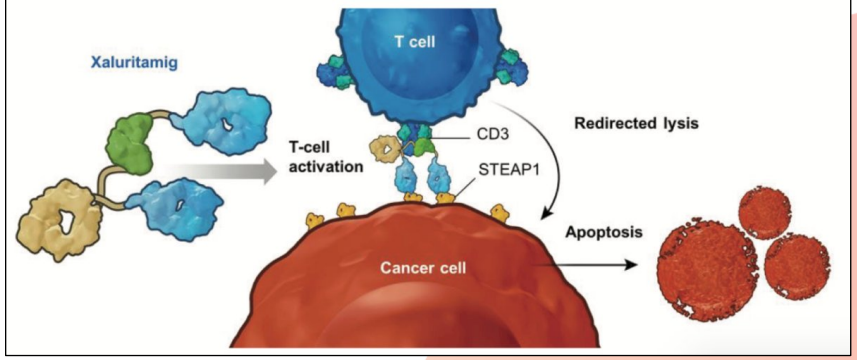
NCT04876651

XALute

Phase 3 study of **xaluritamig** (anti-STEAP1 T-cell engager) vs investigator's choice of cabazitaxel or second ARPi in post-taxane metastatic castration-resistant prostate cancer (mCRPC).

Figure 1: Xaluritamig (AMG 509): XmAb® 2+1 T-cell engager designed to facilitate T-cell-mediated lysis of STEAP1-expressing cells[1-3]



Key inclusion criteria

- Progressive mCRPC
- Prior ARPI
- Prior line of taxane therapy
- Adequate organ function
- ECOG PS 0-1

Estimated enrolment=675

R 1:1

Xaluritamig
1.5 mg Q2W

Stratification by LDH levels, liver metastases (Y/N), prior PSMA therapy (Y/N), intention to treat with cabazitaxel or ARPi switch.

Enzalutamide 160 mg
or abiraterone 1000 mg
or cabazitaxel 25 mg/m2

Primary endpoint

- OS

Main secondary endpoints

- rPFS
- ORR
- Safety and tolerability

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NCT06691984

¡Gracias!

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