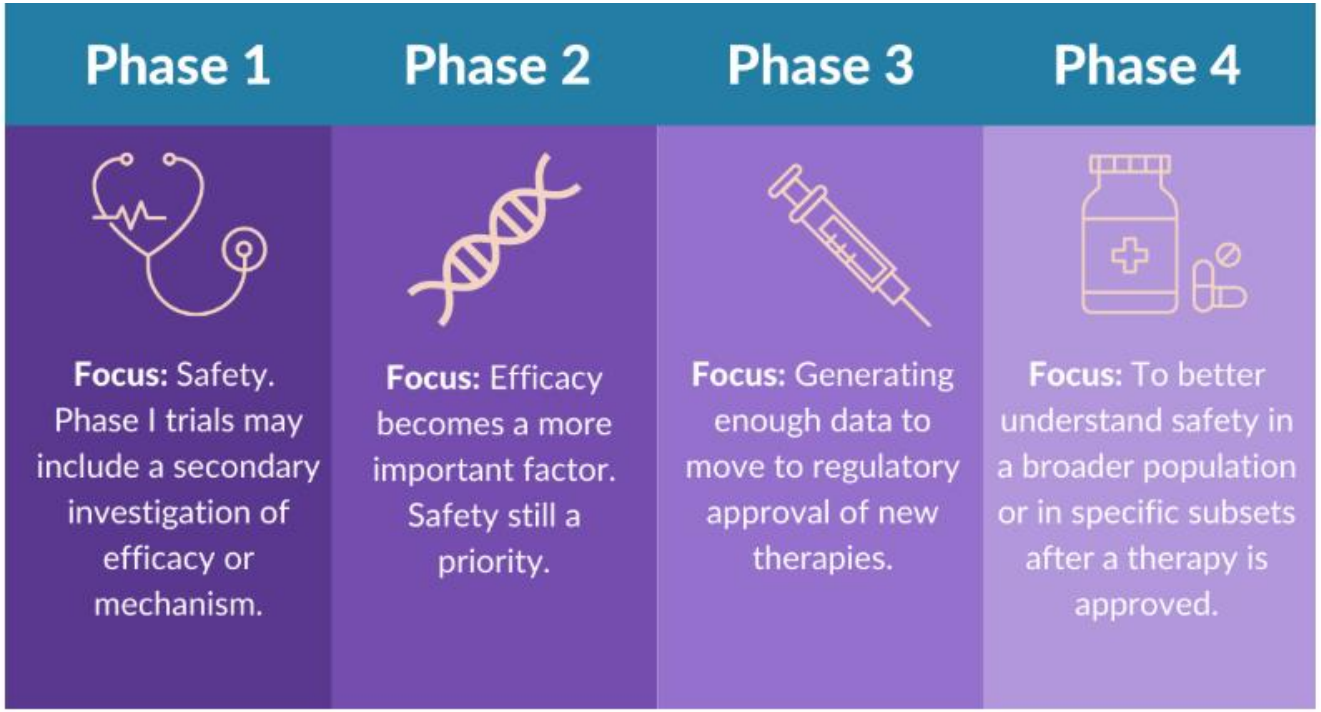
UC San Diego Health | UC San Diego Moores Cancer Center

Oncology Updates – Prostate Cancer: Advanced Diagnostics and Novel Multidisciplinary Treatment Approaches

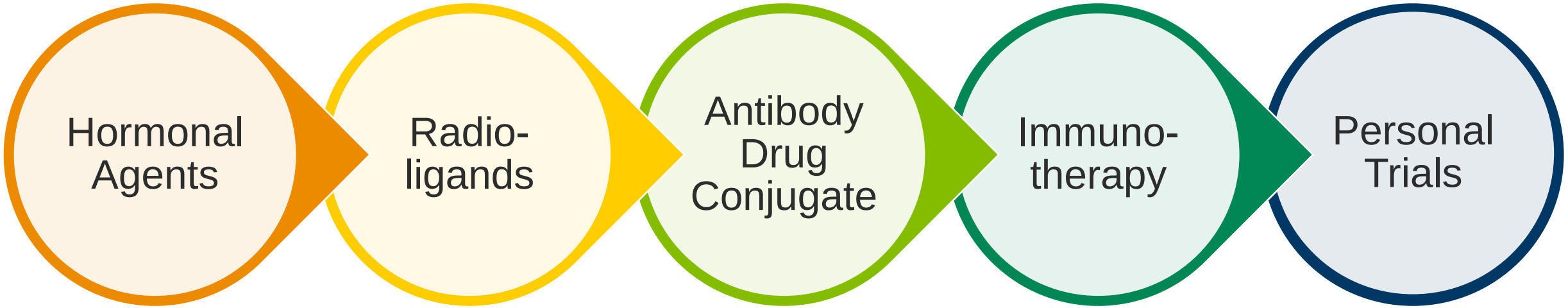
Rana R. McKay, MD, FASCO
Professor of Medicine and Urology
Co-Lead, Genitourinary Oncology Program
Associate Director, Clinical Sciences

What are Clinical Trials?

- Research studies involving patients
- Evaluate new treatments, procedures, or interventions
- Goal: improve patient outcomes & advance knowledge
- Phases: Phase 1 (safety), Phase 2 (effectiveness), Phase 3 (comparison), Phase 4 (long-term)
- Types: Therapeutic vs. Non-therapeutic (focus = therapeutic trials)



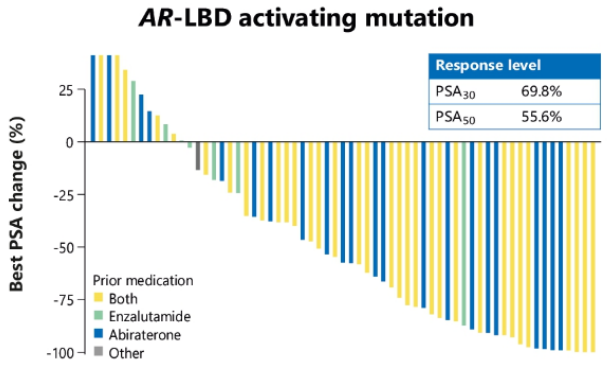
Overview of Emerging Treatments and Paradigms



Hormonal Agents

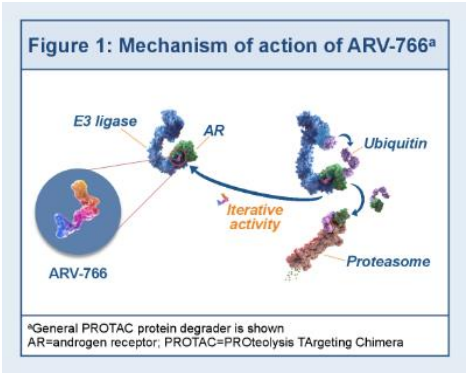
MK-5684

- CYP11A1 inhibitor
- Further blocks androgen production in adrenal gland
- PSA30 70%



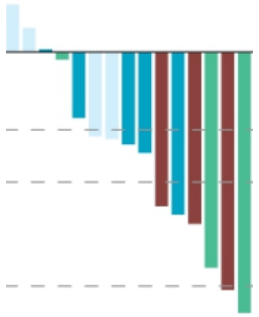
JSB462

- Proteolysis targeting chimera (PROTAC) androgen receptor degrader



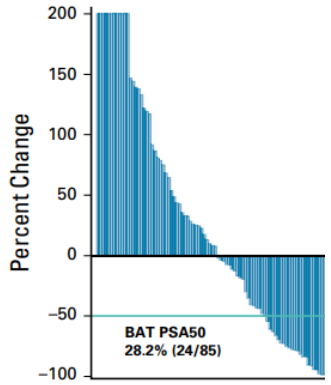
BMS-986365

- Androgen receptor ligand-directed degrader
- PSA30 67%



Bipolar Androgen Therapy

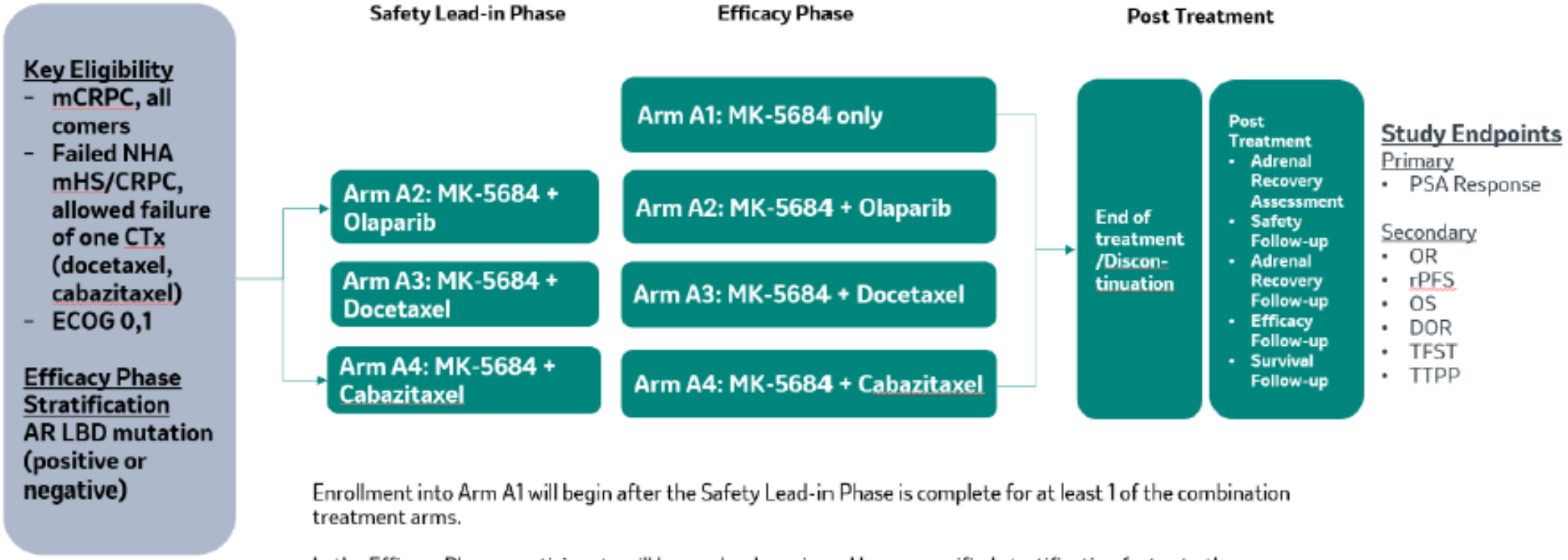
- High dose testosterone replacement
- PSA50 21-28%



MK5684-U01/01A (OMAHA-01A)

Enrolling at UCSD

Schema



Enrollment into Arm A1 will begin after the Safety Lead-in Phase is complete for at least 1 of the combination treatment arms.

In the Efficacy Phase, participants will be randomly assigned by prespecified stratification factor to the open treatment arms using an equal randomization ratio.

Within each arm, the number of AR LBD mutation negative participants will be capped at approximately 50% of the total enrollment.

JSB462 for Hormone Sensitive and Castration Resistant Disease

Pending Enrollment at UCSD

Metastatic Hormone Sensitive

Key eligibility criteria

- ≥ 18 years
- ECOG 0-2
- mHSPC high risk[1]
- No prior ARPI
- Prior taxanes allowed if (neo)adjuvant

R
1:1:1

- Arm 1: JSB462 (100 mg QD) + abiraterone (1000 mg QD) N=50
- Arm 2: JSB462 (300 mg QD) + abiraterone (1000 mg QD) N=50
- Arm 3: ARPI[2] N=50[3]

1 - Visceral metastases and/or ≥4 bone lesions (with at least one outside the vertebral column and/or pelvis).
2 - Abiraterone 1000 mg QD or enzalutamide 160 mg QD per investigator's choice.

Metastatic Castration Resistant

Key eligibility criteria

- ≥18 years
- ECOG 0-2
- mCRPC
- Positive 68 Ga-PSMA-11 PET/CT scan
- Prior progression on ARPI
- 0-2 prior taxanes

R
5:5:3

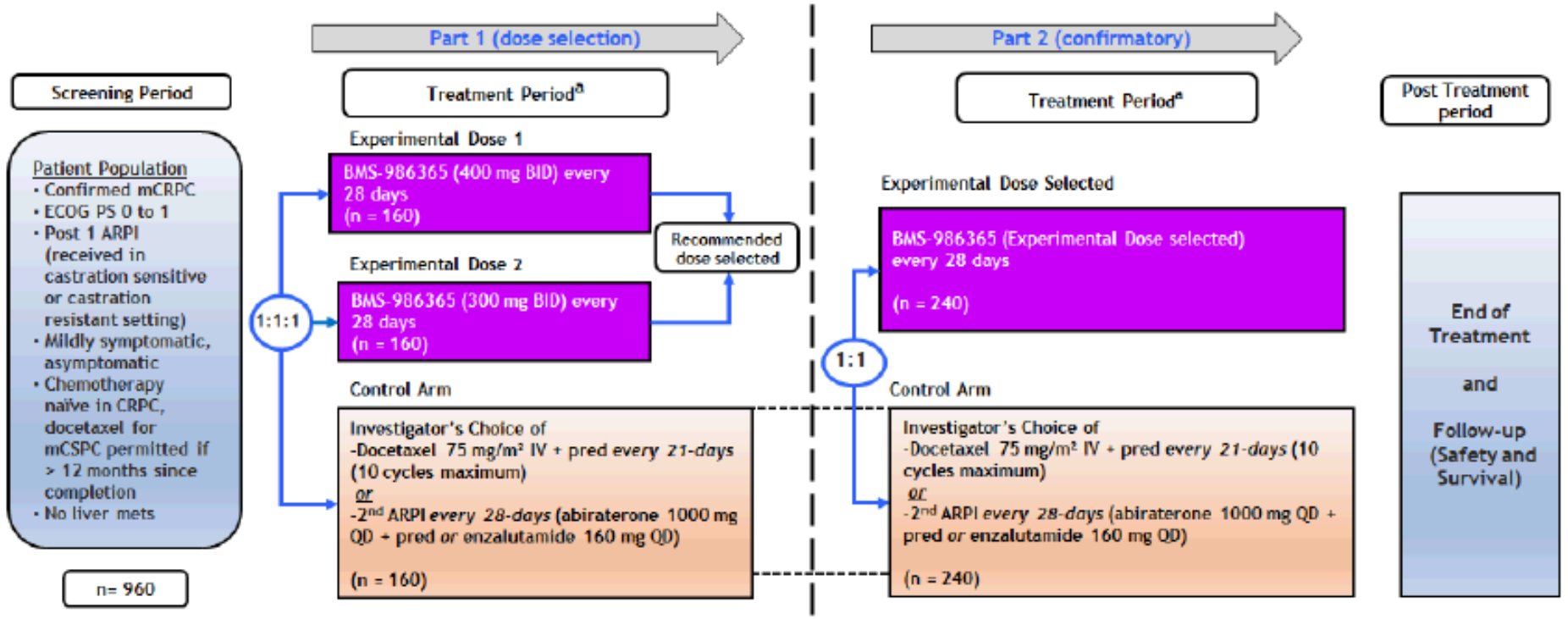
Arm 1	JSB462 100 mg QD + AAA617 (7.4 GBq)	N = 50[1]
Arm 2	JSB462 300 mg QD + AAA617 (7.4 GBq)	N = 50[1]
Arm 3	AAA617 (7.4 GBq)	N = 30[1]

1- An interim safety look will be performed in the first randomized participants (~6-10 participants in Arm 1, ~6-10 in Arm 2 and ~3-6 in Arm 3).

BMS-986365 for Metastatic Castration Resistant Disease

Enrolling at UCSD

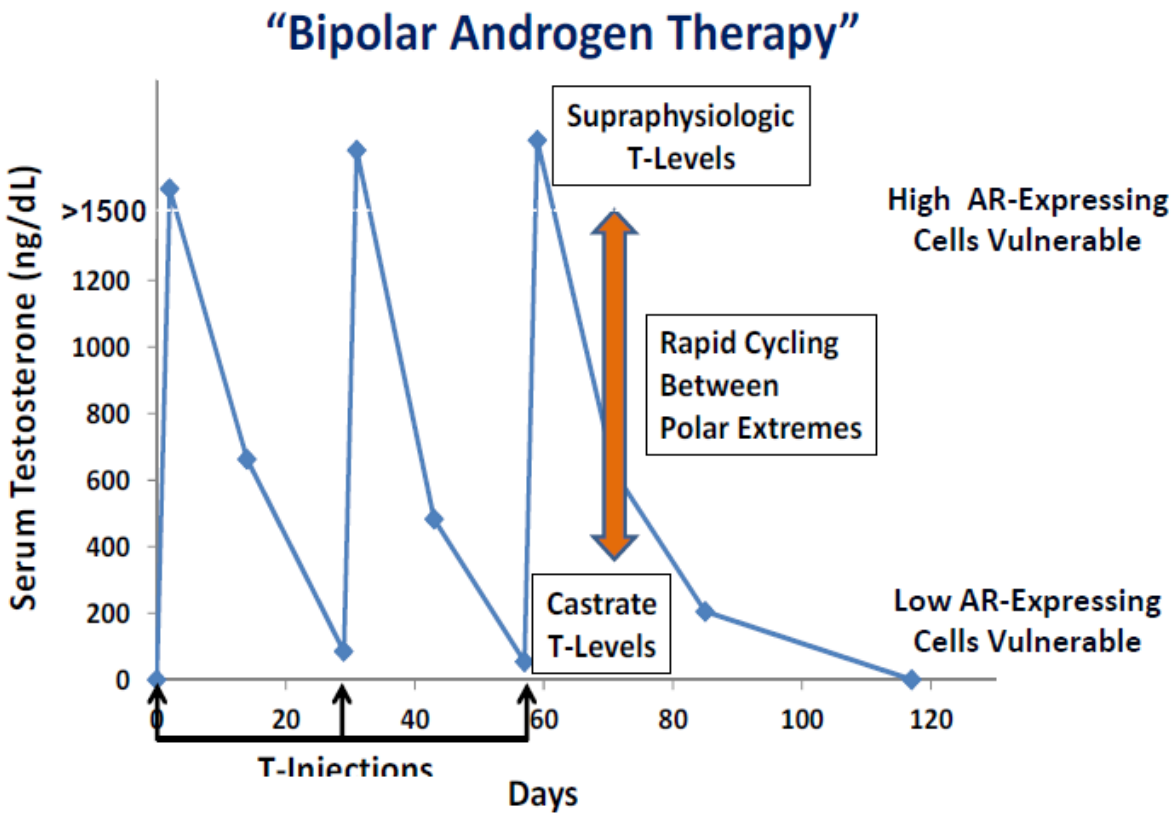
Study Design Schema:

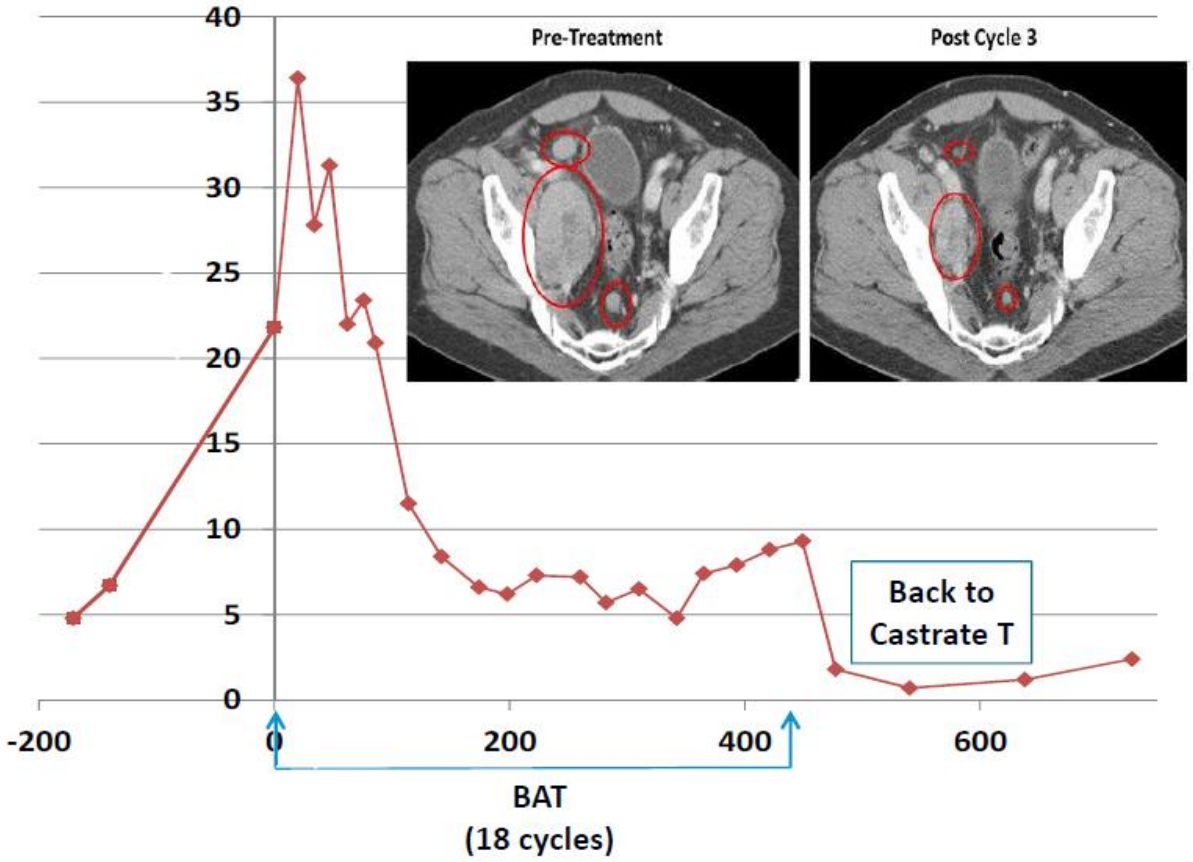


Randomization is stratified by:
- Prior ARPI received (abiraterone vs enzalutamide, darolutamide or apalutamide)
- Investigator's choice (docetaxel vs 2nd ARPI)

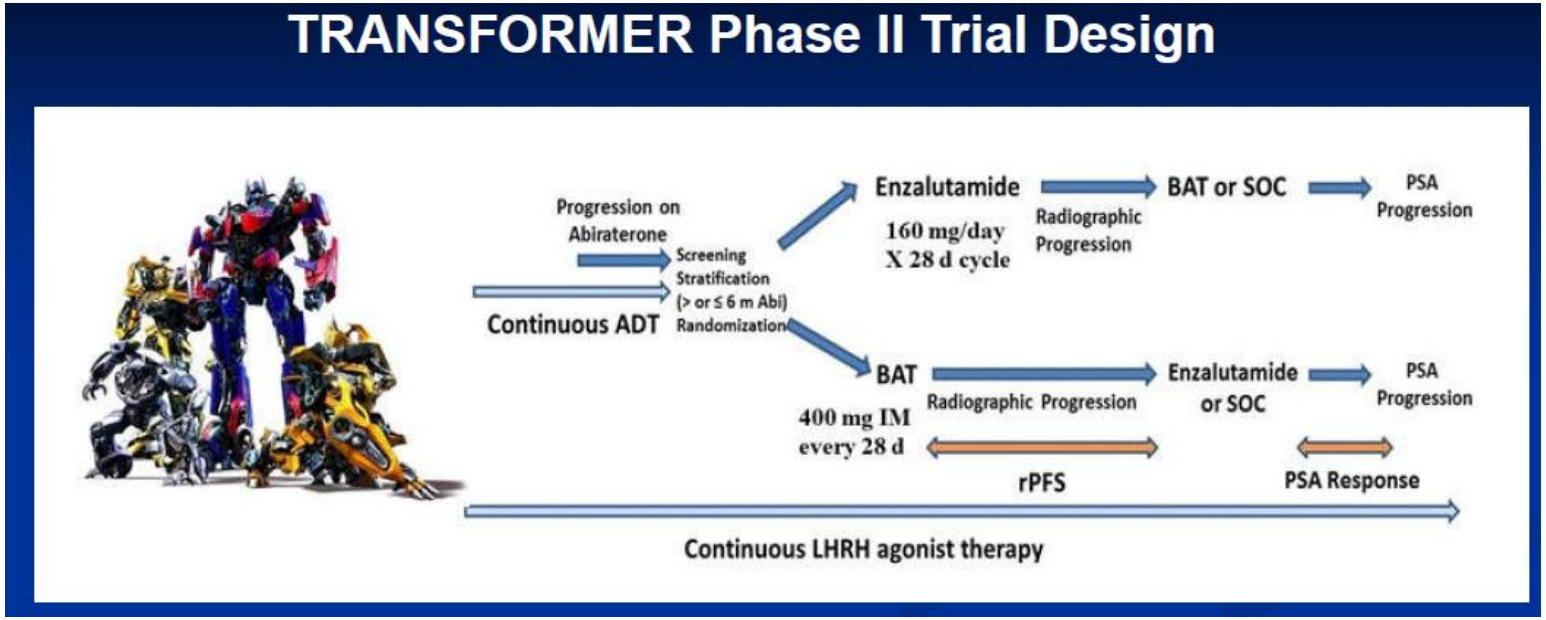
- The investigator's choice of agent, in the control arm, must be prespecified prior to randomization.
- Participants enrolled in the treatment arm corresponding to dose not selected for Part 2 may switch to the selected dose of BMS-986365; if assessed as clinically indicated by the investigator.
- The final efficacy and safety analysis will be performed on participants from selected dose arm and control arm enrolled in Part 1 and Part 2.
- No crossover from BMS-986365 to Control or vice versa be allowed within the trial

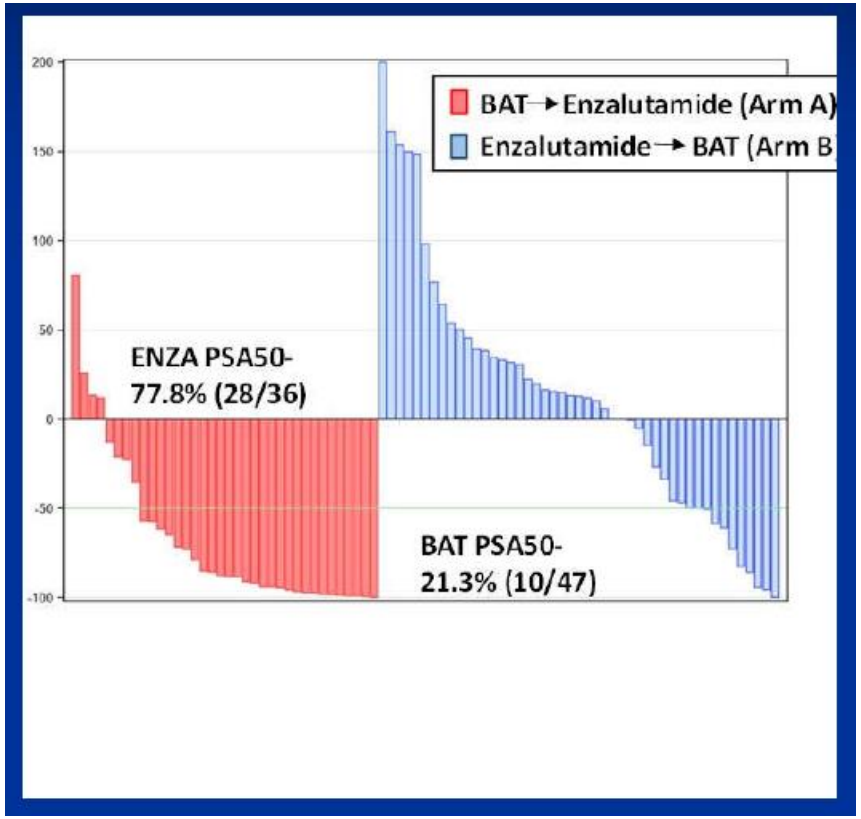
Bipolar Androgen Therapy



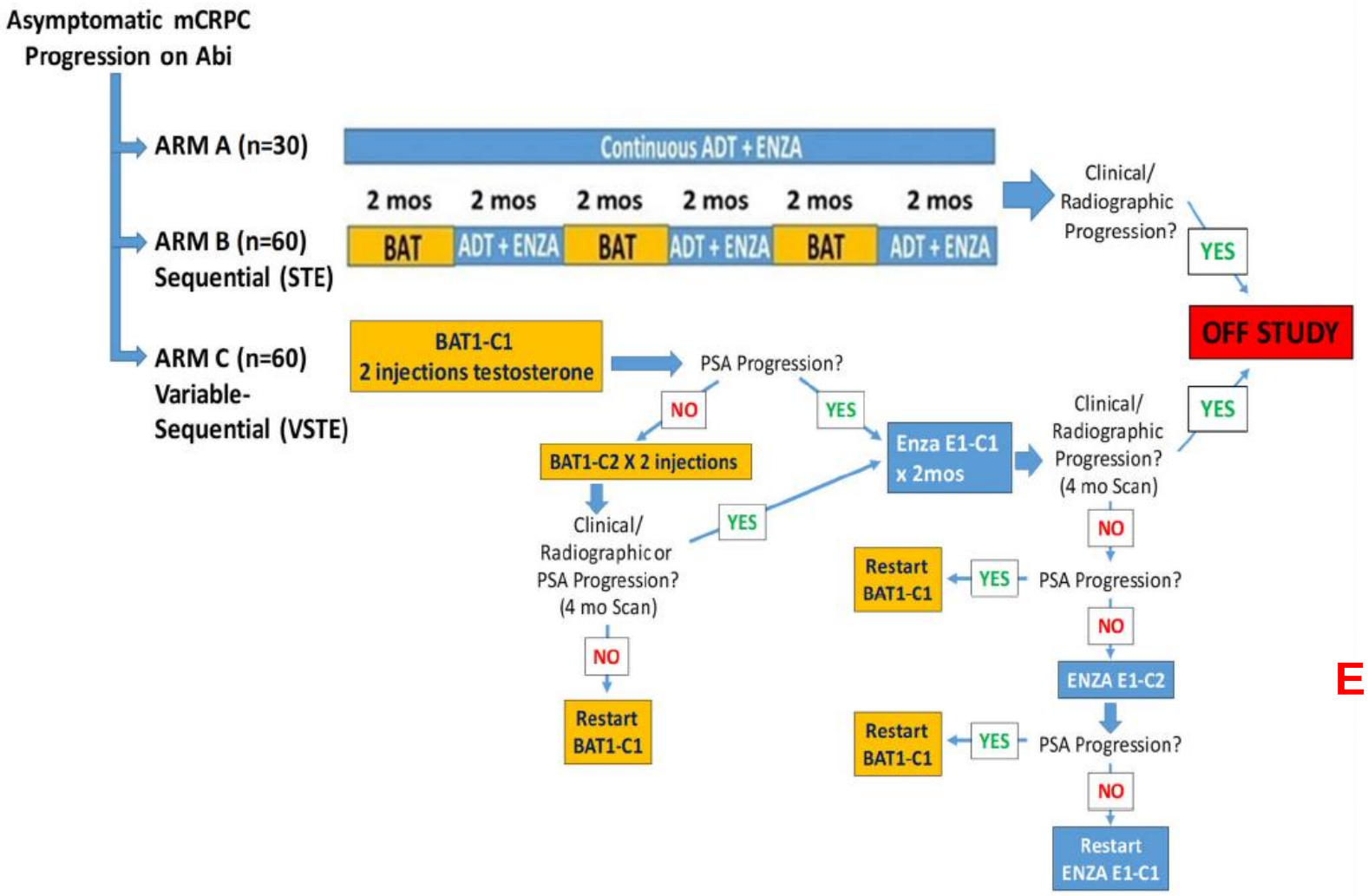


BAT Sensitizes to AR Antagonism



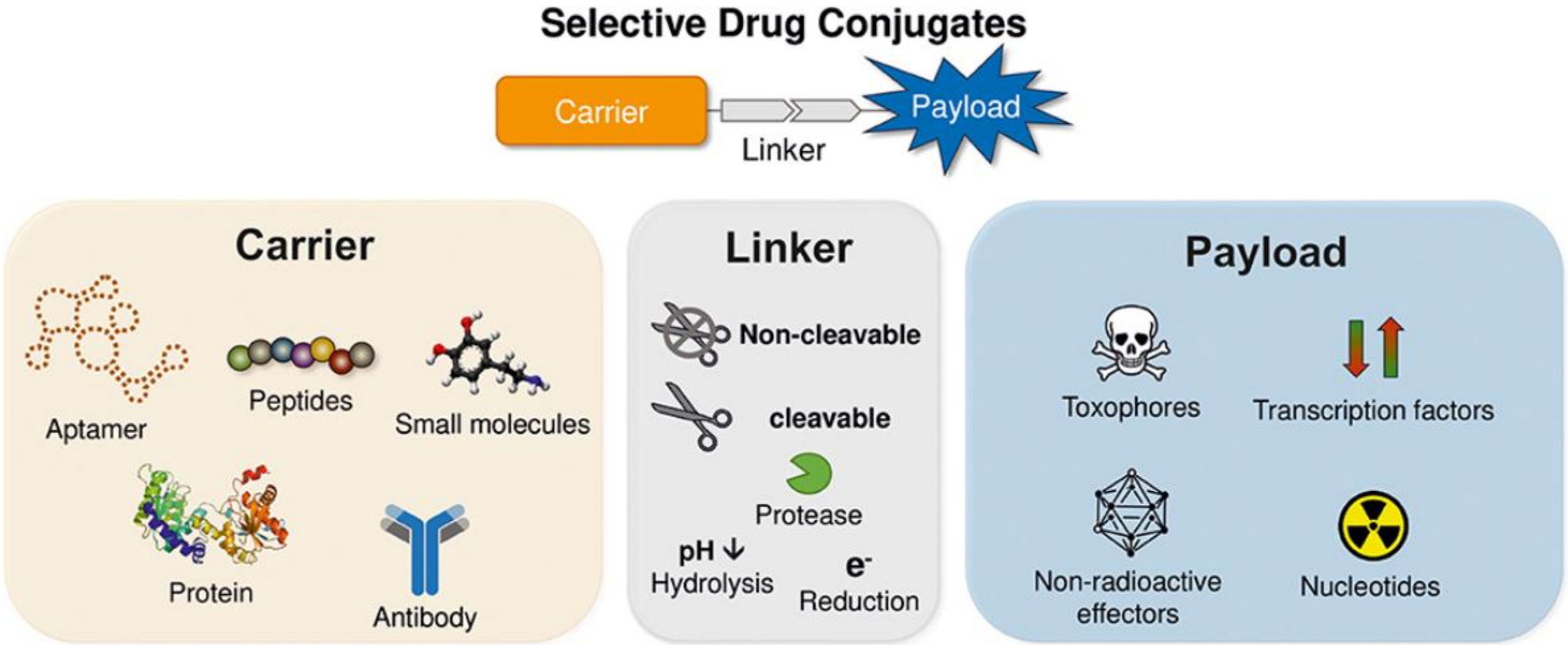


Step-Up Trial (Bipolar Androgen Therapy) – mCRPC



Enrolling at UCSD

Selective Drug Conjugates

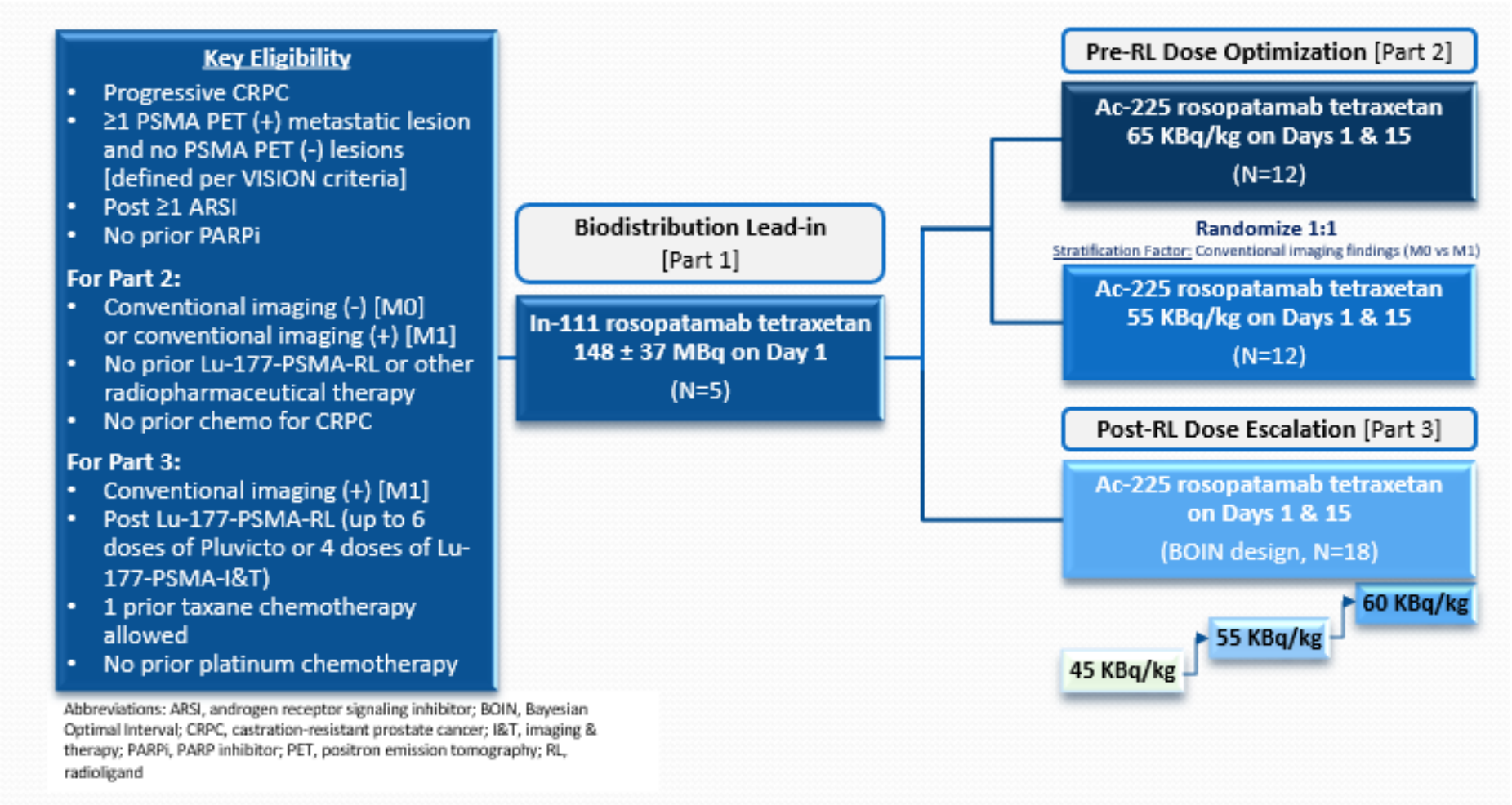


Radioligand Agents

^{177}Lu-PSMA-617	^{177}Lu-PNT-2002	^{225}AC-PSMA-617	^{225}AC-J591
• β emitter • PSMA small molecule	• β emitter • PSMA small molecule	• α emitter • PSMA small molecule	• α emitter • Monoclonal antibody

Ac-225-J591 in mCRPC

Enrolling at UCSD

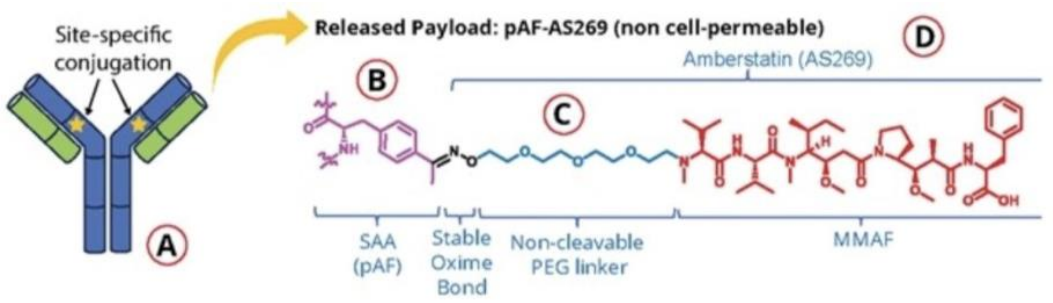


Abbreviations: ARSI, androgen receptor signaling inhibitor; BOIN, Bayesian Optimal Interval; CRPC, castration-resistant prostate cancer; I&T, imaging & therapy; PARPi, PARP inhibitor; PET, positron emission tomography; RL, radioligand

Antibody Drug Conjugates

ARX-517

- PSMA targeting
- Payload MMAF
- Greater PSA responses at higher doses (PSA50 52%)



Ifinatamab deruxtecan

- B7-H3 targeting
- Payload DXd (topoisomerase I inhibitor)
- PSA50 21%

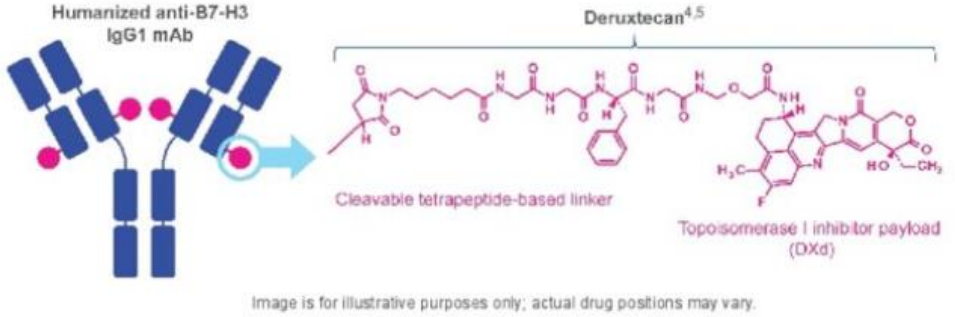
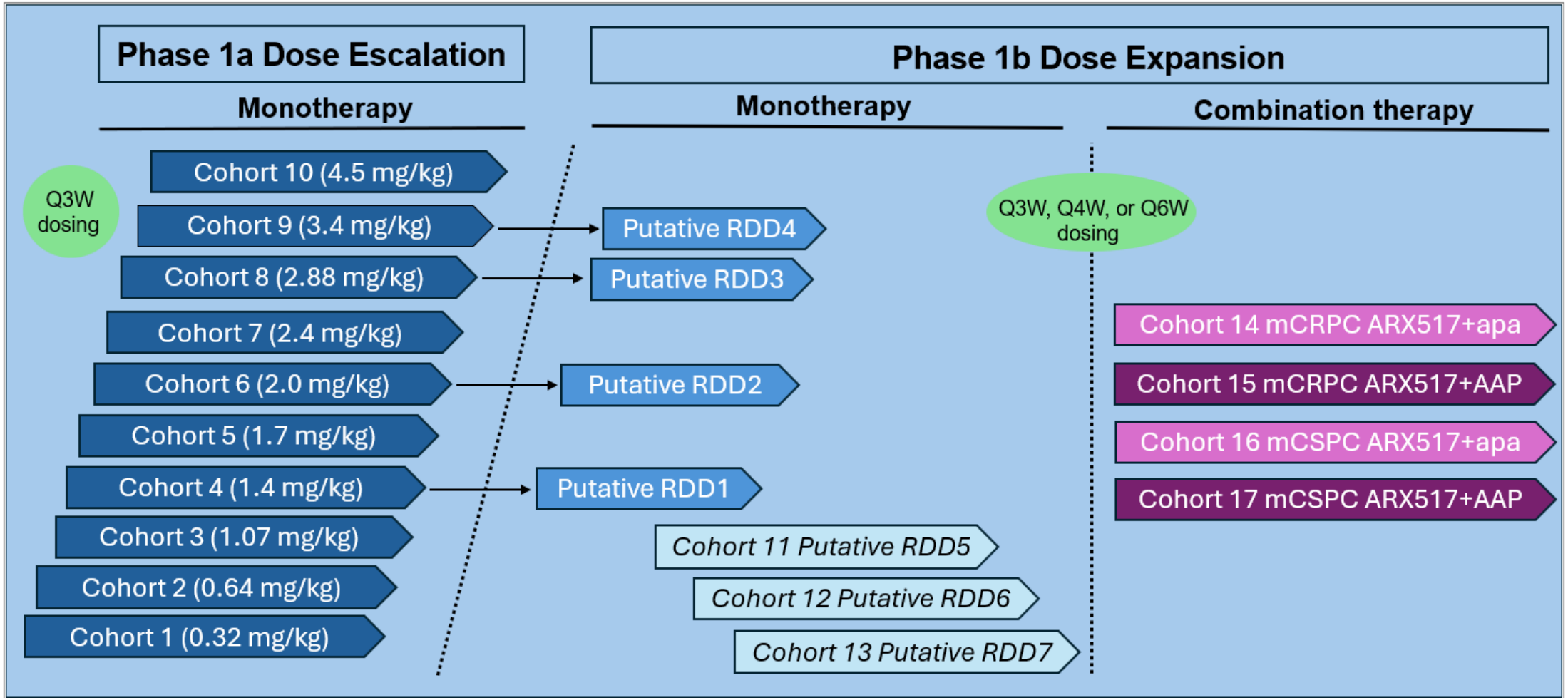


Image is for illustrative purposes only; actual drug positions may vary.

ARX-517 in mCPRC

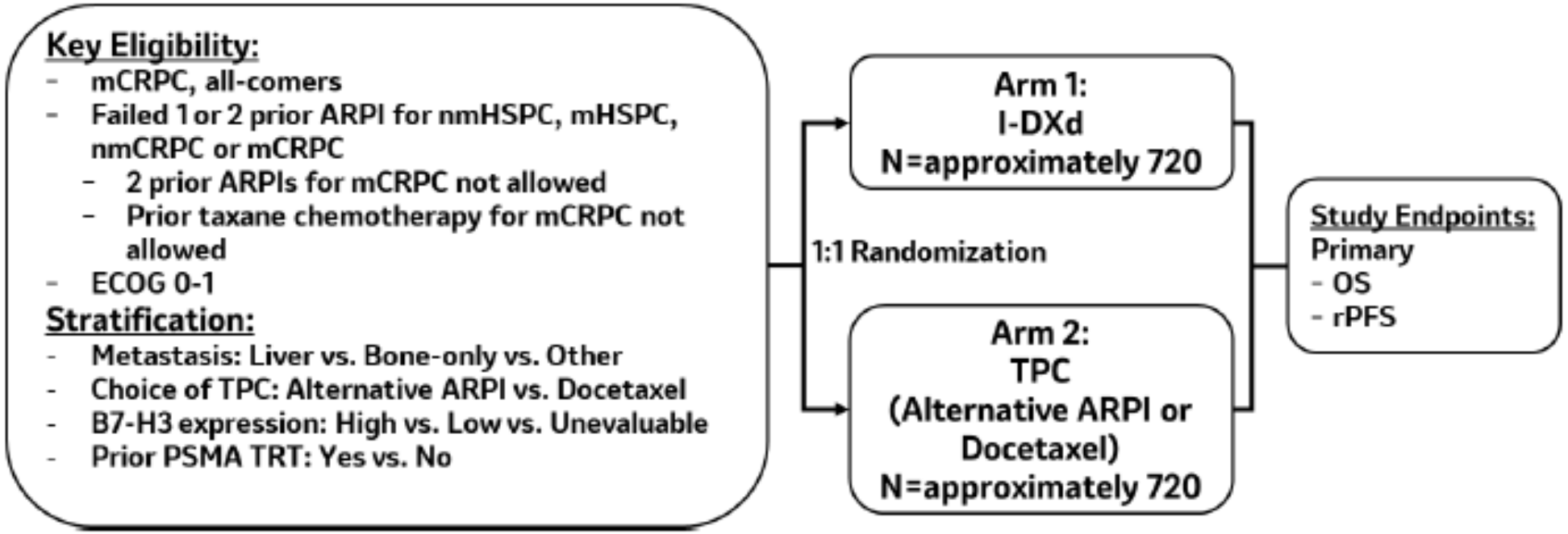
Enrolling at UCSD



Ifinatamab deruxtecan in mCRPC

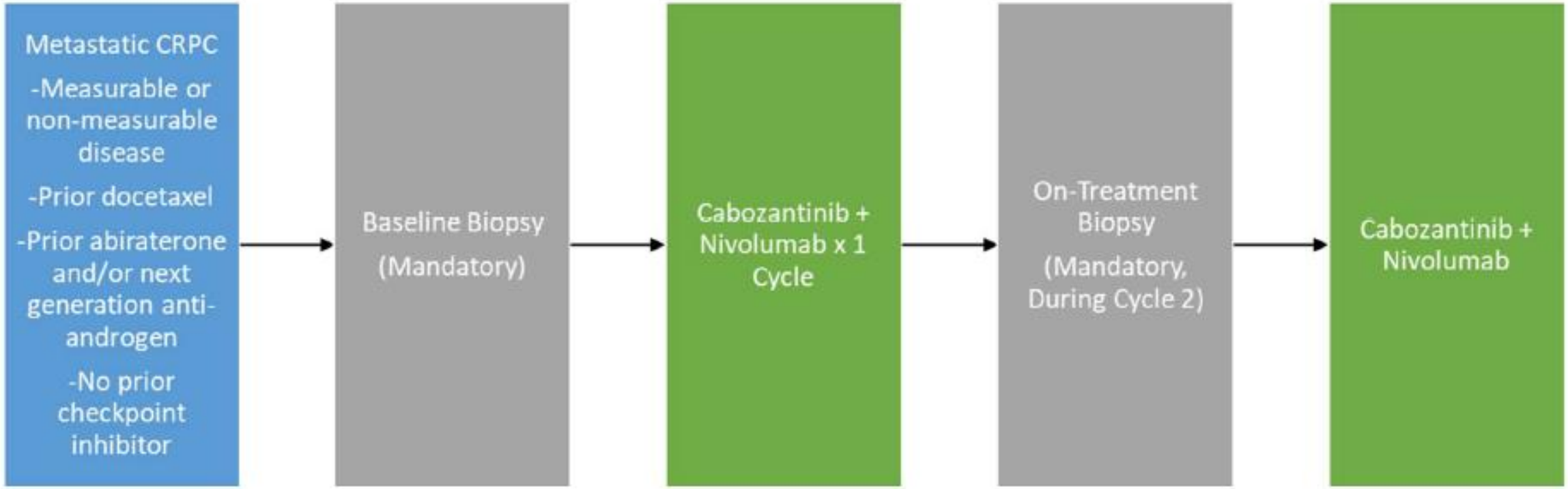
Enrolling at UCSD

Figure 1 Study Schema



ARPI=androgen receptor pathway inhibitor; ECOG=Eastern Cooperative Oncology Group; HSPC=hormone-sensitive prostate cancer; mCRPC=metastatic castration-resistant prostate cancer; mHSPC=metastatic hormone-sensitive prostate cancer; N=number of participants; nmCRPC=non-metastatic castration-resistant prostate cancer; nmHSPC=non-metastatic hormone-sensitive prostate cancer; OS=overall survival; PSMA=prostate-specific membrane antigen; rPFS=radiographic progression-free survival; TPC=treatment of physician's choice; TRT=targeted radionuclide therapy.

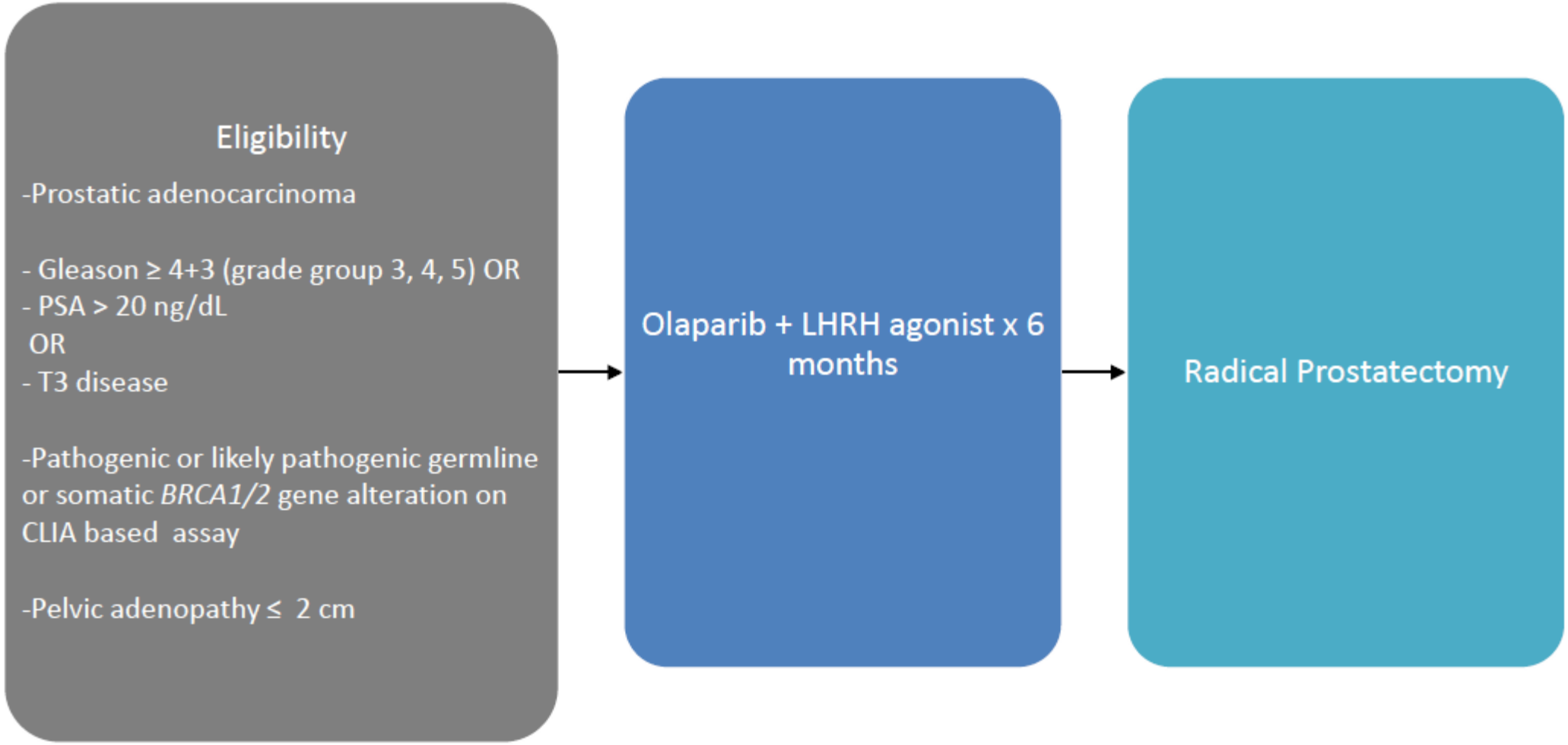
Canopy Trial – mCRPC



Enrolling at UCSD

Neptune Trial

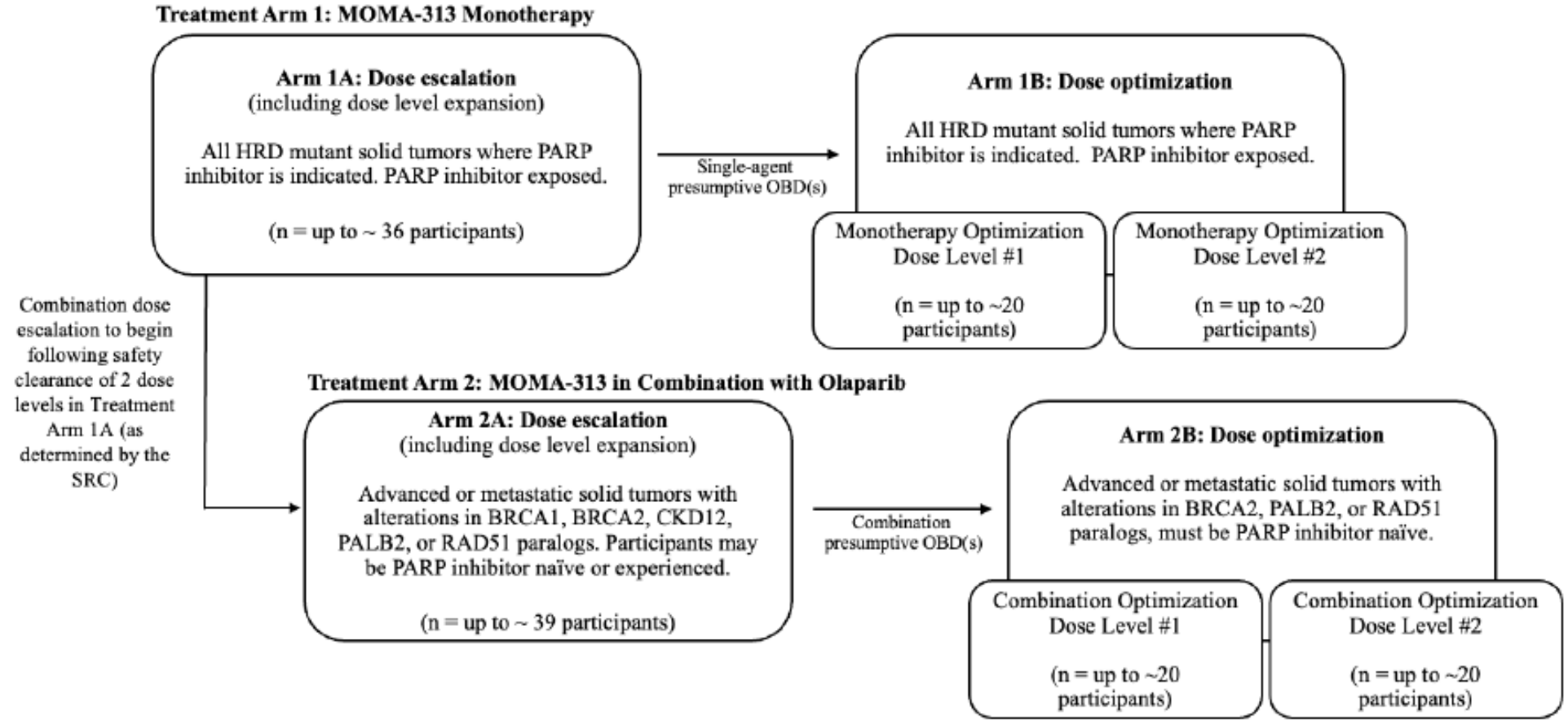
Enrolling at UCSD



MOMA-313, an oral Polθ inhibitor, in mCRPC

Enrolling at UCSD

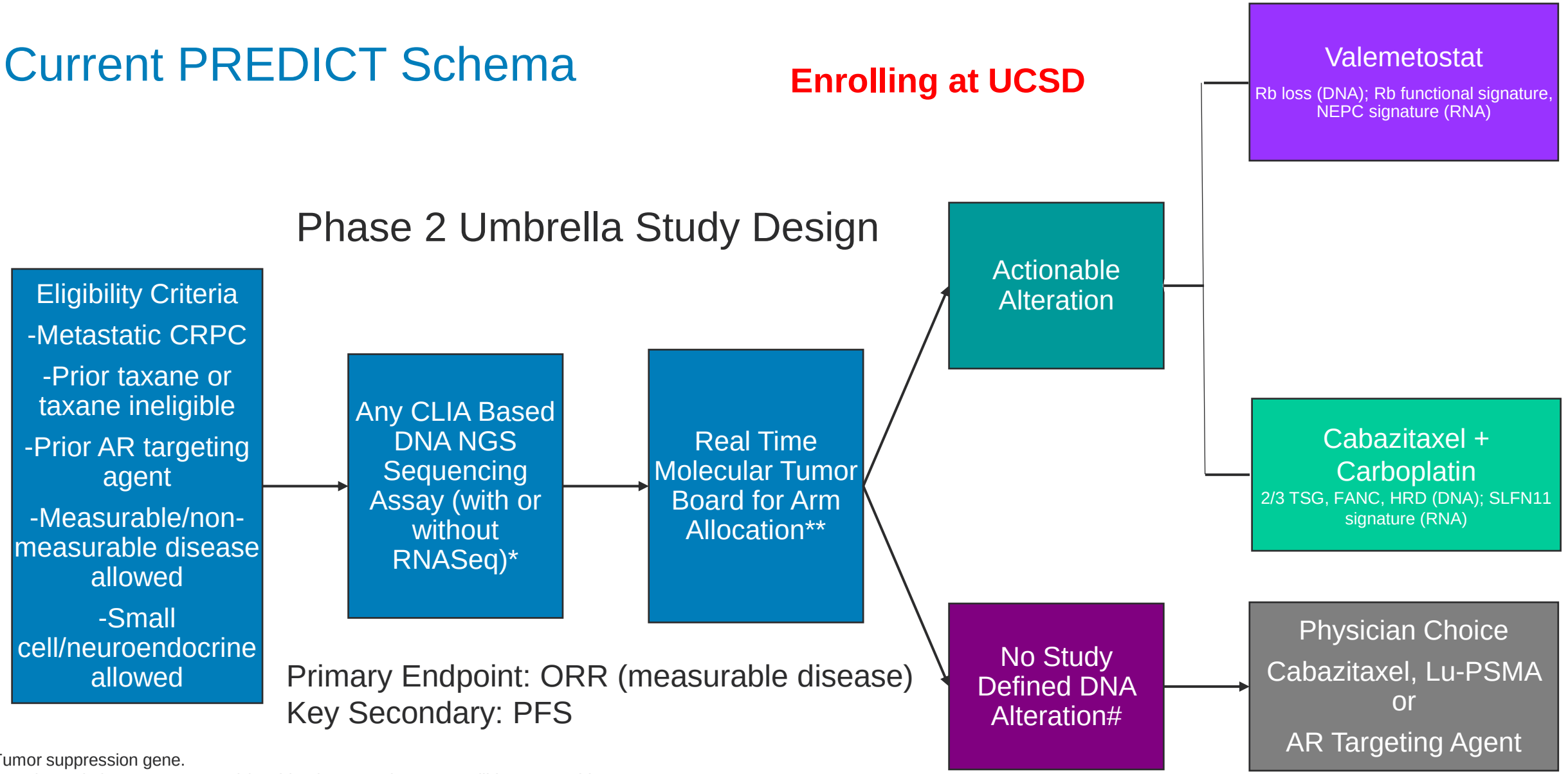
Figure 1: Study Schematic



Current PREDICT Schema

Enrolling at UCSD

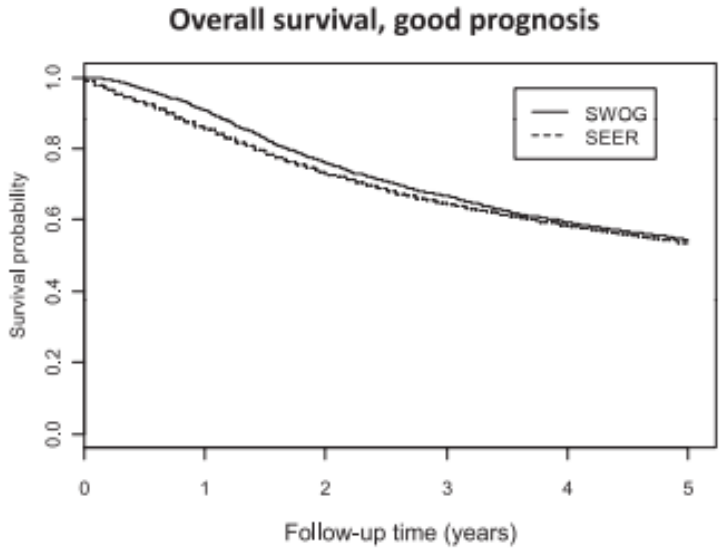
Phase 2 Umbrella Study Design

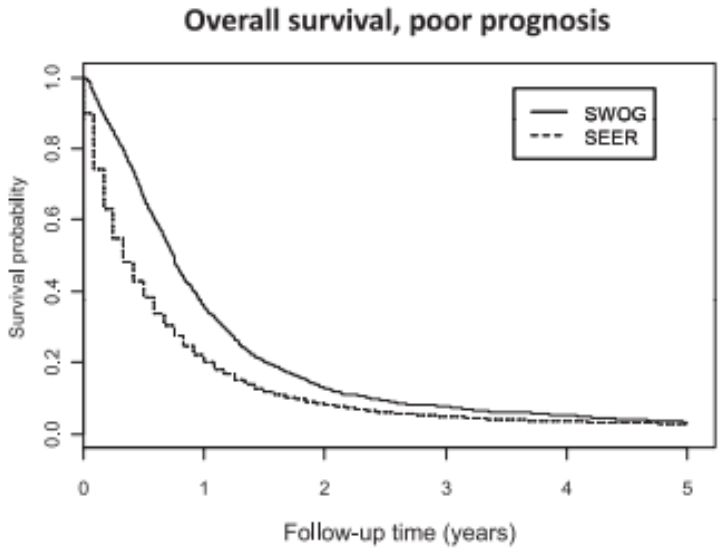


Primary Endpoint: ORR (measurable disease)
Key Secondary: PFS

TSG=Tumor suppression gene.
*Any CLIA tissue (primary or metastasis) or blood sequencing assay will be acceptable.
**Priority for allocation based on DNA. For patients with co-occurring DNA alterations that would qualify an individual to more than one arm, priority is given to the arm with less prevalent alterations projected.
#Patients are required to have tissue sequencing within 12 months of enrollment. Patients with actionable alterations including BRCA1/2 without prior exposure to a PARP inhibitor or patients with MSI/MMR-deficient tumors without prior exposure to PD-1/PD-L1 therapy will not be allowed to enroll.

Survival Improved in Patients Treated on Clinical Trials





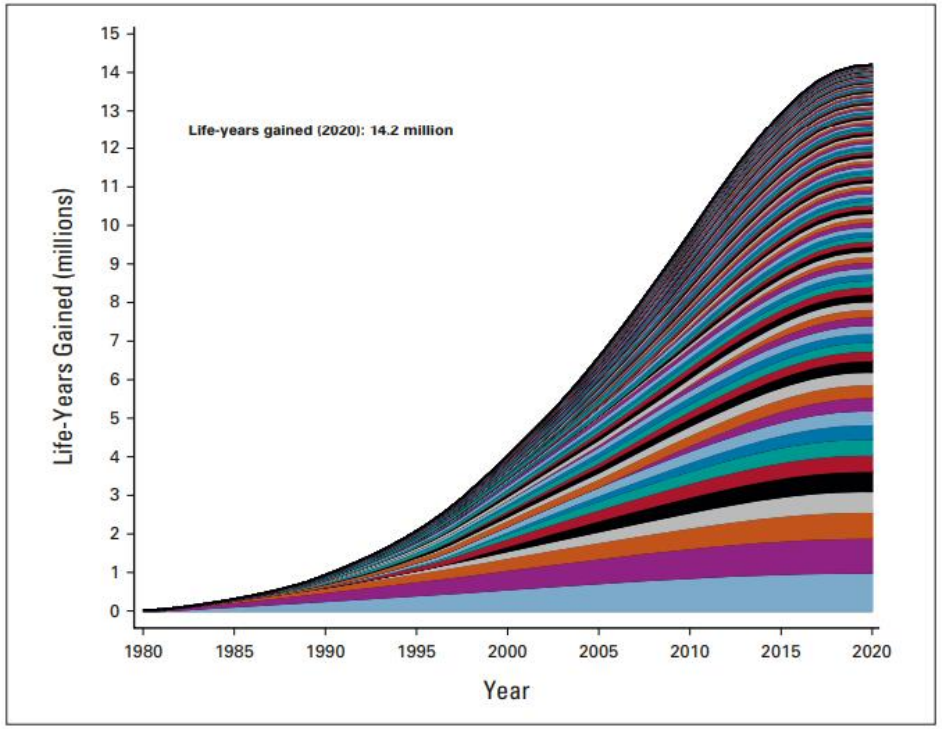


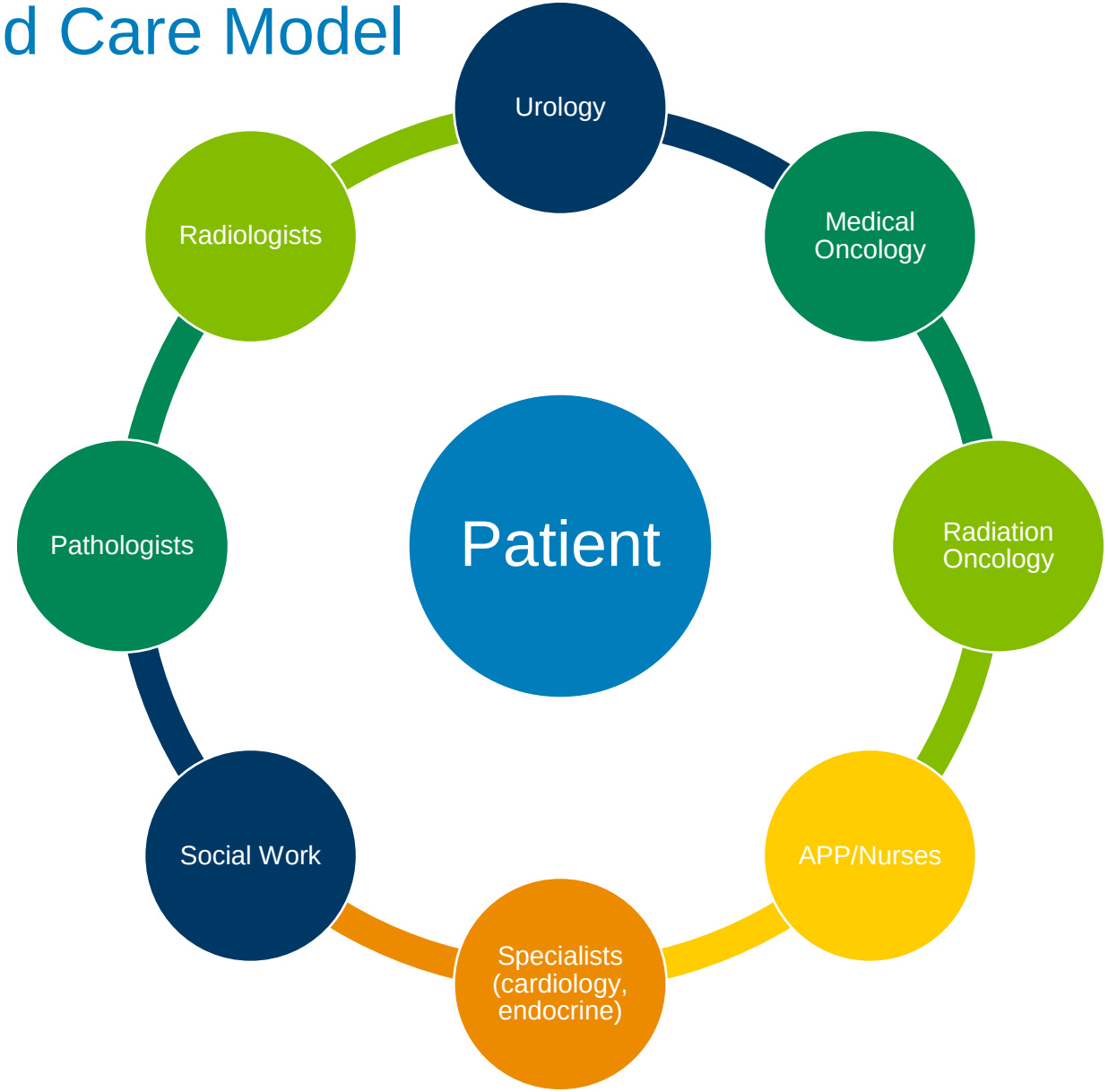
FIG 1. Cumulative life-years gained through 2020 by study. Each color-coded area represents cumulative life-years for 1 of 133 studies for which life-year gains were estimated.

One hundred sixty-two trials comprised of 108,334 patients were analyzed, representing 29.8% (162/544) of trials conducted

Unger et al, JNCI, 2014

Multidisciplinary Clinic – Integrated Care Model

- Weekly multidisciplinary clinic (Friday PM)
- Joint consultation with medical oncology, urology, and radiation oncology
- Integrated platform for molecular tumor profiling
- Screening for clinical trial eligibility
- Personalized treatment strategy



Conclusions

- There have been significant advances in life prolonging therapies for patients with advanced prostate cancer
- The care of patients with advanced prostate cancer is highly multidisciplinary and integrated with urology, medical oncology, and radiation oncology
- Clinical trials have improved outcomes for patients resulting in significantly prolonged survival

UC San Diego Health

Questions