2nd Annual Southern California Genitourinary Cancer Research Forum

Panel: Prostate Studies (Localized, Salvage/BCR, mHSPC, mCRPC)

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Disclosures

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This presentation and/or comments will be free of any bias toward or promotion of the above referenced companies or their product(s) and/or other business interests.

This presentation and/or comments will provide a balanced, non-promotional, and evidence-based approach to all diagnostic, therapeutic and/or research related content.

This presentation has been peer-reviewed and no conflicts were noted.

The off-label/investigational use of AMG509 (xaluritamig), PSCA CAR T cells, carotuximab, Ac225-CEA, talazoparib, AZD 5035 (saruparib), TLX-591, and 225 Ac-PSMA-617

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This presentation and/or comments will be free of any bias toward or promotion of the above referenced companies or their product(s) and/or other business interests.

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Cultural Linguistic Competency (CLC) & Implicit Bias (IB)

STATE LAW:

The California legislature has passed Assembly Bill (AB) 1195, which states that as of July 1, 2006, all Category 1 CME activities that relate to patient care must include a cultural diversity/linguistics component. It has also passed AB 241, which states that as of January 1, 2022, all continuing education courses for a physician and surgeon **must** contain curriculum that includes specified instruction in the understanding of implicit bias in medical treatment.

The cultural and linguistic competency (CLC) and implicit bias (IB) definitions reiterate how patients' diverse backgrounds may impact their access to care.

EXEMPTION:

Business and Professions Code 2190.1 exempts activities which are dedicated solely to research or other issues that do not contain a direct patient care component.

The following CLC & IB components will be addressed in this presentation:

- *We will address genomic and other disease characteristics that may vary according to ancestry.*
- *Will discuss importance of offering clinical trials to all patients without hesitation.*
- *Potential barriers to patient care due to race/ethnicity and/or socioeconomic status.*
- *Known knowledge in disparities in care including published work.*

Case 1: Intermediate-risk localized prostate cancer

A 48 year-old man was recently diagnosed with an **intermediate-unfavorable risk prostate cancer** (T1c, PSA 8, Gleason 4+3). He is in excellent clinical condition and is known for having several female family members on his mother's side with ovarian and breast cancer. On diagnosis he underwent germline testing with the INVITAE panel that reported a pathological variant in the *BRCA2* gene. He comes to discuss treatment.

a) Radical prostatectomy

b) Hormone-radiation therapy with 6 months of ADT

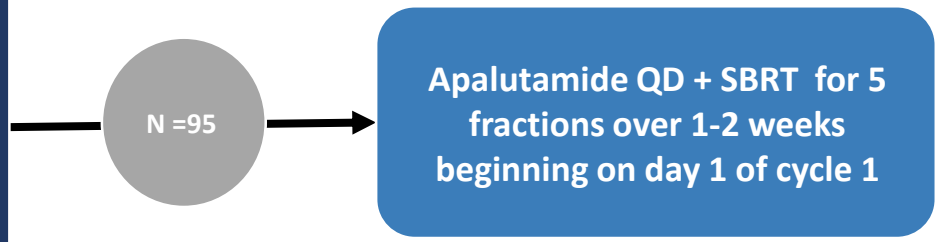
c) HEATWAVE

HEATWAVE

NCT06067269

Phase 2, single-arm

- **Unfavorable intermediate-risk prostate**
  - **2 of the following: PSA 10-20 ng/mL, T2b-2c, ISUP group 2;**
  - **Any 1 of with ISUP grade group 3 disease**
  - **Any 1 with 50% or more cores with prostate cancer)**
- **Decipher genomic classifier score**
- **Have at least one dominant intraprostatic lesion visible on multiparametric MRI**
- **Have undergone a PSMA PET**
- **Testosterone >= 150 ng/dL**
- **ECOG 0-1**



Endpoints

Primary: % patients achieving PSA of < 0.2 ng/mL

Secondary: time to BCR, PROs, radiographic persistence of disease on PSMA/PET and MRI, acute and late toxicities

Case 2: High-risk localized prostate cancer

A 48 year-old man was recently diagnosed with a **very high-risk prostate cancer** (T3b, PSA 48, Gleason 4+5). He is in excellent clinical condition and is known for having several female family members on his mother's side with ovarian and breast cancer. On diagnosis he underwent germline testing with the INVITAE panel that reported a pathological variant in the *BRCA2* gene. He comes to discuss treatment.

a) Radical prostatectomy

b) Hormone-radiation therapy with 24 months of ADT

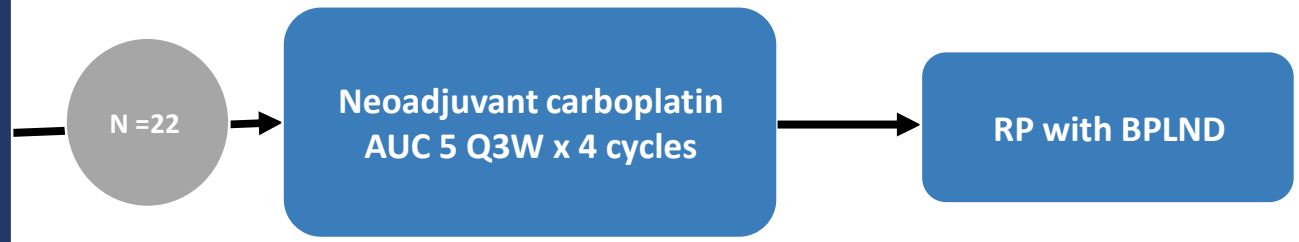
c) SWOG 2210

SWOG 2210

NCT05806515

Phase 2, single arm

- **High or very high-risk disease defined by at least one of the following:**
  - **cT3a to cT4x**
  - **Grade Group 4 or 5 (Gleason sum 8-10)**
  - **PSA > 20 ng/mL prior to registration**
- **Germline mutation (pathogenic/likely pathogenic variant) in BRCA2 or BRCA1 through testing in a CLIA-certified lab**



Endpoints

Primary: pCR rate

Secondary: bPFS, rates of salvage therapy, time to metastases, OS

Case 3: Metastatic HSPC

A 78-year-old man presents to the ER with acute low back pain. Lumbar MRI shows several blastic lesions throughout the spine. His **PSA is 97**, and a bone biopsy confirms **metastatic prostate carcinoma**. CT CAP and bone scan show several **sites of bone-only disease**, including L3-L5, the pelvis, femur, and humerus. The patient comes seeking clinical trials.

a. ADT + ARSI

b. EvoPAR

c. TriplePRO

EvoPAR

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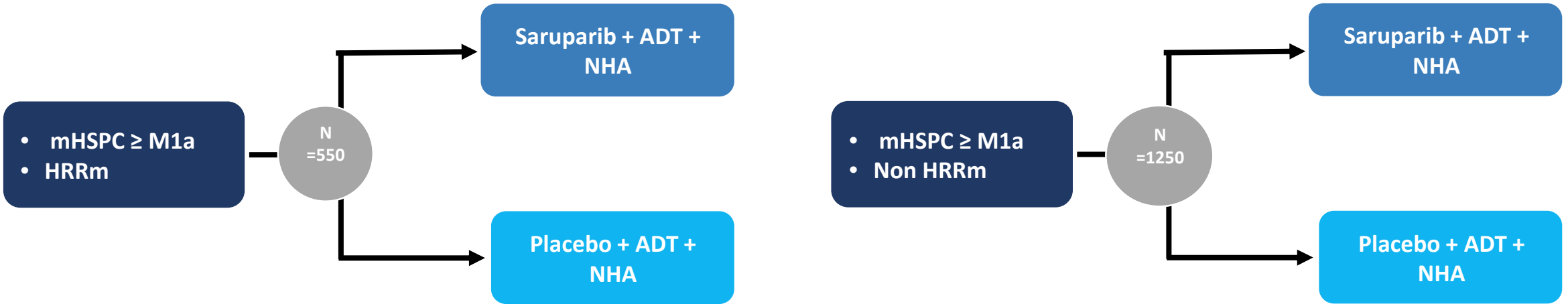
PROVIDENCE

NCT06120491

Phase 3, randomized, 2-cohort, double-blind, placebo-controlled



Notes

Physician's choice NHA = abiraterone, darolutamide, or enzalutamide (ensure minimum 12.5% per NHA used in each cohort).

Prospective tissue + ctDNA testing used for stratification. *BRCAm* capped to 42% in HRRm Cohort (n = 231).

Low volume capped at 37% in Non-HRRm Cohort.

Endpoints

Primary: rPFS in BRCAm/ rPFS non-HRRm

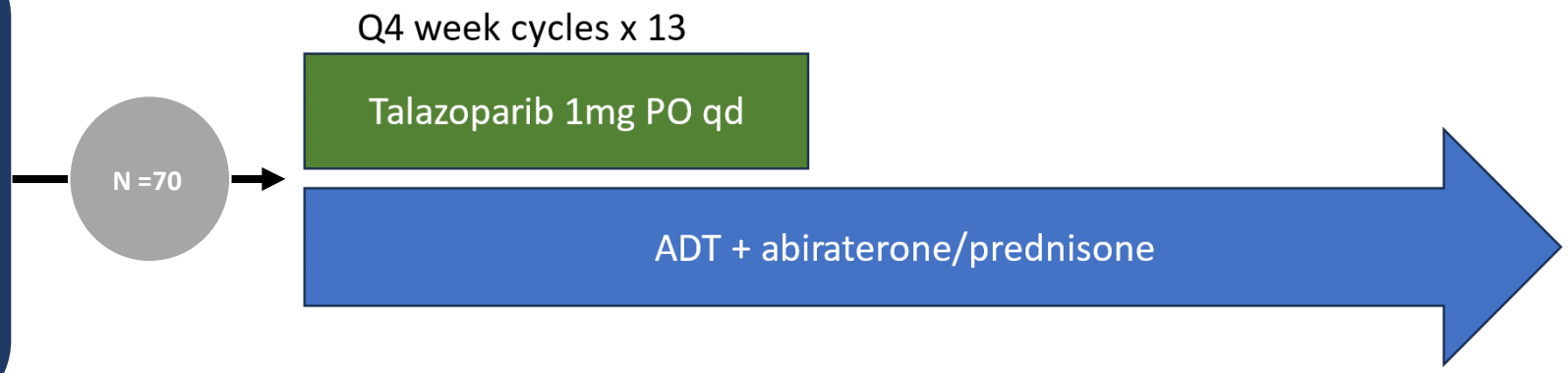
Secondary: rPFS HRR, OS

TriplePRO

NCT 04734730

Phase 2, single arm, open label

- **Metastatic HSPC (measurable disease not required)**
- **6 months since completion of ADT in the neoadjuvant and/or adjuvant setting, and it must not have lasted for more than 36 months**
- **No more than 60 days from first LHRH injection (or surgical castration)**
- **Abiraterone for no more than 3 weeks**



Endpoints

Primary: PSA nadir <0.2 at 12 months

Secondary: ORR, PSA response, rPFS, PROs

Case 3: Metastatic HSPC continuation

A 78-year-old man presents to the ER with acute low back pain. Lumbar MRI shows several blastic lesions throughout the spine. His PSA is 97, and a bone biopsy confirms metastatic prostate carcinoma. CT CAP and bone scan show several sites of bone-only disease, including L3-L5, the pelvis, femur, and humerus. The patient comes seeking clinical trials.

The same patient decided to receive standard of care with ADT+apalutamide. After 6 months of treatment, he has had a PSA response of 0.08 and has not presented with major toxicities. He is be interested in knowing additional options that could improve his quality of life and his survival.

a. Continue treatment

b. Offer treatment to the primary

c. SWOG 1802

SWOG 1802

NCT 03678025

Phase 3, randomized controlled trial

- mHSPC ≥ M1a
- No local tumor recurrence
- PSA ≤10.0 ng/ml
- Must have ≥3 PSA values within the last two years since end of primary treatment
- Serum total testosterone ≥ 100 ng/dL

N =260

Systemic standard of care + definitive treatment (surgery and radiation)

Systemic standard of care

Endpoints

Primary: OS

Secondary: rate of symptomatic local progression, PFS

Case 4: Metastatic CRPC

A 71-year-old man was diagnosed with high-risk prostate cancer and underwent a prostatectomy in 2017 but was lost to follow-up. He returned to the clinic in late 2022 with a PSA of 24 and a PSMA PET scan showing metastatic disease in the bone and liver. He started therapy with ADT and apalutamide without significant toxicities, achieving a PSA nadir of 4. In late 2024, his PSA began to rise, and imaging showed several new sites of disease in the bone and liver. He underwent an NGS with a TMB 14 mt/mB. The patient states that he is not interested in receiving chemotherapy.

a. Best supportive care

b. ProstACT GLOBAL

c. AlphaBreak

d. START-001

ProstACT GLOBAL

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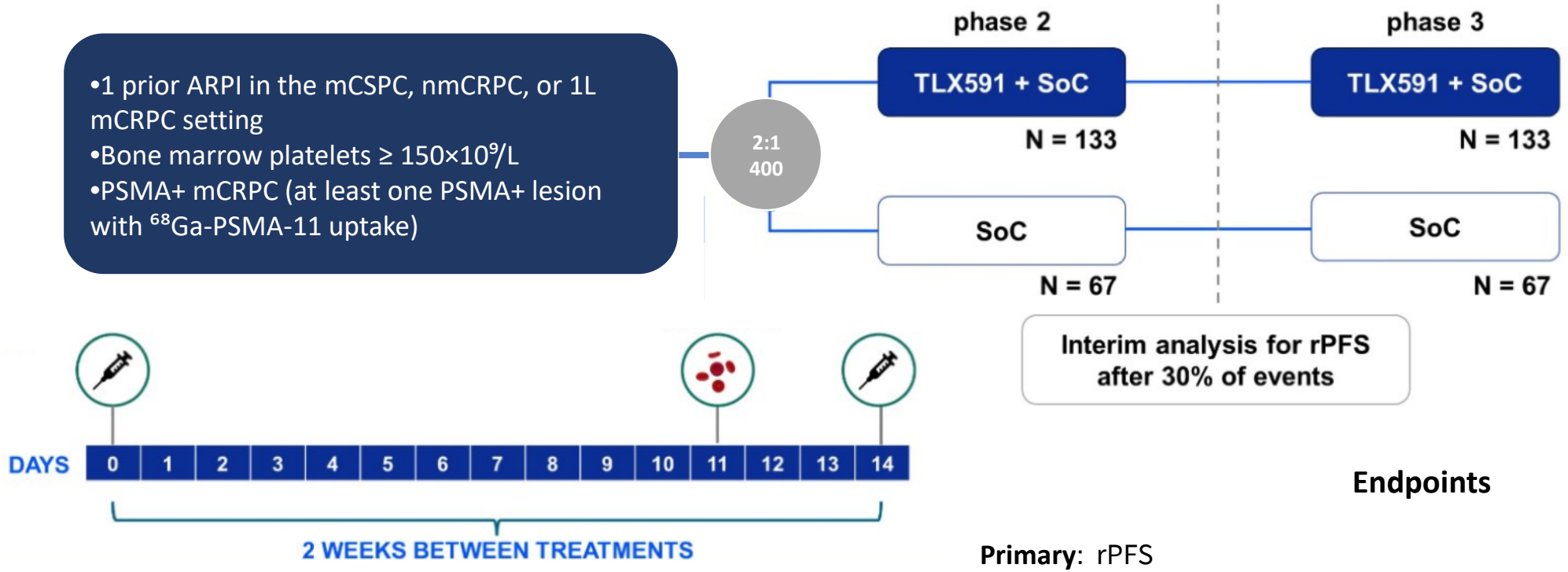
NCT06520345

Phase 2/3, multinational, multicenter, prospective, randomized, controlled open label study.



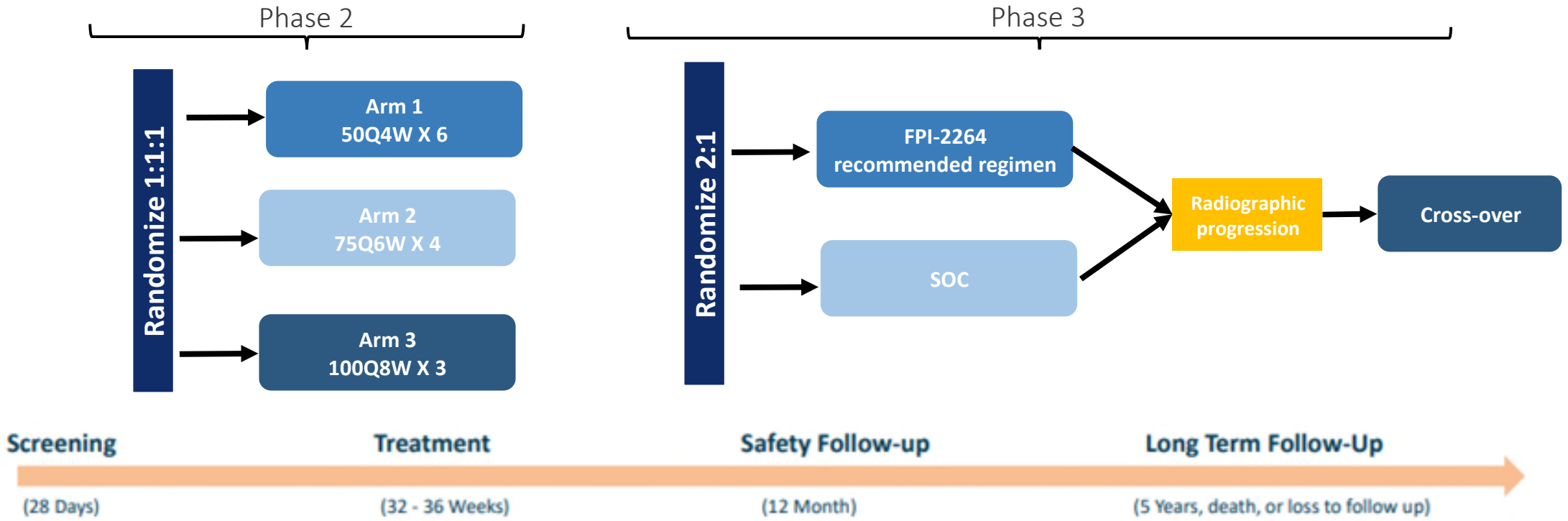
Endpoints

Primary: rPFS
Secondary: OS, ORR, symptomatic skeletal-related events, QoL

SoC physician's choice: ARPI, docetaxel, external Radiation (palliative), hormonal agents, LHRH analogues, bone-targeted agents, corticosteroids, supportive measures (such as pain medication, hydration, and/or transfusions)

AlphaBreak

NCT06402331



MOA:

- 225 Ac FPI-2264: binding its carrier/ligand, PSMA-I&T, to PSMA. The binding allows for the targeted delivery of alpha particles directly to the cancer cells.

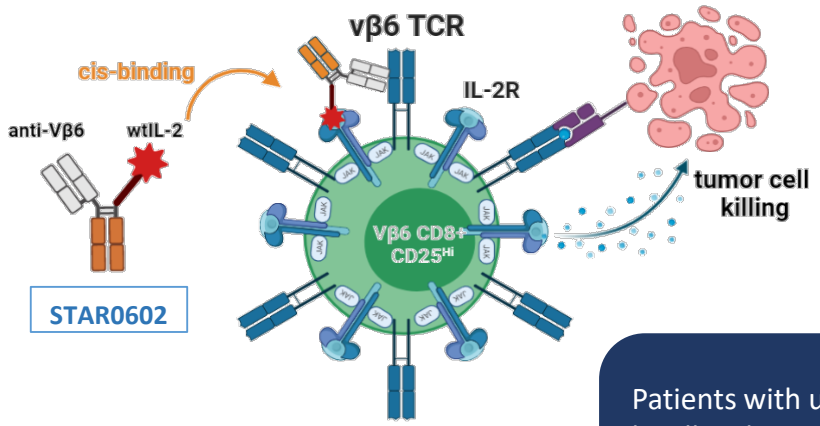
Endpoints

Phase 2: safety and efficacy, PSA50, AE/SAE, PK, Changes in PRO, rPFS
Primary: rPFS
Secondary: PFS, ORR, OS, PSA50, DoR, changes in PRD, time to SSE, PK

START-001

NCT 06067269

Phase 2/3, two-part, open-label, FIH, STAR0602 given via IV infusion, Q2W



Patients with unresectable, locally advanced, metastatic solid tumors with TMB-H, MSI-H/dMMR, or virally associated

Phase I: Dose Escalation

DL5
DL4.5
DL4
DL3
DL2
DL1

RP2D = 0.08 mg/kg

Phase II: Dose Expansion

Optimal Simon's Two-Stage Design

- TMB-H (≥ 10 mut/Mb)
- MSI-H/dMMR
- CRC (both Ras WT and mutant) TMB-H, or MSI-H /dMMR, or both TMB-H and MSI-H/dMMR
- Virally associated tumors
- mTNBC
- Ovarian
- Prostate (mCRPC)
- NSCLC
- Immunogenic tumors

Biopsy:
- **Screening**
- **C1D21**

MOA:

- STAR0602: is a bifunctional antibody-fusion molecule, binds both TCR and IL-2 receptors only on Vβ6/Vβ10 cells (in cis orientation) Once bound to the TCR, STAR0602 promotes the activation and expansion of CD8+(cytotoxic) T-cells

Case 5: Metastatic CRPC

A 66-year-old man was diagnosed with de novo mHSPC in 2017 and started treatment with ADT and 6 cycles of docetaxel. He responded until early 2020, when he developed a new site of disease in the lungs. He began first-line treatment with abiraterone/prednisone until mid-2022, when disease progression occurred. He then received 8 cycles of cabazitaxel but had to discontinue due to new shoulder pain. An MRI showed new sites of bone metastases. A PSMA PET scan demonstrated PSMA avidity in all metastatic sites (bone and lungs). He received 6 cycles of treatment without significant toxicities. He recently underwent somatic testing of his primary tumor that reported an *SPOP* mutation. After 3 months, the patient presented with progression at known sites of disease. Which treatment option would you offer?

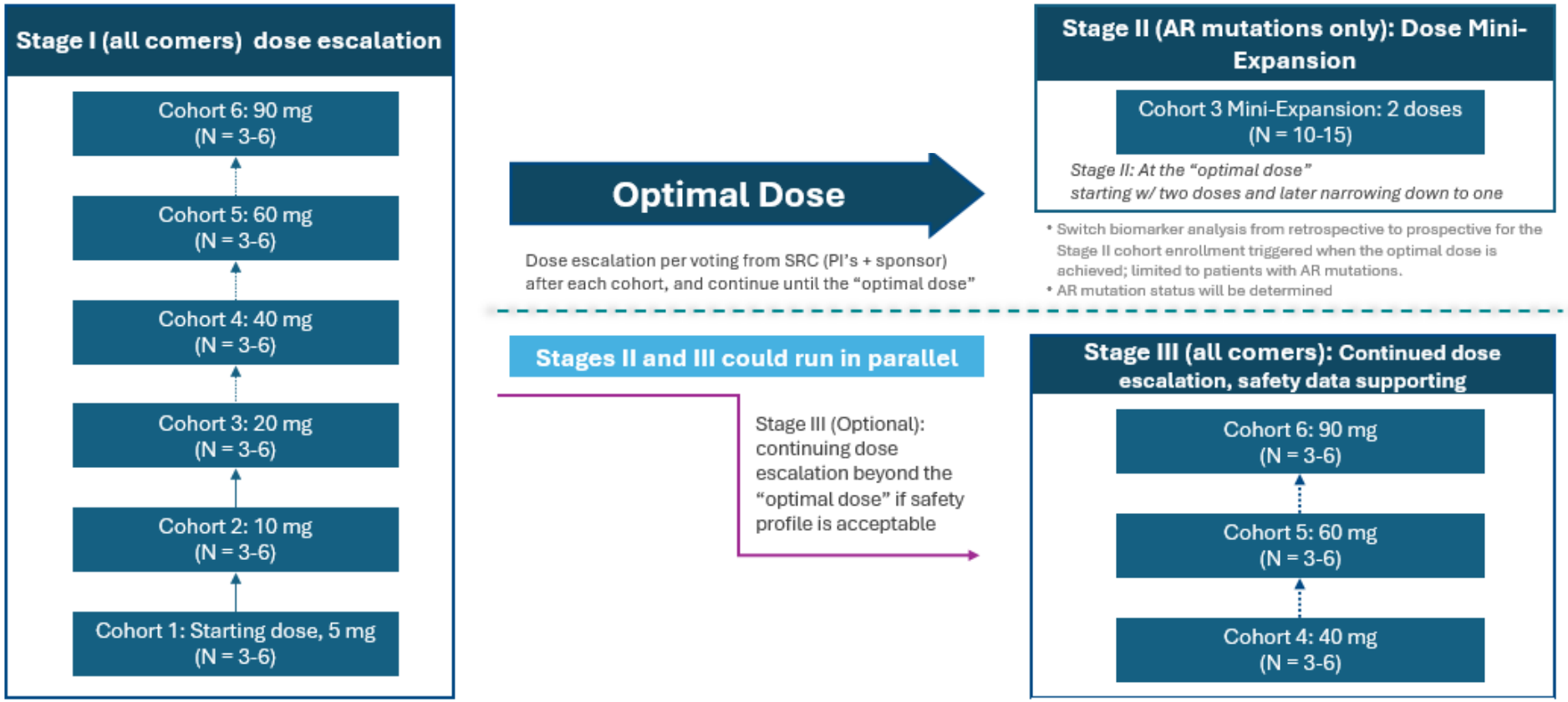
a. INV 9956

b. AMGEN-509

c. MK-5684

INV-9956

NCT06609005



MOA:

- INV-9956: inhibits Cyp11A1, an enzyme that catalyzes the production of pregnenolone. This inhibition prevents the biosynthesis of androgens and other steroids

Endpoints

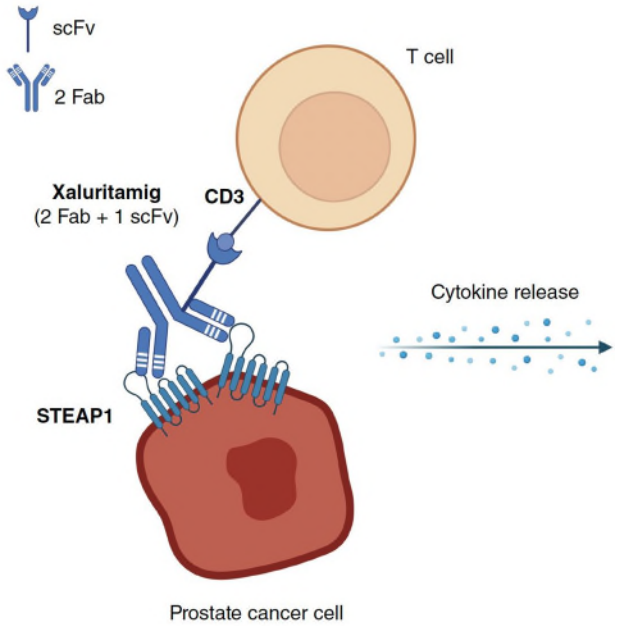
Primary: MTD, RDR

Secondary: safety, PK/PD, rPFS, ORR

AMG 509

NCT 06691984

Phase 3, randomized control trial, open-label



- **mCPRC ≥ 1 metastatic lesion**
- **Testosterone < 50 ng/dL**
- **Prior ARDT and docetaxel (if eligible)**
- **Screening period (28 days)**
- **Prior treatment with RLT, PARPi permitted**

R 2:1
N =675

Xaluritamig

Cabazitaxel or second ARDT

MOA:

- Xaluritamig: six-transmembrane epithelial antigen of the prostate 1 (STEAP1)–targeted T-cell engager

Endpoints

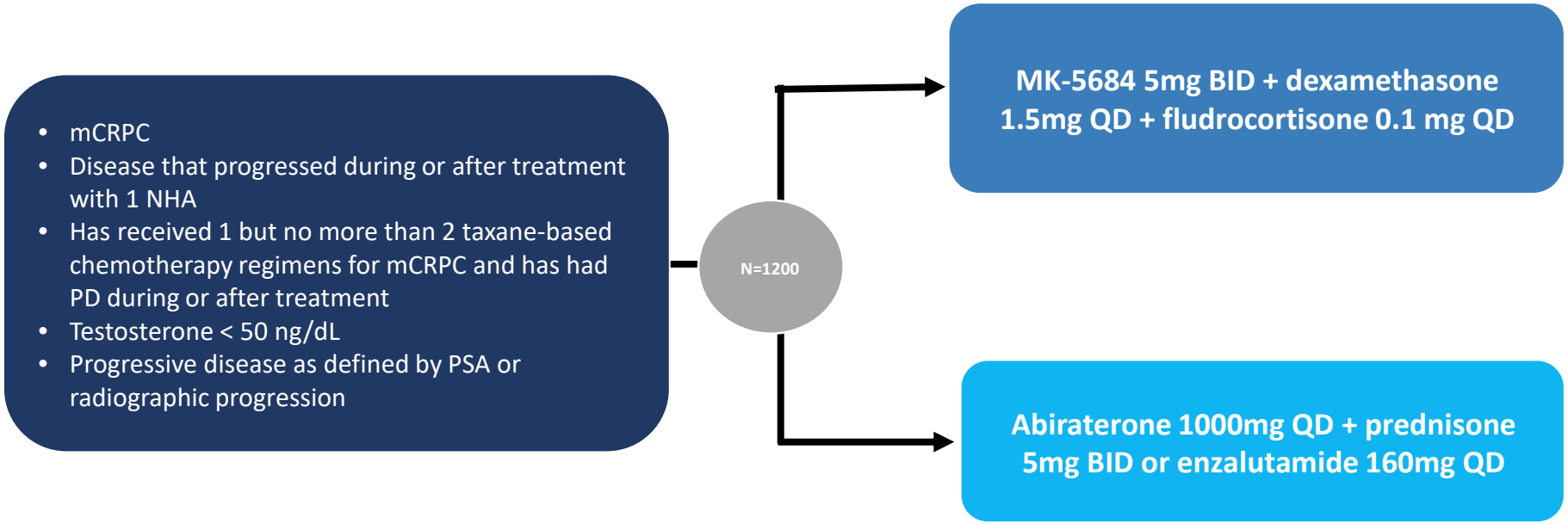
Primary: OS

Secondary: rPFS, ORR, DOR, DCT, PFS, TTR, SSE, QoL, time to worsening, PK/PD

MK-5684 Versus Alternative NHA

NCT 06136624

Phase 3, randomized control trial, open-label, parallel assignment



MOA:

- MK-5684: oral, non-steroidal, selective inhibitor of CYP11A1 (first and rate-limiting enzyme of steroid biosynthesis)

Endpoints

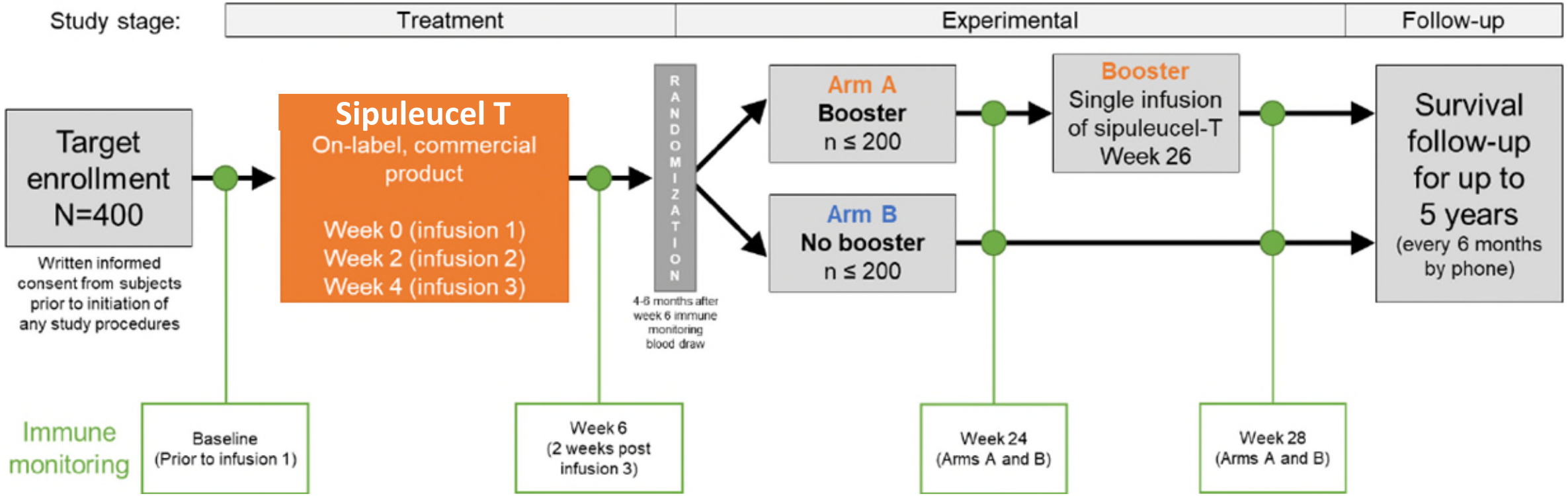
Primary: OS, OS in AR LBD, rPFS

Secondary: time to initiation of the first subsequent anticancer therapy, ORR, DOR, time to pain progression, PSA RR, AE, time to first symptomatic skeletal-related event

Case 5: Metastatic CRPC

A 66-year-old man was diagnosed with de novo mHSPC in 2017 and started treatment with ADT and 6 cycles of docetaxel. He responded until early 2020, when he developed a new site of disease in the lungs. He began first-line treatment with abiraterone/prednisone until mid-2022, when disease progression occurred. He then received 8 cycles of cabazitaxel but had to discontinue due to new shoulder pain. An MRI showed new sites of bone metastases. A PSMA PET scan demonstrated PSMA avidity in all metastatic sites (bone and lungs). He received 6 cycles of treatment without significant toxicities. He recently underwent somatic testing of his primary tumor that reported an *SPOP* mutation. After 3 months, the patient presented with progression at known sites of disease.

The patient enrolled in the MK-5684 trial and is doing great, he asks you if you think any trials that excite you for the future…



Endpoints

Primary: humoral immune response to PAP and PA2024 after sipuleucel-T booster with 2 different measures between arms: the geometric mean of the antibody responses and the rate of response

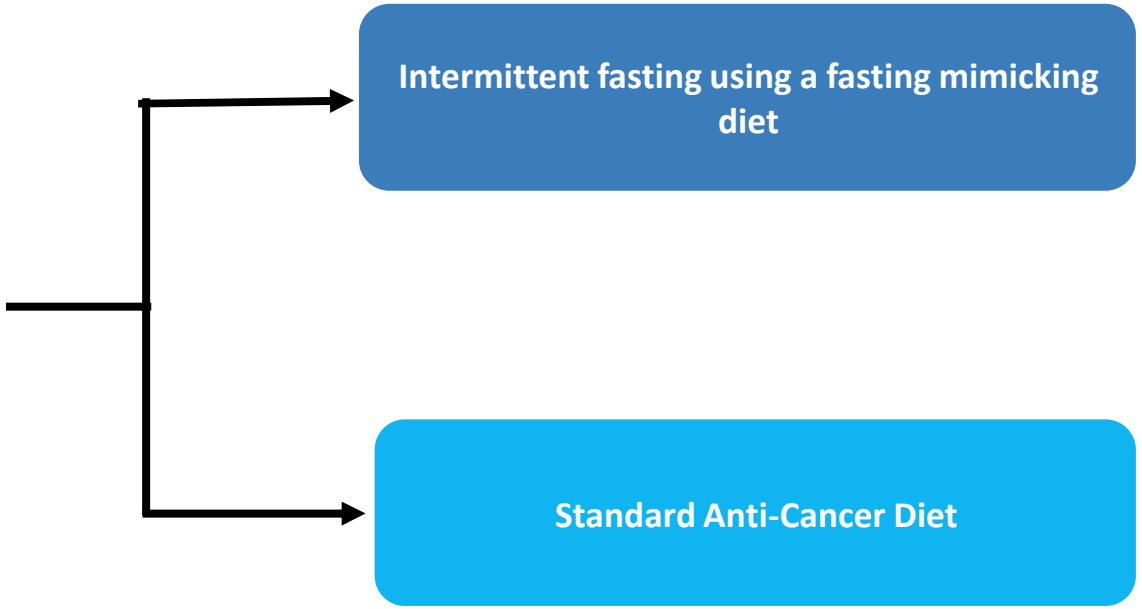
Secondary: OS, safety

FAST-PRO

NCT05832086

Phase 2, randomized two-armed, multi-site study

- Metastatic HSPC (adenocarcinoma prostate histologically confirmed by biopsy AND metastatic disease confirmed biopsy, or MRI scan)
- Men receiving or planning to start first-line intensified ADT with abiraterone, apalutamide, enzalutamide, or darolutamide with or without current or prior chemotherapy



Endpoints

Primary: response to cancer treatment
Secondary: time to development of castration resistance, metabolic toxicity