A Multicenter, Open-Label, Exploratory Platform Study to Evaluate Biomarkers and Immunotherapy Combinations for the Treatment of Patients With Metastatic Castration-resistant Prostate Cancer (PORTER)

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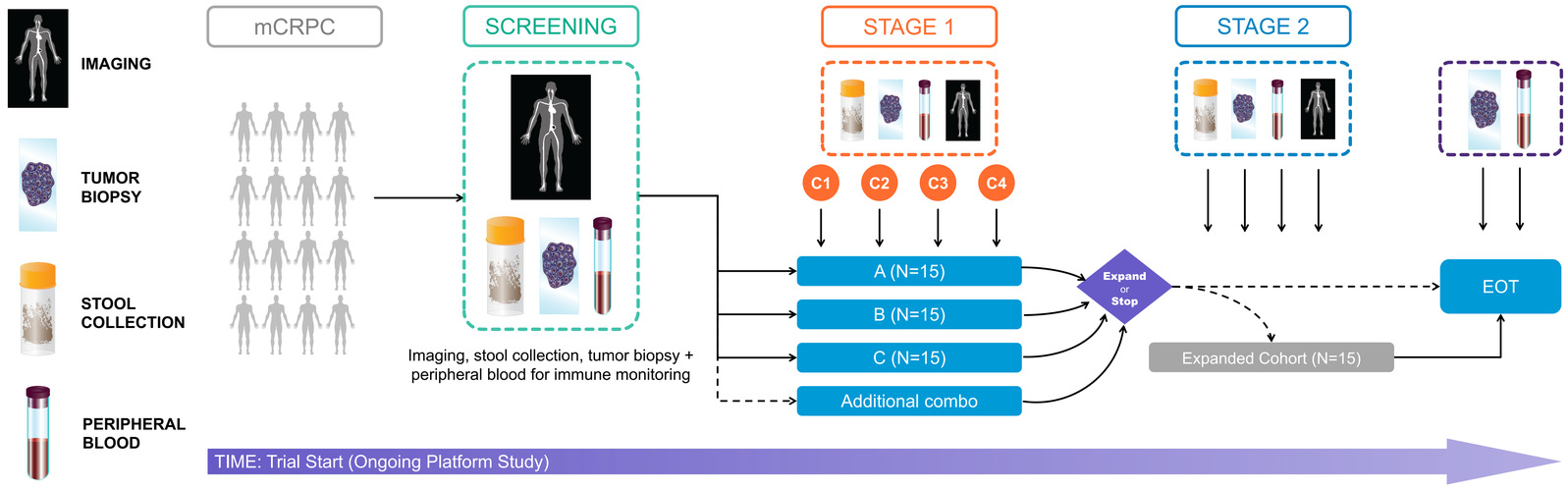
BACKGROUND

Metastatic castration resistant prostate cancer (mCRPC), the lethal form of prostate cancer, has shown limited benefit from immune checkpoint inhibition as monotherapy, with two randomized phase 3 trials with ipilimumab failing to show a survival benefit, and a large phase 2 trial with pembrolizumab demonstrating an overall response rate (ORR) of 3-5%.
Clearly, a deeper understanding of the biology of prostate cancer, inclusive of the immune microenvironment is needed to inform rational combination strategies in this disease.

PORTER is an open-label, non-randomized, multi-arm, multi-stage, exploratory platform study designed to assess the safety and antitumor activity of multiple immunotherapy combinations in participants with mCRPC who have received and progressed on prior secondary androgen receptor signaling inhibitor therapy.
Coupled with deep immune biomarker profiling, this design will enable rapid insights into the immune responses for each combination, providing premise for future larger validation studies, while also generating hypotheses for new cohorts.

PLATFORM STUDY SCHEMA



OBJECTIVES, STAGES AND EXPANSION

Primary Endpoint

- Safety, as assessed by the incidence and severity of adverse events.

Secondary Endpoints:

- Composite Objective Response Rate (PSA reduction ≥ 50%, confirmed CR or PR per RECIST v1.1, or change in circulating tumor cell (CTC) from ≥5 cells/7.5 mL to ≤ 4 cells/7.5 mL)
- Disease Control Rate
- Radiographic Progression-Free Survival
- Overall Survival

Exploratory endpoints:

- Association of tissue, blood and stool biomarkers with treatment and clinical outcomes.

Stages and Expansion

Each cohort has a two-stage design (initial n = 15, expansion n = 15) with a decision to expand based on the safety, clinical activity, and biomarker results observed in the initial stage.

PATIENT POPULATION

Key Common Inclusion Criteria

- Adenocarcinoma of the prostate
- mCRPC
- Castrate-level testosterone (<50 ng/dL)
- Progressed after abiraterone, enzalutamide and/or apalutamide
- Chemo naïve or post chemo if no progression of disease on chemotherapy

Key Common Exclusion Criteria

- Known history of active non-infectious pneumonitis
- Active infection requiring systemic therapy
- Known history of + testing for HIV, Hep B or C
- Known/active CNS metastases

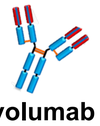
The trial is open & recruiting, for more information on this trial visit:
https://www.parkerici.org/clinical-trial/the-porter-trial/
https://clinicaltrials.gov/ct2/show/NCT03835533

DRUG COMBINATIONS

Cohort A

NKTR-214
(bempegaldesleukin)
0.006 mg/kg
Q3W IV

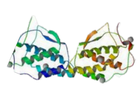
+



Nivolumab
360 mg
Q3W IV

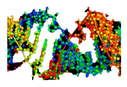
Activating the immune system with a CD122-preferential IL-2 pathway agonist that expands the number of effector cells and potentially overcomes adaptive resistance with anti-PD1.

Cohort B



CDX-301
75 µg/kg
QD x 5 SC

+

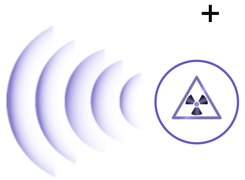


Poly-ICLC
1 mg
b.i.w. x 3W IM

+

Nivolumab
480 mg
Q4W IV

+



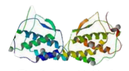
SBRT

Stereotactic body radiation therapy (SBRT):
1-5 metastatic sites, delivered in 3 to 5 fractions; should deliver a total dose of 30 to 50 Gray.

Inducing immunogenic cell death with radiotherapy, mobilizing and activating DCs with a FLT3 ligand and a PAMP adjuvant, Poly-ICLC and and restore T cell effector function with anti-PD-1.

Cohort C

Immune Priming Lead In :
Days 1-5 and 22-26



CDX-301
75 µg/kg
QD x 5 SC

+

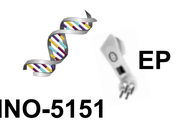
INO-5151
3 mg IM + EP
on Day 8

INO-5151, a DNA vaccine encoding PSA, PSMA, and IL-12 delivered via IM EP plus CDX-301 and nivolumab.

CDX-301, FLT3 ligand, will be administered at a dose of 75 µg/kg SC QD on Days 1–5 & Days 22–26.

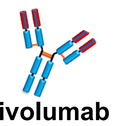
INO-5151 will be administered at a dose of 3 mg via IM followed by EP on Day 8 of the Immune-priming Lead-in.

Immunotherapy Treatment:



INO-5151
3 mg IM + EP
C1,2,3 and Q12W

+



Nivolumab
480 mg
Q4W IV

INO-5151 will be administered at a dose of 3 mg via IM followed by EP starting on Day 1 of Cycle* 1, Cycle 2, and Cycle 3, and every 12 weeks thereafter.

Vaccination with tumor antigens and FLT3 ligand will mobilize and activate dendritic cells, and and the addition of anti-PD-1 will stimulate anti-tumor CD8 T cells.

*A cycle is defined as 4 calendar weeks.

CLINICAL TRIAL STATUS

- First participant enrolled July 2019
- Participating sites:
  - MD Anderson Cancer Center
  - Memorial Sloan Kettering Cancer Center
  - The Mount Sinai Hospital
  - The Angeles Clinic & Research Institute
  - University of California, San Francisco
  - Oregon Health & Science University
- New cohorts using novel immunotherapy combinations are under consideration.

LEGEND

- C = Cycle
- EOT = End of treatment
- N = Sample size
- SC = Subcutaneous
- IM = Intramuscular
- IV = Intravenous
- PR = Partial response
- EP = Electroporation
- PAMP = Pathogen-associated molecular patterns
- QD = Once a day
- b.i.w = Twice a week
- DCs = Dendritic cells
- CR = Complete response

ACKNOWLEDGEMENTS

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