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NCI National Clinical Trials Network

EA8191/INDICATE

For Patients with Prostate Cancer

EA8191 Available Through ECOG-ACRIN Cancer Research Group

Phase III Study of Local or Systemic Therapy **IN**tensification **DI**rected by PET in Prostate **CA**ncer Patients with Post-Prosta**TE**ctomy Biochemical Recurrence (**INDICATE**)

Patient Population

See Section 3.0 for Complete Eligibility Details

Step 0– Registration Eligibility Criteria:

- Male ≥ 18 years old; ECOG PS 0-2; adequate lab values
- Must have had a radical prostatectomy (RP) as definitive therapy for histopathologically-proven prostatic adenocarcinoma; must have biochemical recurrence (BCR) after RP, with rising PSA defined per protocol
- Must be negative or equivocal for extra-pelvic metastatic disease (defined per protocol) by CIM (anatomic imaging with CT and/or MRI and bone scintigraphy, or equivalent) within 26 weeks prior to Step 0 registration
- Must be a candidate for standard of care (SOC) post-prostatectomy radiation therapy (RT) to the prostate bed and pelvic nodes with androgen deprivation therapy (adjuvant); must not have started androgen deprivation therapy for BCR prior to baseline study PET/CT
- No history of seizures/known condition that may cause predisposal to seizures within 1 year prior to registration
- No history of inflammatory bowel disease
- HIV/HBV/HCV patients permitted per protocol
- Patients with known history/current symptoms of cardiac disease/history of treatment with cardiotoxic agents, should be NYHA class I or II (by patient symptoms) or A or B (by objective assessment)
- Must not have had prior pelvic radiation therapy for any reason

Step 1- Randomization Eligibility Criteria:

- Must have completed a baseline SOC PET scan, per protocol, with results of extra-pelvic metastases involvement known (positive or negative)
  - ◊ Patients with negative extra-pelvic metastases: PET-imaging status of intra-pelvic nodes must be known (positive or negative)
  - ◊ Patients with positive extra-pelvic metastases: the number of extra-pelvic lesions must be known (1-5 or > 5 extra-pelvic lesions)

Treatment Plan

See Section 5.0 for Complete Treatment Details

All patients will receive a SOC PET/CT (mid thigh level to skull base or skull vertex) on a qualified PET/CT scanner at baseline, prior to any treatment planning/delivery (during Step 0 registration or up to 16 weeks prior). Patients will then be placed into one of two cohorts:

PET-Negative for Extra-Pelvic Metastases:

- Arm A– Planned SOC RT + STAD
- Arm B– Planned SOC RT + STAD + Apalutamide

PET-Positive for Extra-Pelvic Metastases

- Arm C– Planned SOC RT + STAD +Apalutamide
- Arm D– Planned SOC RT + STAD + Apalutamide + Metastasis-Directed RT to PET-positive lesions
- A repeat ^{18}F-fluciclovine PET/CT will ***only*** be performed in patients who received ^{18}F-fluciclovine for PET1 and were enrolled on Arms C/D. The repeat PET will be performed at time of PSA progression or 12 months after completion of enhanced systemic therapy, whichever occurs first

NOTES:

- *SOC RT is external beam RT to the prostate bed and pelvic lymph nodes; SOC RT can start anywhere from 7 days prior to STAD initiation up to 3 months after the start of STAD*
- *For STAD, see protocol for acceptable GnRH agonist/antagonist (goserelin, leuprolide, triptorelin, relugolix, degarelix); patients should start STAD within 14 days after Step 1 randomization*
- *Apalutamide is 240 mg PO (taken whole) once daily for 6 months; must be started within 14 days of starting STAD*
- *RT dose and fractionation to the prostate bed and pelvic nodes will follow standards as detailed in NRG-GU002 or NRG-GU008, i.e., 30 Gy in 3 fractions for SBRT or 50 Gy in 10 fractions for Non-SBRT*

Study Chair:
Neha Vapiwala, MD, FACR, FASTRO

Patient Enrollment

All Sites: Oncology Patient Enrollment Network (OPEN) https://open.ctsu.org

Protocol Information

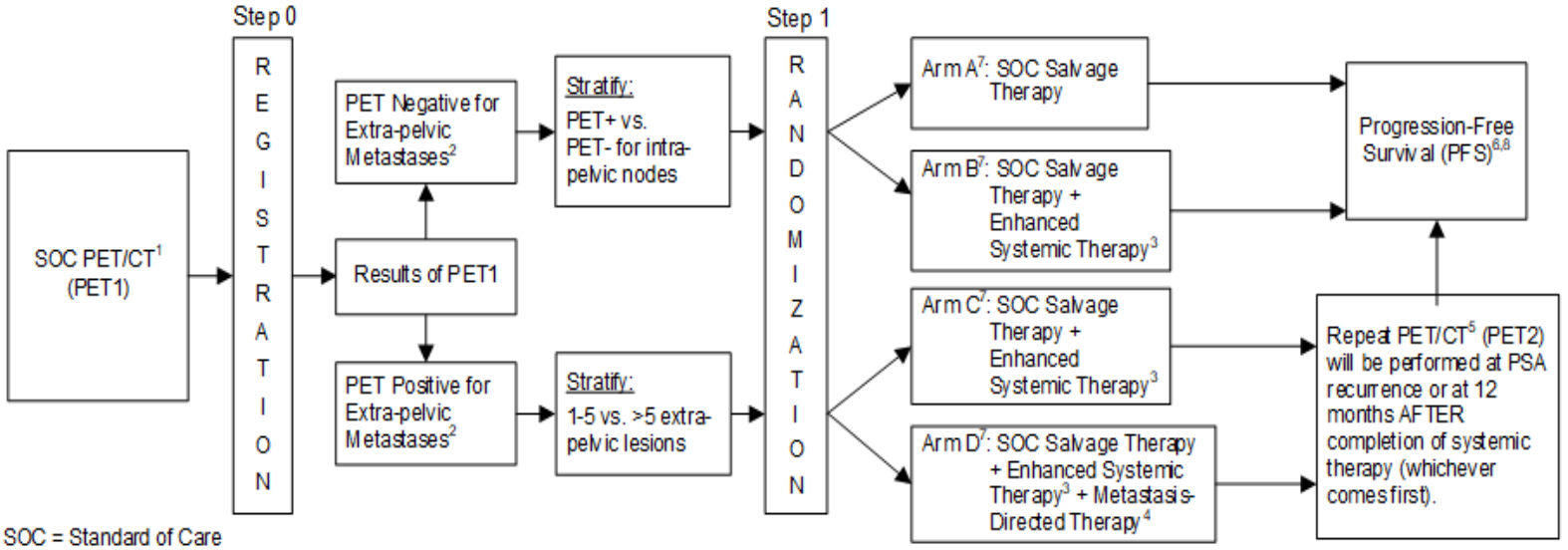
ECOG-ACRIN Operations-Boston: 857-504-2900, http://ecog-acrin.org (Member Login)

Please Enroll Your Eligible Patients!

ECOG-ACRIN cancer research group

EA8191

Schema



SOC = Standard of Care

1. PET1 must follow all imaging requirements outlined in Section 3.1.5 (regarding the PET/CT scanner qualifications and timing of the PET1). Whole body PET/CT (mid thigh level to skull base or skull vertex) for recurrent prostate cancer after radical prostatectomy who are negative or equivocal for extrapelvic metastatic disease by conventional imaging modality (anatomic imaging with CT and/or MRI and bone scintigraphy; see Section 7.8).
2. Extra-pelvic metastases defined as any PET-positive lesions outside of standard salvage RT fields (prostate bed + whole pelvis). PET 1 and PET2 must be performed with the same radiotracer and same scanner.
3. Enhanced Systemic Therapy = Short Term Androgen Deprivation Therapy (STAD) with GnRH agonist/antagonist + apalutamide for 6 months.
4. See section 5.1.3, under Radiation Therapy.
5. PET2 is considered a research scan, is required only for patients who used ^{18}F-Fluciclovine on PET1, and is to be read locally clinically with later central review. Whole body PET/CT (mid thigh level to skull base or skull vertex) for prostate cancer. PET2, along with SOC conventional imaging will be performed at PSA progression or at 12 months after completion. PET2 and SOC imaging are due within one month of the date of the confirmation of progression.
6. Progression-free survival (PFS) consisting of the following events:
   - Radiographic progression by conventional imaging
   - Symptomatic disease - cancer-related symptoms, not treatment-related adverse events
   - Death
7. SOC salvage therapy = prostate bed + pelvic lymph node RT + GnRH agonist/antagonist Short Term Androgen Deprivation Therapy (STAD) therapy for 6 months. Patient should start STAD therapy within 14 days after Step 1 randomization. Radiation may start anywhere from 7 days prior to STAD initiation up to 3 months after the start of STAD. For patients receiving apalutamide, it should be started within 14 days of starting STAD.
8. SOC conventional imaging test options may include but are not limited to: Computed Tomography (CT), Magnetic Resonance Imaging (MRI), ^{99m}Tc- MDP/HDP Planar Bone Scan with or without SPECT, ^{18}F-Sodium Fluoride PET/CT, ^{11}C-Choline PET/CT (See Section 7.8. for more details).