v.02/10/25 (Add. #10)

NCI National Clinical Trials Network

EA8191/INDICATE

For Patients with Prostate Cancer

Please Enroll Your Eligible Patients!

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 protocol Section 3 for complete eligibility criteria

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 meeting criteria per protocol
- Must have no definite evidence for extra-pelvic metastatic disease (may be determined by conventional imaging modalities [CIM] or study-eligible PET within 26 weeks prior to Step 0 registration [see protocol for details])
- 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 (ADT); must not have started short term ADT for BCR prior to baseline PET (see protocol for details)
- No history of seizures/known condition that may cause predisposal to seizures within 1 year prior to registration
- No history of inflammatory bowel disease or GI disorder affecting absorption that is expected to increase risk of complication from RT to an unacceptable level
- 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 completed a course of prior pelvic external beam RT that would overlap with EA8191 SOC RT fields, such that normal tissue constraints cannot be met

Step 1- Randomization Eligibility Criteria:

- Must have completed a baseline SOC PET/CT or PET/MR scan using a FDA-approved radiotracer, to establish presence/absence of extra-pelvic metastases on PET
  - ◊ PET results that are negative for extra-pelvic metastases: PET-imaging status of intra-pelvic nodes must be known (+/-). PET results that are positive for extra-pelvic metastases: the number of extra-pelvic lesions must be known (1-5 or > 5 extra-pelvic lesions)

Treatment Plan

See protocol Section 5 for complete treatment details

All patients will receive a SOC PET/CT or PET/MR, utilizing any FDA-approved radiotracer for prostate cancer, prior to any treatment planning/delivery. This can be completed during Step 0 registration or up to 16 weeks prior to Step 0 registration. Patients will then be placed into one of two cohorts:

PET-Negative for Extra-Pelvic Metastases:

- Arm A– Planned SOC RT + ADT for 6 months
- Arm B– Planned SOC RT + ADT + apalutamide

PET-Positive for Extra-Pelvic Metastases

- Arm C– Planned SOC RT + ADT + apalutamide
  - ◊ Patients who experience radiographic progression or have persistent extra-pelvic disease after protocol treatment may receive metastasis-directed RT as clinically indicated
- Arm D– Planned SOC RT + ADT + apalutamide for 6 months + upfront metastasis-directed RT
- A repeat PET2 is applicable to a subset of patients in Arms C/D (patients imaged at PET1 with Axumin will complete PET2 with Axumin; patients imaged at PET1 with POSLUMA will complete PET2 with POSLUMA])

Note:

- *SOC short term ADT consists of GnRH agonist or antagonist (see protocol for ADT options); ADT may start anytime between 7 days prior to Step 0 registration and 14 days after Step 1 randomization*
- *SOC RT consists of external beam RT to the prostate bed and pelvic lymph nodes; it can start between 7 days prior to short term ADT initiation up to 3 months after ADT initiation (must start after Step 1 randomization)*
- *Apalutamide is 240 mg PO (taken whole) once daily for 6 months; must start after Step 1 randomization and within 28 days of starting short term ADT*
- *RT dose and fractionation will follow institutional practice, i.e., 30 Gy in 3 fractions (SBRT)/50 Gy in 10 fractions (Non-SBRT)*

Study Chair:
Neha Vapiwala, MD, FACR, FASTRO, FASCO

NCTN Study Champions
- ***NRG:*** Bridget Koontz, MD
- ***SWOG:*** Evan Yu, MD
- **Alliance:** Rana McKay, MD

Patient Enrollment (Oncology Patient Enrollment Network [OPEN])

https://open.ctsu.org/open 1-888-823-5923

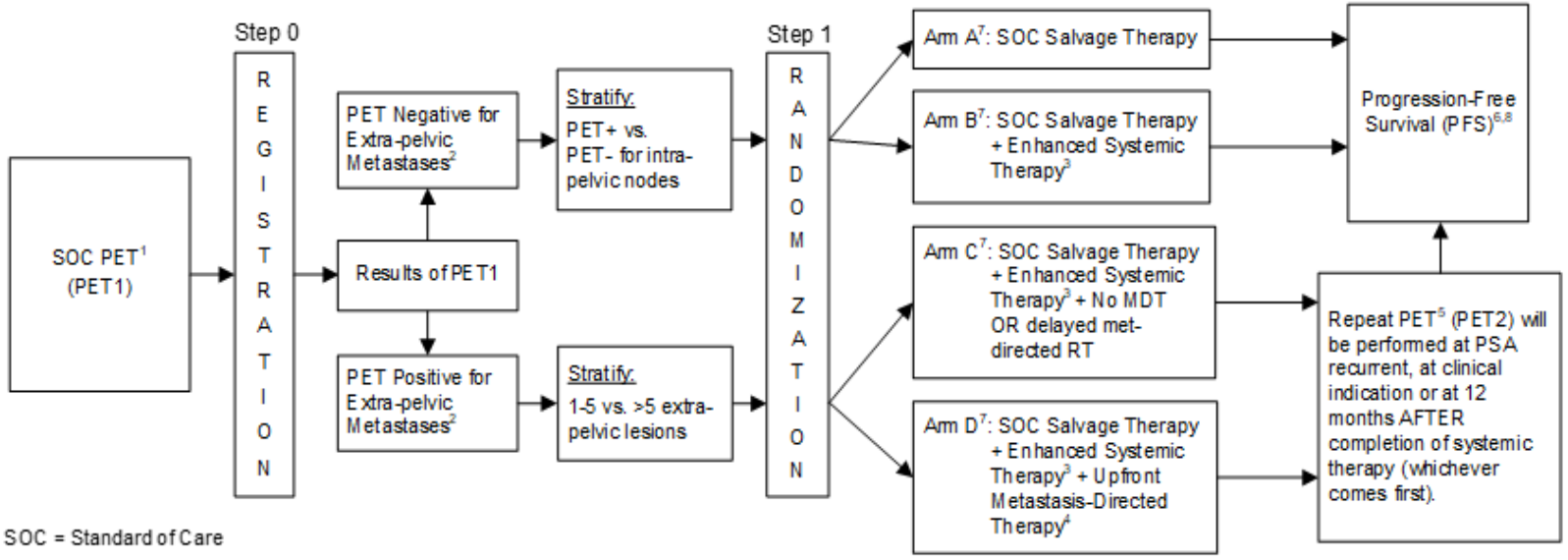
Protocol Information (ECOG-ACRIN Operations – Boston)

http://ecog-acrin.org (Member Login) 1-857-504-2900

ECOG-ACRIN cancer research group

EA8191

Schema



SOC = Standard of Care

1. PET1 must follow all imaging requirements outlined in Section 3.1.4.
2. Extra-pelvic metastases defined as any PET-positive lesions outside of standard salvage RT fields (prostate bed + whole pelvis). Refer to Section 7.5 for PET2 information.
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 and is to be read locally clinically with later central review, whole body PET (mid thigh level to skull base or skull vertex) for prostate cancer. PET2, and if applicable, SOC CIM, will be performed at PSA progression, at clinical indication, or at 12 months after completion of systemic therapy. 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 or SOC PET
   - 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 short term ADT therapy anytime between 7 days prior to Step 0 registration and 14 days after Step 1 randomization. Radiation may start anywhere from 7 days prior to short term ADT initiation up to 3 months after the start of short term ADT. Apalutamide should be started within 28 days of starting short term ADT.
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, PET (See Section 7.8. for more details).