

## Randomized Phase III Trial of 68Ga-PSMA-11 PET/CT Molecular Imaging for Prostate Cancer Salvage Radiotherapy Planning [PSMA-SRT]

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**Background:** Salvage radiotherapy (SRT) for prostate cancer (PCa) biochemical recurrence (BCR) after prostatectomy offers long-term biochemical control in about 50% of patients. SRT is commonly initiated in patients with PSA < 1 ng/mL, a threshold at which standard-of-care imaging is insensitive for detecting recurrence. As such, SRT target volumes are usually drawn in the absence of radiographically visible disease. 68Ga-PSMA-11 PET/CT (PSMA) is highly sensitive to detect and localize PCa BCR. However, it is unclear if incorporation of PSMA imaging into the planning of SRT could improve its likelihood of success. The purpose of this trial is to evaluate the success rate of SRT for PCa BCR after prostatectomy with and without planning based on PSMA. Here we present the study protocol.

**Methods:** This is an interventional phase 3 randomized controlled prospective open label clinical trial with parallel assignment designed for superiority. Patients who are planned to undergo SRT for PCa BCR with PSA > 0.1 ng/mL are eligible. The choice of treating the prostate bed with/without pelvic lymph nodes, with/without androgen deprivation therapy, is left to the discretion of the treating radiation oncologist (RO). RO may or may not change the radiation plan depending on the findings of the PSMA scan. Any other imaging is allowed for SRT planning if done per routine care. The primary endpoint is the success rate of SRT measured as biochemical progression-free survival (PFS) after initiation of SRT (time-frame: from date of initiation of SRT to first occurrence of progression). Biochemical progression is defined by PSA ≥ 0.2 ng/mL and rising. Based on literature data we hypothesized that 1) the incorporation of PSMA to SRT planning will improve 5-year PFS by 20%, 2) the 5-year PFS will be 60% in standard Arm 1 and 80% in interventional Arm 2, and 3) 13% of subjects randomized to Arm 2 will have extra-pelvic metastasis detected by PSMA and will not be included in analysis of the primary endpoint. We will randomize 193 patients (1:1.13 ratio) to proceed with standard SRT (control arm 1, n=90) or undergo PSMA scan (free of charge for patients) prior SRT planning (investigational arm 2, n=103). Patients will be followed for 5 years after the date of initiation of SRT.

### **Discussion:**

Potential pitfalls in study design include drop-out of patients randomized to the control arm as patients may be able to undergo PSMA scans in other institutions and potential FDA approval of PSMA PET imaging probes in the near future (no randomization to standard arm would be then acceptable).

This is the first prospective randomized phase 3 trial designed to determine whether PET/CT can improve outcome of SRT in patients with BCR. Positive outcome would enable better patient selection, important step towards individualized medicine.

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## **Conflict of Interest**

This is an investigator-initiated trial with institutional funding. Study is funded by the Ahmanson Translational Theranostics Division (UCLA).

Johannes Czernin is founder and board member of Sofie Biosciences and a Founder of Trethera Therapeutics.

No other potential conflict of interest relevant to this article was reported.