**ARN-509+Abiraterone acetate+Leuprolide with Stereotactic, Ultra-Hypofractionated Radiation (AASUR) in Very High Risk Prostate Cancer: A Single Arm, Phase II Study**

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**Background:** Our central hypothesis is the combination of Apalutamide and Abiraterone, inhibiting two unique components of the androgen pathway, with leuprolide and stereotactic, hypofractionated radiation therapy will significantly reduce the rate of biochemical recurrence at 3 years in very high risk prostate cancer

**Methods:** This is Phase 2 trial of 58 patients with very high risk prostate cancer. Very high risk prostate cancer is defined as radiographically node negative patients with 2 high risk features (including radiographic T3-T4 disease) *or* >4 cores of Gleason 8-10 disease *or* primary pattern 5 disease. Patients will receive 6 months of Apalutamide (ARN-509), Abiraterone, and Lupron with stereotactic body radiotherapy (SBRT; 7.5-8 Gy x 5 fractions) delivered at month 3. Toxicity associated with this novel combination of therapies will be monitored continuously with a sequential stopping rule utilized to assure termination of the trial should toxicities exceed historical controls.

**Results:**

Primary Objective

- To determine the rate of biochemical failure at 36 months post treatment.

Secondary Objectives

- To determine the rate of positive prostate biopsies at 24 months (required) after completion of anti-androgen therapy.
- Evaluate the effects of treatment on HR-QOL outcomes, comparing baseline to subsequent follow-up using the EPIC-26.
- To evaluate the predictive and prognostic capacity of the following biological correlatives:
    - MSK-IMPACT™ (Integrated Mutation Profiling of Actionable Cancer Targets)
    - Circulating tumor cells (CTCs)
    - Circulating tumor DNA (ctDNA)

**Conclusions:** The trial opened approximately 1 month ago and will be enrolling at five institutions.

**Conflict of Interest**: None

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