ARN-509 (apalutamide) + Abiraterone acetate + Leuprolide with Stereotactic, Ultra-Hypofractionated Radiation (AASUR) in Very High-Risk Prostate Cancer

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Background: Radiotherapy and long course (18-28 months) androgen deprivation therapy (ADT) is a current standard of care in very high risk prostate cancer; however, biochemical failure remains frequent. We hypothesize that stereotactic, hypofractionated radiotherapy (SBRT) delivered with a total of 6 months of apalutamide, abiraterone, and leuprolide will result in a superior 3-year rate of biochemical control compared to the historical control of conventionally fractionated radiation therapy (42-48 treatments) and long term ADT in patients with very high risk prostate cancer (Gleason 9-10 or 2 high risk features or > 4 Gleason 8 cores). **Methods:** We present a single arm, phase 2 trial to determine the efficacy of anti-androgen therapy combined with SBRT in very high-risk prostate cancer, with the proportion of patients who have had biochemical failure (nadir+2) by 36-months post completion of anti-androgen therapy as the primary endpoint. Eligible patients will receive 6 months of leuprolide, abiraterone, and apalutamide to begin 3 months prior to SBRT with continuation 3 months post-SBRT. Patients will be assessed every 4 weeks (±1 week) (cycle = 28 days) throughout study treatment, and at least once during SBRT. A prostate biopsy will be required prior to the start of SBRT; 2 additional biopsies (at 24 months and, if applicable, metastatic progression) will be performed; partial exome analyses using the MSKCC genomic platform (IMPACT) will be performed on all biopsies; additional correlatives include circulating tumor cell evaluation and cell-free DNA measurement pre and post treatment. **Results:** 56 of planned 58 patients have been enrolled. The trial is open at 5 sites and managed by the Prostate Cancer Clinical Trials Consortium. Clinical trial information: NCT02772588 **Conclusions:** Interim analysis will ensure early trial termination should toxicities exceed historical controls. The regimen, if proven in a phase 3 setting, would enable very high-risk prostate cancer patients to receive curative therapy with potentially decreased morbidity compared with extended androgen ablation.

Conflict of Interest:

SMM (Consulting/Advisory Role – Bristol Myers Squib, Travel funding – Bristol Myers Squib, Research Funding - Janssen)

MJZ (Consulting/Advisory Role – Augmenix)

HIS (Leadership - Asterias Biotherapeutics, Consulting/Advisory Role - Ambry Genetics Corporation/Konica Minolta Inc.; Amgen; Janssen Biotech, Inc.; Janssen Research & Development; OncLive Insights; Physician Education Resource; Sanofi Aventis; WIRB-Copernicus Group, Research Funding - Illumina (Inst); Innocrin Pharma (Inst); Janssen (Inst), Travel/Accommodations/Expenses - Asterias Biotherapeutics; Onclive; Physician Education Resource; Sanofi; WIRB-Copernicus Group)

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WA (Honoraria – CARET, Consulting/Advisory Role – Clovis Oncology, Research Funding – AstraZeneca; Clovis Oncology; GlaxoSmithKline (Inst); Zenith Epigenetics, Travel/Accommodations/Expenses – GlaxoSmithKline)

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