**Short Term Androgen Deprivation Therapy Without or With Pelvic Lymph Node Treatment Added to Prostate Bed Only Salvage Radiotherapy: The NRG Oncology/RTOG 0534 SPPORT Trial**

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**Purpose/Objective(s):** To determine in a three-arm randomized trial whether there are incremental gains in freedom from progression (FFP) from the addition of 4-6 months of short term androgen deprivation therapy (STADT) using antiandrogen plus an LHRH agonist, without or with pelvic lymph node treatment (PLNRT), to prostate bed salvage radiotherapy (PBRT).

**Materials/Methods:** Patients were randomized to PBRT alone (Arm 1), PBRT + STAD (Arm 2), and PLNRT + PBRT + STAD (Arm 3). The FFP primary endpoint included PSA nadir+2, clinical failure, or death from any cause, with censoring for secondary salvage therapy initiated prior to these events. The sample size provided 90% statistical power to detect a 10% absolute FFP improvement at 5 yr in Arm 2 compared to Arm 1 and a 10% absolute improvement at 5 yr in Arm 3 compared to Arm 2 at an overal alpha level of 0.025. On the third planned interim analysis for efficacy and futility based on 1191 eligible patents with 5 yr minimum follow-up, the treatment arms were compared in a stepwise approach to determine if the Haybittle-Peto (HP) threshold boundary of p < 0.001 (one sided) was crossed. Futility evaluation tested the alternative hypotheses at p < 0.001. Adverse events were graded using CTCAEv3.0.

**Results:** There were 1792 patients enrolled from 2008 - 2015. Median follow-up for those living is 5.4 yr. Ineligible patients included 18, 17, and 21 in Arms 1, 2, and 3. The patient and tumor characteristics for the 1736 eligible patients include a median age of 64 yr (range 39-84), black in 13%, baseline Zubrod status of 0 in 93%, seminal vesicle involvement in 15%, pre-radiotherapy PSA of ≤1.0 ng/ml in 89%, Gleason score < 8 in 83%, and pT2 margin positive or pT3 in 72%. Arms 1, 2, and 3 had 5 yr

FFP rates of 71.1%, 82.7% and 89.1%. Arm 3 had the highest rate compared to Arm 1 (p < 0.0001), exceeding the HP boundary. The hazard ratio (HR) between arms 3 and 1 was 0.44 (95% CI: 0.32-0.59). Arm 3 was then compared to Arm 2, yielding a difference of 6.4% (p=0.0063) and a HR of 0.71 (95% CI: 0.51-0.98). In all eligible patients followed for up to 8 years, there were 45, 38 and 25 patients who developed distant metastasis (DM) in Arms 1, 2 and 3. Without second salvage censoring, the DM hazard ratio for Arm 3 vs Arm 1 was 0.52 (95% CI: 0.32-0.85) and for Arm 3 vs. Arm 2 was 0.64 (95% CI: 0.39-1.06). With IMRT use in 87% of cases, highest late grade 3+ toxicity was observed in 4.3%, 4.9% and 6.0% for renal/genitourinary events and 0.7%, 0.4%, and 1.1% for gastrointestinal

events in Arms 1, 2, and 3.

**Conclusion:** This is the first report of the primary endpoint and is the first randomized trial to show significant incremental improvements in FFP going from PBRT only to PBRT+STAD to PLNRT+PBRT+STAD. The addition of PLNRT resulted in early, meaningful, reductions in failure.

Follow-up of patients will further elucidate the magnitude of the differences between arms 2 and 3.