

## 52 RTOG 0215 Treatment of Erectile Dysfunction (ED) in Patients Treated With Neoadjuvant and Concurrent Androgen Deprivation (AD) and Radiotherapy (RT) for Prostate Cancer (PC)

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**Purpose/Objective(s):** The purpose of this randomized, double-blinded crossover trial was to determine if there is a difference in ED between men treated with sildenafil vs placebo after external beam RT and short-term neoadjuvant and concurrent (either  $\leq 120$  days or  $> 120$  days) AD for PC. Conventional wisdom held that ED after RT plus AD would be equivalent to that after RT alone once AD was discontinued. However, in our own previous work, rates of ED were higher with combined RT and AD even after AD was discontinued, as compared to RT alone.

**Materials/Methods:** For this study, eligibility included being a minimum of 6 months and a maximum of 5 years post RT/AD therapy and pretreatment ED measured by International Index of Erectile Dysfunction (IIEF) question # 1, "How often were you able to get an erection during sexual activity?" responses 0–3 "no sexual activity" to "sometimes". Patients (pts) were randomized to 12-wks of sildenafil or placebo followed by 1 wk of no treatment then 12-wks of the alternative. IIEF was measured pre-treatment, 12 wks after start of initial agent and 12 wks after the alternative. The primary endpoint was improved erections, measured as IIEF post-treatment score 4–5, "most times or almost always/always". The marginal model for binary cross-over data was used to model sildenafil effect while adjusting for potential period or treatment-by-period interaction (carryover) effects. Maximum likelihood estimate and 95% CI were calculated for difference in probabilities of a positive response between placebo and sildenafil.

**Results:** The study closed due to slow accrual with 115 pts. 61 pts (55%) completed all 3 IIEF assessments, and of these, 34 men had received  $\leq 120$  days AD and 27 men had received  $> 120$  days AD. Results are presented in the Table. Although the test result is underpowered due to limited accrual (35% of planned 332 pts), overall sildenafil effect was highly significant ( $p = 0.009$ ) with difference in probabilities of response between sildenafil and placebo of 0.17 [0.06, 0.29].

**Conclusions:** Findings of this study are provocative and encouraging given accrual of less than half the planned sample. Sildenafil significantly improved ED for a subset of pts treated with RT + AD. AD duration ( $\leq 120$  days or  $> 120$  days) may be a predictor of response to sildenafil with the longer duration associated with higher rates of non-responders. The results suggest a synergistic interaction between RT and duration of AD on the response of erectile dysfunction to intervention.

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## 53 Can External Beam Radiotherapy for Prostate Cancer Help Improve Urinary Symptoms in Men With High IPSS Scores?

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**Purpose/Objective(s):** In patients with prostate cancer who present with high International Prostate Symptom (IPSS) scores, the effect of definitive External Beam Radiation Therapy (EBRT) on urinary symptoms is not well defined. Furthermore, it is unclear if high IPSS scores predict for greater acute or late genitourinary toxicity.

**Materials/Methods:** Of 855 men treated with RT for localized prostate carcinoma at University of Chicago from 1988–2005, 378 were treated with EBRT and had pre- and post-RT IPSS scores available for analysis. 63 patients had pre-RT IPSS scores  $\geq 15$  and are the focus of this study. Median age was 69 years; 15% of patients had  $\geq T3$  disease and 44% had  $\geq$  Gleason 7 disease. Median PSA was 8.0 ng/mL. All patients received EBRT (median dose: 74 Gy, range: 45–76.4 Gy); 65% were treated with IMRT and 54% received hormones. Two men received a brachytherapy boost; 6 were treated after radical prostatectomy. Pre-RT, first post-RT and last post-RT IPSS scores were documented. Change in IPSS scores from baseline was analyzed using the paired t-test and Wilcoxon signed-rank test. Pre-RT IPSS scores were also analyzed against acute and late GU toxicity by Chi-square analysis. Toxicity was graded according to RTOG criteria; the use of medicines for urinary symptoms after RT was documented and classified as Grade 2 toxicity.

**Results:** At a median f/u of 38 months, biochemical control (nadir+2) at 4 yrs was 76%. Median pre-RT IPSS score was 18.0 (range: 15–34) with 44% of men presenting with a pre-RT IPSS score  $\geq 20$ . 19 patients (30%) were taking a urinary medication prior to RT. Overall, EBRT was relatively well tolerated. Acute grade 2 or 3 GU toxicity occurred in 51% and 2% of patients, respectively; late grade 2 or 3 GU toxicity was noted in 58% and 8% of patients, respectively. There was no grade 4+ acute or late toxicity. When tested as a continuous variable, higher IPSS score was not associated with higher rates of Grade 2+ acute ( $p = 0.3797$ ) or late GU toxicity ( $p = 0.3142$ ). At first f/u (median 1 month, range: 0.7–12), post-RT IPSS scores (median 17, range: 0–32) improved by a median of 3.5 points ( $p < 0.0001$ ); no change was observed in urinary quality of life (QOL) scores. In 46 (87%) patients with a  $\geq 2$  yr IPSS f/u (median 4 yrs), post-RT IPSS scores (median: 13, range: 0–34) were less than pre-RT scores by a median 4.0 points ( $p < 0.0001$ ). Only 23% of patients had IPSS scores  $\geq 20$  at last f/u; 50% had a post-RT IPSS score  $< 15$ . QOL scores also improved (median improvement: 1,  $p < 0.0001$ ). On subset analysis of IPSS scores at  $\geq 2$  yrs, 5 of 7 measures improved after EBRT (incomplete emptying, frequency, intermittency, urgency, and weak stream, all  $p < 0.05$ ). Of 61 men analyzable for post-RT urinary medication use, 35 (57%) were taking an agent for urinary symptoms at last f/u, 12 (20%) had tried and discontinued use, and 14 (23%) never tried medications. Comparison of the 63 men with pre-RT IPSS scores  $\geq 15$  to the 315 men with pre-RT IPSS scores  $< 15$  did not demonstrate higher rates of Grade 3+ acute toxicity (2% vs 3%,  $p = 0.6519$ ) or late GU toxicity (8% vs 5%,  $p = 0.3565$ ).

**Conclusions:** EBRT is well tolerated in patients with high IPSS scores. Men with baseline IPSS scores  $\geq 15$  do not have higher rates of severe GU toxicity. In combination with urinary medications, RT can decrease IPSS scores as early as 1 month and lead to a lasting improvement in urinary QOL.

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