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Randomized, Double-Blinded, Placebo-Controlled Crossover Trial of Treating Erectile Dysfunction with Sildenafil After Radiotherapy and Short-Term Androgen Deprivation Therapy: Results of RTOG 0215

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Abstract

Introduction—Erectile dysfunction (ED) may be the most commonly observed adverse event (AE) associated with the combination of radiation therapy (RT) and androgen deprivation therapy (ADT). A significant number of men are trying phosphodiesterase type 5 inhibitors (PDE5s) such as sildenafil to treat ED, yet sildenafil studies to date shed little light on the response to ED after ADT.

Aim—The purpose of this trial was to evaluate sildenafil in the treatment of ED in prostate cancer patients previously treated with external beam RT and neoadjuvant and concurrent ADT.

Methods—In this randomized, double-blinded crossover trial, eligible patients received RT/ADT for intermediate risk prostate cancer and currently had ED as defined by the International Index of Erectile Function (IIEF). Patients were randomized to 12 weeks of sildenafil or placebo followed by 1 week of no treatment then 12 weeks of the alternative. Treatment differences were evaluated using a marginal model for binary crossover data.

Main Outcome Measures—The primary end point was improved erectile function, as measured by the IIEF.

Results—The study accrued 115 patients and 61 (55%) completed all three IIEF assessments. Sildenafil effect was significant ($P = 0.009$) with a difference in probabilities of erectile response of 0.17 (95% confidence interval: 0.06, 0.29), and 0.21 (0.06, 0.38) for patients receiving 120 days of ADT. However, as few as 21% of patients had a treatment-specific response, only improving during sildenafil but not during the placebo phase.

Conclusions—This is the first controlled trial to suggest a positive sildenafil response for ED treatment in patients previously treated with RT/ADT, however, only a minority of patients responded to treatment. ADT duration may be associated with response and requires further study. The overall low response rate suggests the need for study of additional or preventative strategies for ED after RT/ADT for prostate cancer.

Keywords

Erectile Dysfunction; Sildenafil; Prostate Cancer; Patient Reported Outcomes; Radiation Therapy; Phosphodiesterase Type 5 Inhibitors Following Prostate Cancer Treatment

Introduction

The Prostate Cancer Outcomes Study found that 61.5% of men reported erectile dysfunction (ED) within 2 years following standard four-field radiotherapy (RT) for prostate cancer (PC) [1]. The advent of newer RT technologies, i.e., three-dimensional conformal RT (3D-CRT) and intensity-modulated RT, increased the possibility of sparing a greater amount of normal tissue, and as a result, 3-year post-treatment ED rates ranging from 38% to 41% are now reported [2,3]. However, improvements in normal tissue sparing with 3D-CRT may be offset by androgen deprivation therapy (ADT) [4]. Multiple clinical trials have shown improved disease outcome when RT is combined with neoadjuvant or adjuvant ADT (RT/ADT) for localized disease [5-7]. However, even short-term ADT increases the rate of ED [8,9], which may be the most commonly observed adverse event (AE) associated with the combination of RT/ADT. ADT alone carries a risk of ED of at least 80% [10]. Conventional wisdom previously held that erectile function after discontinuation of short-term ADT would be equivalent to that after RT alone. However, in our previous work where we reported ED rates of 45% for RT only, 33% for RT/ADT after ADT discontinued and 15% for age-matched controls, rates of ED were 12% higher with RT/ADT even after ADT was discontinued [11].

A significant number of men are trying phosphodiesterase type 5 inhibitors (PDE5-Is) such as sildenafil (Viagra®, Pfizer Inc., New York, NY, USA) to treat ED. Sildenafil is an oral medication that works by enhancing smooth muscle relaxation and inflow of blood into the corpora cavernosa, which occurs in conjunction with sexual stimulation [12]. With minimal side effects, sildenafil has shown efficacy in treating ED after RT in several small, single-institution nonrandomized studies. Among men with various histories and concomitant medical conditions, including men who underwent prior radical prostatectomy or RT, studies suggest that about two-thirds of patients with ED respond to sildenafil [13-18]. However, sildenafil studies to date shed little light on the response to ED after ADT. Unlike RT that primarily causes ED through neurovascular changes over time, ADT affects the central hormonal pathways mediating sexual activity by reducing plasma testosterone levels similar to that of castration. In addition, androgens are key regulators in the expression of many neuronal and endogenous vasodilators (e.g., PDE5-Is) and in connective tissue metabolism; and therefore, ADT can further contribute to ED by impairing the response to endogenous vasodilators [19]. However, the efficacy of the PDE5-Is in treating ED following RT/ADT has not been well studied. As a result, the Radiation Therapy Oncology Group (RTOG) sought to address this void by conducting a randomized clinical trial (0215) to evaluate sildenafil in the treatment of ED in PC patients previously treated with RT and neoadjuvant and concurrent ADT. Partner satisfaction with ED treatment outcomes was also assessed and will be reported separately.

Methods

Protocol Development

This symptom management trial was developed as a companion to RTOG 9910, a phase III treatment trial evaluating ADT/RT in intermediate-risk PC. However, in accordance with current Community Clinical Oncology Program (CCOP) funding, which supports infrastructure only, obtaining additional extramural funding was necessary for the distribution of study drug and placebo, which delayed opening of the companion by 3 years after the parent trial opened. Institutional Review Board approval was obtained from the American College of Radiology and all participating sites.

Patients

Patients receiving treatment at RTOG member or CCOP institutions were candidates for inclusion. Eligibility criteria included clinical T1b-T4 adenocarcinoma of the prostate, no known nodal (N0) or distant metastases (M0), and serum total prostate-specific antigen (PSA) that was ≤ 100 ng/mL before ADT initiation. All patients were treated with external beam RT without brachytherapy. Intensity-modulated radiation therapy (IMRT) was excluded from the parent study. ADT had to include a luteinizing hormone-releasing hormone analogue with or without an anti-androgen that was continuously administered for 8–28 weeks prior to RT, maintained until RT completion, and then discontinued post-RT. Initially, a minimum of 6 months to a maximum of 18 months must have elapsed since RT completion, but as accrual lagged, the maximum time since RT was expanded to 5 years. In addition, participants were required to have baseline ED as measured by ratings of 0–3 on the International Index of Erectile Function (IIEF) Q1 (“How often were you able to get an erection during sexual activity?”).

Study Design

This was a randomized, double-blind, placebo-controlled two-way crossover clinical trial. Patients were randomized to receive a 12-week supply of either sildenafil or placebo followed by a 1-week washout period before receiving a 12-week supply of the alternative. A flexible dosing schedule was used starting with a 50-mg dose (1 pill) 1-hour prior to

desired sexual activity and increasing up to 100 mg (2 pills) daily as needed. Additional pills were made available if necessary. Patient pill diaries were used to record the number of pills used on each date. Patients were requested to take at least two pills per month (6 pills per 12-week period). Patients who took fewer than three pills per period were considered to be non-compliant. AEs were reported according to the Common Toxicity Criteria version 2.0.

Study personnel and patients were blinded to treatment assignment for the duration of the study. Patients were stratified before randomization using the Zelen treatment allocation scheme to ensure that within each stratum a balanced number of patients would be allocated to each treatment arm [20]. Stratification factors included: (i) prior use of sildenafil after RT (i.e., no; yes/unsatisfactory response; yes/satisfactory response); (ii) ADT duration (i.e., 120 days; >120 days); and (iii) score on the baseline pretreatment IIEF Q1 (i.e., 0–1; 2–3).

Patient-Reported Outcomes (PROs)

PRO measures were assessed with the IIEF, the Sexual Adjustment Questionnaire (SAQ), and Locke's Marital Adjustment Test. Participants were asked to complete PROs at pretreatment, week 12, and 12 weeks after crossover.

The IIEF is a 15-item validated questionnaire developed as a measure of erectile function [21]. Questions specific to erectile function include how often in the past 4 weeks were you able to—"get an erection during sexual activity (Q1)," "penetrate your partner (Q3)," and "maintain your erection (Q4)." Item scores range from 0 to 5: no sexual activity (0); almost never/never (i); a few times (ii); sometimes (iii); most times (iv); and almost always/always (v). The domains of sexual function assessed by this instrument include: erectile function, orgasmic function, sexual desire, intercourse satisfaction, and overall satisfaction [22]. Of specific interest was the erectile function domain; scores range from 1 to 30, with higher scores indicating higher levels of erectile function. The series of RT related trials on which we based our hypothesis used Q1 as the primary outcome; however, as time elapsed since the design of the trial, it has become more common to use the sum of Q3/Q4 as the primary outcome in ED trials. We therefore report both for comparison.

The RTOG-modified SAQ is a 20-item questionnaire adapted from the original [23] to reduce patient burden. Psychometric analysis of the modified version demonstrated acceptable reliability and validity and identified five subscales: dysfunction, satisfaction, desire, activity, and fatigue. The RTOG-modified SAQ scores range from 0 to 100, with higher scores indicating an improved quality of sexual life [24].

Statistical Methods

The primary end point of this study was improvement in erectile function as measured by a score of 4 on IIEF Q1 post-treatment. Non response/failure was defined as a score of 0–3. The marginal model for binary data [25] was selected to evaluate the efficacy of sildenafil while adjusting for potential period or interaction effects. An effect size of 0.367 was determined as clinically meaningful for this trial assuming that 20% of patients would respond to placebo [26], and (based on lower-bound data from the single institution, nonrandomized RT and sildenafil series [22,27-30]) 75% of patients would respond to sildenafil.

Based on a two-sided comparison at the 0.05 significance level, and adjusting for retrospectively ineligible patients, a sample size of 332 patients would ensure 90% statistical power to detect this difference. The analysis was based on intention to treat and noncompliant patients were included if all IIEF assessments were completed.

Secondary end points included the SAQ and the IIEF erectile function domain. Composite scores were computed using the guidelines associated with each PRO instrument [22,24,31]. Patients must have completed all items in the IIEF erectile function domain and must have completed 15 out of the 20 SAQ items to have a composite score. Missing SAQ item values were determined based on the average values of the completed items. The change scores from placebo to sildenafil treatment were determined for each patient. The paired *t*-test was utilized to test for a significant treatment difference in the mean change scores at the 0.05 significance level. A clinically meaningful change (CMC) for the SAQ was determined to be 7.0 [24]. A CMC for the IIEF erectile function domain was assumed to be the standard deviation of the baseline scores. The treatment difference in the proportion of patients achieving a CMC was evaluated using McNemar's test at the 0.05 significance level.

Results

Pretreatment Characteristics

The study accrued 115 patients (35% of planned sample size) from January 3, 2003 to February 17, 2006, and closed because of slow accrual. One patient was ineligible and three patients withdrew their consent (Figure 1). The racial and ethnic distributions of the 111 eligible patients were: 1% Asian; 26% African American; 72% Caucasian; 1% were not reported; and 4% were of Hispanic/Latino ethnicity.

Patient characteristics were well-balanced between treatment arms. The mean age was 70 years (range 52, 86). The majority of patients (70%) on each arm had no or poor sexual function upon study entry as indicated by a score of 1 on IIEF Q1 and had not previously used sildenafil after RT (82%). Median time from completion of RT was 12 months (range 5.5, 48). The majority of patients (83%) were within 24 months of RT completion. Mean radiation dose was 70.5 Gy (range 70.20, 73.80). Mean testosterone level at study entry was below normal values of 24–95 ng/mL at 14.2 ng/mL (range 0.01, 683). In this study, 96 patients (86%) were castrate at study entry and 11 patients (10%) had subnormal (5–24 ng/mL) testosterone levels. More than three-quarters of the participants had a partner (77%).

Patients were asked about prior sildenafil use (Table 1) and use of mechanical or other agents for ED. Only 4 patients reported prior use of vacuum pump device and no patients reported a penile implant or other agents. Our study was activated January 3, 2003. Vardenafil was not approved by the Food and Drug Administration (FDA) until August 19, 2003 and tadalafil was not approved by the FDA until November 21, 2003. No patient reported use of these agents.

Mild AEs caused by sildenafil were reported by 4% of all patients including two patients reporting mild changes in vision. Additionally, one patient reported moderate flushing and two patients reported severe headaches. Mild AEs caused by placebo were also reported by 4% of all patients including one patient with abnormal vision. Additionally, three patients on placebo reported moderate headache, flushing, or nasal congestion. No severe AEs caused by placebo were reported.

Compliance

There were no significant differences in pill compliance between the treatment arms. Sixty-seven percent of patients completed both treatment periods per protocol (>150 mg per period). The median number of pills taken during period 1 was 21 (range 3–138). The median number of days pills were taken was 14 (range 2–84). The median number of pills taken during period 2 was 26 (range 3–117). The median number of days pills were taken was 15 (range 3–84).

Completion of PRO Measures and Missing Data

Patients missing the baseline, after placebo, or after sildenafil assessment were excluded from analysis of the primary end point. Standard multiple imputation methods were not applied because of the binary primary end point and crossover trial design. Sixty-one patients (55%) completed all three IIEF assessments and were included in the analysis of the primary end point. Thirty-nine patients (35%) completed one post-treatment assessment and were included in analysis of the secondary end points. Eleven patients (10%) did not complete any post-treatment assessments. Patients included in the primary analysis were more likely to have completed treatment per protocol ($P < 0.01$). Therefore, the data cannot be assumed to be missing completely at random, and excluding patients with missing data may lead to biased results. However, minimal bias is anticipated as there were no significant differences in the key prognostic factors that could influence treatment response, e.g., prior use of sildenafil, age, partnership status, baseline IIEF score, or duration of hormones between patients excluded from and included in analysis (Table 1).

Response to Sildenafil

IIEF item scores are reported in Table 2. Per the IIEF Q1 score, stratified response rates are detailed in Table 3. Overall, 40 patients (66%) did not respond to either placebo or sildenafil; 6 patients (10%) responded to both placebo and sildenafil; 13 patients (21%) responded to sildenafil, but not placebo; and two patients (3%) responded to placebo, but not sildenafil (Figure 2). Sensitivity analyses with respect to missing data indicate that, if the data were complete, the percentage of patients not responding to either treatment could be as low as 36%. However, with complete data, the percentage of patients responding to sildenafil, but not placebo could only be as large as 31%. A sildenafil effect adjusted for period effects could not be estimated within each stratum because of the small number of informative patients with discordant responses. Overall, there was not a statistically significant period or carry-over effect ($P = 0.40$ and 0.64 , respectively). The response to sildenafil within Arm 1 was equivalent to the sildenafil effect within Arm 2 ($P = 0.52$), and the overall sildenafil effect was statistically significant ($P = 0.009$). The estimate of the difference in response between the placebo and sildenafil treatments was 0.17 [95% confidence interval (CI): $0.06, 0.29$] for all patients and 0.21 [$0.06, 0.38$] among patients receiving 120 days of ADT. There were insufficient numbers of differential responders to accurately examine a difference in patients receiving >120 days of ADT.

Erectile Function and Sexual Adjustment

Based on the Q3/Q4, nonresponders scored 0–8 and responders scored 9–10. There were 59 patients with baseline to follow-up Q3/Q4 data, of which 47 (79%) did not respond to either treatment, 1 (2%) responded to both treatment and placebo, 10 (17%) responded to sildenafil only, and 1 (2%) responded to placebo only. Sildenafil effects on the IIEF Q3/ Q4 and the IIEF erectile function domain (Q1–Q5, Q15) were evaluated and the mean improvements from placebo to sildenafil were 1.26 and 4.03, respectively (both $P < 0.001$) (Figure 3).

For the SAQ total score, the mean improvement was 2.58 ($P = 0.02$). Although statistically significant, these magnitudes are not clinically significant. Based on the proportion of patients achieving a CMC, there was no sildenafil effect on the SAQ (18% placebo only vs. 23% sildenafil only, $P = 0.53$). There was, however, a significant sildenafil effect on the IIEF erectile function domain score (8% placebo only vs. 25% sildenafil only, $P = 0.03$).

Discussion

Patients who are treated for localized PC generally have a low risk of cancer-specific mortality, but may have their life complicated by long-term treatment-related side-effects.

The importance of sexual functioning as a quality-of-life (QOL) issue is significant. In a controlled study of 522 men, satisfaction with sexual life was found to be a powerful predictor of satisfaction with life as a whole [32]. Similarly, among cancer survivors, a QOL study concluded that cancer survivors enjoy QOL similar to their noncancer counterparts in all but one aspect of daily life: sexual functioning [33].

There have been five observational reports of the efficacy of sildenafil in the treatment of ED in patients who have either received RT alone [14] or RT/ADT [17,18,34,35]. All of these studies were nonrandomized, single-institution studies with convenience samples of small sizes ranging from 21 to 50 patients, with one study accruing 152 subjects [34]. Mean age among three of the studies [17,18,35] were similar to the current sample of men who completed the IIEF at age 69, with one study reporting on men with a mean age of 65.7 years [14] and another on men with a mean age of 62 years [34]. As in the current study, three [14,18,35] of the four studies employed 3D-CRT, one reported on patients treated with 3D-CRT or brachytherapy [34] and one study used a four-field technique [17]. Most prescribed sildenafil 50 mg titrated to 100 mg as needed, but not all studies reported on compliance, doses taken or frequency of use. The sildenafil response rates for improvement in erectile function ranged widely from 26% to 91%. However, all studies used different metrics for reporting response. One study used a measure of ED that was not validated [18] and one used a validated measure other than the IIEF [14,35]. Three studies used the IIEF [14,17,34] but reported on different domains or items and one, which excluded patients treated with ADT, reported response by individual IIEF items and overall response was reported with the single global item that assessed frequency of ability to achieve firm erections, which was not part of the scoring of the IIEF [14].

The study by Weber and colleagues, reported an improved total IIEF score in 50% of patients who had received concomitant hormones [17]. Compared with the current study where patients had been off hormones a mean of 14.6 months, the patients in this study had been off hormones a mean of 20.5 months. While testosterone levels were not reported in the study by Weber and no conclusions can be drawn, it is plausible to hypothesize that the better response to sildenafil in men previously treated with concomitant hormones may have been associated with better testosterone recovery over the additional 6 months before starting sildenafil post-RT compared with the current study. Of note is that the Weber study treated patients using the less precise four-field technique, which theoretically should have had higher rates of ED compared with the more normal tissue-sparing conformal technique employed in the current study, regardless of testosterone status.

The study by Teloken et al. [34] specifically assessed response to sildenafil in patients previously treated with ADT. ADT resulted in lower response rates to sildenafil at 24-month follow-up as compared with patients treated with RT alone (47% vs. 61%, $P = 0.032$), however how long patients had been on ADT, how long ADT had been discontinued, and testosterone recovery were not reported [34].

To date, there has only been one other controlled trial of the efficacy of sildenafil for ED in PC patients, but this trial excluded patients who had previously been treated with ADT [36]. In this randomized, double-blind, crossover, placebo-controlled trial, PC patients were treated with 3D-CRT alone. In terms of ED, sildenafil was found to be effective in 45% of the patients vs. 8% after placebo, and successful intercourse was reported in 55% of the patients after sildenafil vs. 18% after placebo. We observed a lower response rate (31%) to sildenafil than reported by this study [36], but their work excluded patients treated with ADT. We also observed a lower response rate than reported in the smaller nonrandomized studies of patients treated with RT/ADT [17,18,35] or RT alone [14].

Differences in findings among the current and previous studies may be related to study design or patient characteristics. In terms of design, this study was prospective, placebo-controlled, and used validated self-report questionnaires to ascertain sildenafil efficacy. Further, although this study did not meet its accrual goal, it included almost twice the number of analyzable participants ($N = 61$) than the sum of patients treated with RT/ADT in other nonrandomized reports ($N = 35$) [17,18,35]. In terms of patient characteristics, it is possible that sildenafil may have been less effective than in previous trials because most of our participants had substantially impaired erectile function at baseline. For example, the mean IIEF Q1 (erectile frequency) score was 0.89 in the current study as compared with 1.7 in the randomized study by Incrocci et al. [36] and 2.19 in the study by Kedia et al. [14], neither of which included ADT. The men in this study were also slightly older than many of the other studies reported here, and were hypogonadal at study entry.

Patients may also have had ED prior to ADT/RT, so there may have been multiple causes for their ED; it is possible this may have contributed to a lesser than previously observed sildenafil response rate. Furthermore, our study did not require the use of highly conformal image-guided RT methods to minimize dose to erectile tissues and their vascular supply. These factors may have contributed individually or in some collective fashion to the results. Nonetheless, these observations suggest that future research should focus on alternatives to reverse ED in this patient population through earlier intervention or through preventative strategies.

In this study, patients who received a shorter duration of ADT (< 120 days) appeared to receive a greater benefit in erectile response to sildenafil than was noted in the overall study group. This raises a question for future research whether there is a synergistic effect of RT/ADT that continues after the ADT discontinuation on erectile function and response to PDE5-Is.

The major limitations of this study were the lower than expected accrual and the amount of missing data, a common challenge with PROs, which prevented a more conclusive examination of the possible effect of ADT duration on response to sildenafil therapy. To this point RTOG is prospectively testing a new method of electronic PRO data capture to assess if this technology is able to decrease data attrition.

In addition, while many factors may have contributed to slow accrual, the additional burden of obtaining extramural funding for symptom management trials is a major barrier to the conduct of such trials in the cooperative group setting. While the NCI-funded analysis of the cooperative group protocol development process has recently been published, few solutions have been proposed that may help inform new initiatives trying to streamline the process specifically for symptom management trials [37].

Another study limitation was the incomplete recovery of testosterone levels, which may have reduced both the total number of days the drug was used (because of decreased libido) and the response rate. Testosterone recovery to normal levels was not an eligibility criterion to this study, nor was testosterone level followed longitudinally in these patients. Further, emerging data on other biomarkers may be pertinent in future work that may better predict responders vs. nonresponders to ED interventions. For example, one recent report of single nucleotide polymorphisms (SNPs) suggests that men with the XRCC1 rs25489 G/A (Arg280His) genotype were more likely to develop ED after RT than men who had the G/G genotype (67% compared with 24%; $P = 0.048$) [38].

A limitation to this and most similar trials is the absence of data on co-morbidities. There are several well documented factors that may contribute to ED including diabetes, smoking, and psychological issues, as well as certain medications, all highly prevalent in aging men, that

may affect response to ED medications. They were not included in this trial for pragmatic reasons of patients being on two trials simultaneously and the concern for patient burden. However, future trials would be strengthened by assessing these factors. Finally, while a flexible daily dosing of sildenafil was encouraged, only a minimum of two pills per month was required per protocol with a minimum of three pills per 12-week period considered for analysis. The median number of pills taken during each 12 week period 1 and 2 was 21 and 14, respectively. Since the protocol was written in 2002 a number of sexual rehabilitation articles following radical prostatectomy have been published suggesting more frequent dosing of at least three times per week [39] or daily [40] may be more efficacious, although some studies indicated no difference compared with on-demand dosing [41,42]. A more intensive dosing and possibly a longer regimen may be necessary for optimal results and should be considered in future trials. As with penile rehabilitation with radical prostatectomy, starting ED treatment earlier in this patient population may also have benefit, however the challenge of compliance with earlier treatment in patients with low libido while on ADT would need careful consideration.

Conclusions

It is important to understand ED in the context of ADT used in combination with RT because of the frequent use of ADT with RT in men with localized PC. This is the first randomized controlled trial to demonstrate that at least some patients with ED who received prior RT and short-term ADT will respond to sildenafil. Nonetheless, the findings raise the concern that only about one in four patients respond better to sildenafil than to placebo and that overall sexual adjustment for the group demonstrated no clinically significant improvement. These findings, if substantiated in larger trials, may have a significant impact on patient decision making if the incremental improvements in intermediate stage PC treated with ADT are weighed against the incidence of ED and low response to PDE5-Is. However, the results noted in this study are suggestive and should be considered as an exploratory basis for a larger clinical trial that includes an assessment of the interaction among PDE5-Is, ADT duration, hypogonadal status, and possible genetic predictors of response.

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Figure 1.
CONSORT diagram.

Figure 2. Responses to International Index of Erectile Function (IIEF) Question 1 after each treatment. IIEF Q1: How often were you able to get an erection during sexual activity? Numbers in parentheses represent frequency counts. Responders (+) have score of: 4—most times or 5—almost always/always. $n(x, y)$ represents response status to placebo and sildenafil treatments, respectively.

Figure 3.

Mean International Index of Erectile Function (IIEF) scores at baseline and after each treatment. Scores: 0—no activity; 1—almost never/never; 2—a few times; 3—sometimes; 4—most times; 5—almost always/always. *IIEF Q1 (primary end point): how often were you able to get an erection during sexual activity? IIEF Q3: When attempting intercourse, how often were you able to penetrate your partner? IIEF Q4: During intercourse, how often were you able to maintain your erection after penetration? IIEF-erectile function (EF) domain score (Q1–Q5, Q15).

Table 1
Baseline characteristics of patients with missing and complete International Index of Erectile Function (IIEF) assessments

	Patients missing IIEF assessments (N = 50)		Patients completing all IIEF assessments (N = 61)		P value
Age (years)					
Mean (standard deviation)	71 (7)		69 (7)		0.22
Range	52–82		55–86		
Radiation dose (Gy)					
Mean (standard deviation [SD])	70.6 (0.82)		70.4 (0.63)		0.64
Range	70.2–72.2		70.2–73.8		
Serum testosterone level (ng/ml)					
Mean (SD)	14.3 (56)		14.7 (88)		0.97
Range	0.01–294		0.23–683		
Months from completion of radiation therapy/androgen deprivation therapy					
Mean (SD)	16.1 (11.2)		14.6 (9.4)		0.45
Range	3.1–48.9		3.6–48.3		
	N	%	N	%	
Treatment arm					
Arm 1 (sildenafil/placebo)	24	48	30	49	0.99
Arm 2 (Placebo/sildenafil)	26	52	31	51	
Treatment completed per protocol					
No	32	64	5	8	<0.01
Yes	18	36	56	92	
Zubrod performance status					
0	48	96	56	92	0.45
1	2	4	5	8	
Prior use of mechanical agents after RT					
No	50	100	57	93	0.13
Yes	0	0	4	7	
Prior use of organic nitrates					
No	47	94	61	100	0.09
Yes	3	6	0	0	

	Patients missing IIEF assessments (N = 50)	Patients completing all IIEF assessments (N = 61)	P value
Penile implant			
No	50	61	100 NA
Prior use of sildenafil after RT			
No	43	49	80 0.70
Yes—unsatisfactory response	4	6	10
Yes—satisfactory	3	6	10
IIEF Question 1 Score			
0–1	35	43	70 0.99
2–3	15	18	30
Hormonal therapy duration			
120 days	25	34	56 0.57
>120 days	25	27	44
Partner status			
No partner	7	19	31 0.10
Not married to partner	6	7	12
Married to partner	37	35	57
Partner willingness to participate in study			
No partner	7	19	31 0.01
No	24	14	27
Yes	19	28	46

T-test (continuous) or Fisher's exact test (discrete).

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Table 3

Response rates to International Index of Erectile Function (IIEF) Question 1 *

	N	Placebo responders only	Sildenafil responders only	Placebo and sildenafil responders	Placebo and sildenafil nonresponders
All patients	61	2 (3%)	13 (21%)	6 (10%)	40 (66%)
Prior use of sildenafil					
No/unsatisfactory response	55	2 (4%)	12 (22%)	5 (9%)	36 (65%)
Yes/satisfactory response	6	0 (0%)	1 (17%)	1 (17%)	4 (67%)
Baseline IIEF Question 1 Score					
0–1	43	1 (2%)	6 (14%)	2 (5%)	34 (79%)
2–3	18	1 (6%)	7 (39%)	4 (22%)	6 (33%)
Hormonal therapy duration					
120 days	34	2 (6%)	9 (26%)	4 (12%)	19 (56%)
>120 days	27	0 (0%)	4 (15%)	2 (7%)	21 (78%)

Responders have score of 4—most times or 5—almost always/always.

* IIEF Q1: How often were you able to get an erection during sexual activity?