RTOG 0831: A Randomized, Double-Blinded, Placebo-Controlled Phase III Trial to Evaluate the Effectiveness of a Phosphodiesterase 5 Inhibitor, Tadalafil, in Prevention of Erectile Dysfunction in Patients Treated With Radiotherapy for Prostate Cancer

Fast Facts

Tadalafil/placebo provided
AJCC 6th Ed; CTC v.4;

Patient Eligibility
1. Clinical stage T1b-T2b (AJCC, 6th ed.; Appendix IV) adenocarcinoma of the prostate within 6 months of registration
2. Clinically negative lymph nodes as established by imaging (pelvic ± abdominal CT or MR), nodal sampling, or dissection within 3 months prior to registration. Patients with lymph nodes equivocal or questionable by imaging are eligible if the nodes are ≤ 1.5 cm. Lymph node assessment is optional, and at investigator discretion, for patients with Gleason Score <7.
3. No evidence of bone metastases (M0) on bone scan within 3 months prior to registration. Equivocal bone scan findings are allowed if plain films are negative for metastasis. Bone metastases assessment is optional, and at investigator discretion, for patients with Gleason Score <7.
4. Baseline serum PSA value performed with an FDA-approved assay (e.g., Abbott, Hybritech) within 3 months prior to registration.
   a. Any of the following combinations of factors (NOTE: tumor found in 1 or both lobes on biopsy, but not palpable, will not alter T stage):
      i. T1b-T2b disease, Gleason Score <7 and serum total PSA that is <20 ng/ml or
      ii. T1b-T2b disease, Gleason Score ≥7 and PSA that is <15 ng/ml
5. Serum total testosterone level prior to the initiation of RT within normal range according to institutional guidelines
6. Zubrod Performance Status 0 or 1 (Appendix III)
7. Age ≥ 18 years
8. Treatment that will consist of either external beam RT alone to the prostate ± seminal vesicles only at a dose between 75 Gy and 79.2 Gy or brachytherapy alone (NOTE: treatment with combined external RT and brachytherapy excludes patient participation)
9. Completion of entire IIEF Form (QF Form) prior to registration
10. Pretreatment (before starting prostate cancer treatment) erectile function as measured by IIEF (QF form) Question 1, “How often were you able to get an erection during sexual activity?” – with responses of:
    a. “sometimes (about half the time)” [response 3] or
    b. “most times (much more than half the time)” [response 4] or
    c. “almost always/always” [response 5]
11. History of prior tadalafil use: Document usual dosage per sexual encounter, date of last dose, and patient’s response (No; Yes—Unsatisfactory Response; Yes—Satisfactory Response). Regardless of past experience, the patient is eligible if he agrees to adhere to protocol and take only tadalafil or placebo prescribed on study.
12. Although patients with partners are targeted for recruitment, patients without partners or without partners willing to participate are eligible. Patients (and spouses/partners, if willing to participate) must be able to provide study-specific informed consent.

Patient Ineligibility
1. The patient’s participation in another medical research study that involves the treatment of ED
2. Previous or concomitant invasive cancer (AJCC Stage >0), other than localized basal cell or squamous cell skin carcinoma (AJCC Stage 0-II), or a hematological malignancy (e.g., leukemia, lymphoma, myeloma) unless continually disease free for at least 5 years
3. History of myocardial infarction within the last year
4. Heart failure in the last 6 months
5. Uncontrolled arrhythmias, hypotension (<90/50 mm Hg), or uncontrolled hypertension (>170/100 mm Hg)
6. Stroke within the last 6 months
7. Use of LHRH agonist androgen suppression (e.g., Lupron, Zoladex), anti-androgen (e.g., Casodex, Eulexin, Nilandron), or estrogenic (e.g., diethylstilbestrol) agents within the last 6 months
8. Current use of any organic nitrate or as needed nitrates (e.g., use of nitroglycerin)
9. Current use of cimetidine, ketoconazole,itraconazole, erythromycin, or ritonavir
10. Known moderate to severe renal insufficiency or end-stage renal disease
11. Known severe hepatic impairement
12. Use of mechanical (vacuum) devices, intracorporeal, intraurethral, topical, or oral (sildenafil, tadalafil, vardenafil) agents as therapy for ED or supplements to enhance sexual function within 5-7 days prior to the start of RT. Patients who discontinue these therapies remain eligible if they can meet eligibility in Section 3.1
13. Pretreatment (before starting prostate cancer treatment) ED as measured by IIEF (QF form) Question 1, “How often were you able to get an erection during sexual activity?” – with responses of:
   a. “no sexual activity” [response 0] or
   b. “almost never/never” [response 1] or
   c. “a few times (much less than half the time)” [response 2]
14. Prior penile implant or history of bilateral orchiectomy
15. Prior prostatectomy, prostatic cryosurgery or high-intensity focused ultrasound (HIFU), radionuclide prostate brachytherapy, or chemotherapy for prostate cancer
16. Prior or anticipated combined external RT and brachytherapy
17. Prior or anticipated external RT to the pelvic ± para-aortic lymph nodes
18. Acquired Immune Deficiency Syndrome (AIDS) based upon current CDC definition; note, however, that HIV testing is not required for entry into this protocol. The need to exclude patients with AIDS from this protocol is necessary because the treatments involved in this protocol may be significantly immunosuppressive. Protocol-specific requirements may also exclude immunocompromised patients.
19. Anatomical genital abnormalities or concurrent conditions that in the estimation of the physician would prohibit sexual intercourse or prevent study completion
20. Major medical or psychiatric illness which, in the opinion of the investigator, would prevent completion of treatment or would interfere with follow-up

**Spouse/Partner Eligibility Criteria**
1. A male or female partner is eligible.
2. Signed study-specific informed consent (Appendix IA)

**Pre-Study Parameters**
1. History/physical w/DRE, performance status, AE and testosterone assessment, concurrent medication list
2. Labs including testosterone, PSA
3. IIEF
4. SAQ (Patient) optional
5. LMAT (Married patients) optional
6. LMAT (spouse) optional
7. SAQ-P (spouse/partner) optional
8. EPIC-Use of erectile aids (Patient) optional

**Treatment**

Tadalafil/placebo to begin within 7 days of RT start date and continue for 24 weeks. Questionnaires to be completed by patient/partner at 2, 4, 20-24, 28-30, 52-54 and 104 weeks post-treatment initiation.