ORIGINAL RESEARCH—ERECTILE FUNCTION

Sexual Function in Men with Lower Urinary Tract Symptoms and Prostatic Enlargement Secondary to Benign Prostatic Hyperplasia: Results of a 6-Month, Randomized, Double-Blind, Placebo-Controlled Study of Tadalafil Coadministered with Finasteride

Sidney Glina, MD, PhD,*† Claus G. Roehrborn, MD,‡ Adil Esen, MD,§ Alexey Plekhanov, MD, PhD,¶ Sebastian Sorsaburu, MD,** Carsten Henneges, PhD,†† Hartwig Büttner, MD, FECSR,‡‡ and Lars Viktrup, MD, PhD**

*Instituto H. Ellis, São Paulo, Brazil; †Department of Urology, Ipiranga Hospital, São Paulo, Brazil; ‡Department of Urology, University of Texas Southwestern Medical Center, Dallas, TX, USA; §Urology Department, University Medical Faculty, Dokuz Eylul University, Izmir, Konak, Turkey; ¶Department of Urology, Andros Clinic, St. Petersburg, Russia; **Lilly Research Laboratories, Eli Lilly and Company, Indianapolis, IN, USA; ††Global Statistical Sciences, Lilly Deutschland GmbH, Bad Homburg, Germany; ‡‡Eli Lilly Biomedicines BU, Lilly Deutschland GmbH, Bad Homburg, Germany

DOI: 10.1111/jsm.12714

ABSTRACT

Introduction. Tadalafil (TAD) 5 mg coadministered with finasteride (FIN) 5 mg significantly improves lower urinary tract symptoms (LUTS) in men with benign prostatic hyperplasia (BPH) and prostatic enlargement. However, its effects on erectile/sexual function have yet to be fully described.

Aim. Assess the effects of TAD/FIN coadministration (compared with placebo [PBO]/FIN) on erectile and sexual function in sexually active men with LUTS and prostatic enlargement secondary to BPH with or without baseline comorbid erectile dysfunction (ED).

Methods. A randomized, double-blind, PBO-controlled study of 695 men (610 sexually active; 450 with baseline ED; 404 sexually active with baseline ED) conducted at 70 sites in 13 countries. TAD 5 mg or PBO once daily coadministered with FIN 5 mg once daily for 26 weeks.

Main Outcome Measures. International Index of Erectile Function (IIEF) domain and single-item scores; proportions of patients who demonstrated minimal clinically important differences (MCIDs) in IIEF-Erectile Function domain scores (IIEF-EF; MCID defined as ≥4-point improvement); and sexual dysfunction adverse events (AEs).

Results. Compared with PBO/FIN, TAD/FIN resulted in improvements for all IIEF domain and single-item scores assessed among patients with baseline ED ($P \leq 0.002$ for all measures) and among patients without baseline ED ($P \leq 0.041$ for all measures). Compared with PBO/FIN, significantly larger percentages of sexually active men with baseline ED treated with TAD/FIN achieved an IIEF-EF MCID after 4, 12, and 26 weeks of therapy ($P < 0.001$ for odds ratio comparisons between TAD/FIN and PBO/FIN at all 3three postbaseline timepoints). The incidence of sexual AEs was low: five TAD/FIN patients and seven PBO/FIN patients reported sexual AEs, including ED, decreased/lost libido, and ejaculation disorders.

Conclusions. TAD/FIN coadministration for the treatment of men with LUTS and prostatic enlargement secondary to BPH concurrently leads to statistically significant improvements in erectile/sexual function and is well-tolerated, regardless of the presence/absence of ED at treatment initiation. **Glina S, Roehrborn CG, Esen A, Plekhanov A, Sorsaburu S, Henneges C, Büttner H, and Viktrup L. Sexual function in men with lower urinary tract symptoms and prostatic enlargement secondary to benign prostatic hyperplasia: Results of a 6-month, randomized, double-blind, placebo-controlled study of tadalafil coadministered with finasteride. J Sex Med 2015;12:129–138.**

Funding/Support and Role of the Sponsor: Eli Lilly and Company helped design and conduct and provided support for this study. Data collection and management and all statistical analyses were performed and retained by the sponsor. All of the authors interpreted the data and participated in the preparation, review, and approval of this manuscript.
Trial Registration: ClinicalTrials.gov ID# NCT01139762

Key Words. 5-Alpha Reductase Inhibitors; Benign Prostatic Hyperplasia; Ejaculatory Function; Erectile Dysfunction; Finasteride; Lower Urinary Tract Symptoms; Orgasmic Function; Phosphodiesterase Type 5 Inhibitors; Tadalafil

Introduction

The 5-alpha reductase inhibitors (5-ARIs), dutasteride and finasteride (FIN), are indicated for treating lower urinary tract symptoms (LUTS) secondary to benign prostatic hyperplasia (BPH) in men who also have confirmed prostatic enlargement [1,2]. However, significant LUTS improvement is not observed before 6–12 months of 5-ARI therapy, and sexual adverse events (AEs), such as erectile dysfunction (ED), decreased/lost libido, and ejaculation disorders, are reported in 5–15% of treated patients [3–6]. To achieve earlier LUTS improvement, 5-ARIs are coadministered with alpha blockers [3,7,8]; this regimen is recommended by the European Association of Urology (EAU) and the American Urological Association for earlier LUTS improvement [1,2]. However, sexual AEs are reported with greater frequency following alpha blocker/5-ARI coadministration compared with 5-ARI monotherapy [6,9].

The coadministration of a 5-ARI with tadalafil (TAD)—a long-acting phosphodiesterase type 5 inhibitor (PDE5I) [10]—may result in early LUTS improvement in this patient population with fewer reported sexual side effects. In fact, the EAU recently included PDE5I therapy, either alone or in combination with 5-ARIs, as part of their treatment algorithm for male LUTS [2], and the TAD product label includes TAD/FIN coadministration for men with LUTS secondary to BPH (BPH-LUTS) and prostatic enlargement [10]. However, recent evidence suggests that TAD/FIN may confer other benefits to these patients. In a recent 12-week, South Korean study of men with BPH-LUTS and prostatic enlargement, TAD coadministered with dutasteride (though not an approved therapy) resulted in LUTS improvements that were similar to tamsulosin/dutasteride-treated patients; moreover, the erectile function of TAD/dutasteride-treated men was significantly improved compared with those receiving tamsulosin/dutasteride [11]. Additionally, in a recent 26-week study investigating the coadministration of TAD 5 mg once daily with FIN once daily for 26 weeks in men with BPH-LUTS and confirmed prostatic enlargement who had received no prior 5-ARI therapy, Casabé and colleagues demonstrated that TAD/FIN coadministration resulted in significant LUTS improvements (compared with placebo [PBO]/FIN) after 4, 12, and 26 weeks of treatment with relatively few sexual side effects. Moreover, study participants who were sexually active and had ED at baseline exhibited significant ED improvements with TAD/FIN (compared with PBO/FIN) at all three postbaseline timepoints [12]. The results observed for ED improvements from these studies warrant further investigation.

Aims

The aim of our study was to further assess the effects of TAD/FIN coadministration for 26 weeks (vs. PBO/FIN) on erectile and sexual function in sexually active men with BPH-LUTS and prostatic enlargement with or without baseline comorbid ED.

Methods

The study was an international, randomized, double-blind, PBO-controlled trial of men with BPH-LUTS and prostatic enlargement with or without comorbid ED at baseline that was conducted at 70 sites in 13 countries from November 2010 to September 2012. The study was performed in accordance with the Declaration of Helsinki and all applicable regulations. Institutional review boards at each site approved the study, and all participants provided written informed consent before undergoing study procedures.

Descriptions of the study's design, patient eligibility criteria, and results for LUTS improvements (per changes in International Prostate Symptom Score [IPSS] total scores and subscores) and ED improvements (per changes in Interna-