European Urology

European Urology 47 (2005) 846–854

An Evaluation of an Alternative Dosing Regimen with Tadalafil, 3 Times/Week, for Men with Erectile Dysfunction: SURE Study in 14 European Countries☆

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Accepted 22 February 2005

Available online 9 March 2005

Abstract

Objective: To examine the preference for 2 dosing regimens (on demand or 3 times/week) for tadalafil, a phosphodiesterase 5 inhibitor with a duration of effectiveness up to 36 hours in men with erectile dysfunction (ED).

Design and methods: SURE is a 14 European country, multicenter, crossover, and open-label study. Men with ED ($N = 4262$) were randomized to tadalafil 20 mg treatment on demand (maximum one dose per day and before sexual activity) or 3 times/week for 5–6 weeks. After a 1-week washout period, patients were crossed over to the alternate regimen for 5–6 weeks. The patient's response to a treatment preference question (TPQ) was used to determine the preferred treatment regimen.

Results: The mean age of the randomized patients was 55 years and 85.2% reported a history of ED for one year or greater. Overall, the responses of 3861 men to the TPQ assessment showed that 57.8% preferred the on-demand regimen and 42.2% preferred the 3 times/week dosing. Both regimens were efficacious and well tolerated.

Conclusions: In this study, while 57.8% of men preferred the on-demand regimen of tadalafil 20 mg, a substantial number (42.2%) preferred the 3 times/week treatment. The two regimens provide additional treatment options by giving men with erectile dysfunction unique flexibility in dosing with tadalafil.

Keywords: Erectile dysfunction; SURE study; On demand; 3 times/week; Alternate; Tadalafil

1. Introduction

Tadalafil, sildenafil citrate, and vardenafil HCL are phosphodiesterase type 5 (PDE5) inhibitors that are effective and well tolerated for treating ED of varied

☆ See Acknowledgment for a complete list of SURE Study investigators.

Abbreviations: ED, erectile dysfunction; EF, erectile function; IIEF, International Index of Erectile Function; PDE5, phosphodiesterase type 5; SEP, Sexual Encounter Profile; TEAE, treatment-emergent adverse events; TPQ, Treatment Preference Question; SURE, Scheduled Use versus on demand Regimen Evaluation.

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0302-2838/$ – see front matter
doi:10.1016/j.eururo.2005.02.019

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functional severity (mild, moderate, and severe) and etiology (organic, psychogenic, and mixed) [1–3].

Tadalafil is approved for treatment of ED in over 80 countries including the United States and Europe. Tadalafil, unique among commercially available inhibitors of PDE5, is effective up to 36 hours after dosing [4].

In most trials conducted with tadalafil to date, the drug has been administered on demand. With effectiveness that lasts up to 36 hours, tadalafil could provide nearly continuous coverage when taken on a regular basis, allowing patients to choose when to have sexual intercourse. This study was done to assess the patient's preference for an alternative dosing regimen, 3 times/week, which takes advantage of the 36 hours of efficacy of tadalafil. The standard assessments of efficacy and safety were used and the treatment preference question (TPQ) was administered in this study to determine patient preference for tadalafil 20 mg taken on demand or 3 times/week.

2. Materials and methods

2.1. Study design

This randomized, crossover, open-label study was conducted in 14 European countries. The first patient was enrolled in October 2002 and the last patient visit was in July 2003. The protocol and informed consent document were approved by ethical review boards at each investigative site. The study was conducted in accordance with the protocol, the ethical principles stated in the Declaration of Helsinki 2002, and applicable laws.

This study compared a fixed dose of tadalafil 20 mg taken on demand or 3 times/week for 10 to 12 weeks in men with erectile dysfunction (ED). Medical history, physical examination, laboratory safety tests, and an electrocardiogram were performed at the screening visit. Patients who met all enrollment criteria were randomly allocated to one of the two treatment sequences. Efficacy was measured with standard assessments. Adverse events were collected throughout the treatment phase, including the 1-week washout period, and during the extension phase (post-treatment).

The first phase of the study was a 3 to 4 week run-in, treatment-free period (Fig. 1). The treatment phase consisted of two treatment periods in which the patient followed either an on-demand treatment regimen or 3 times/week regimen for a period of 5 to 6 weeks, wash-out for one week, and then followed the opposite treatment regimen for a period of 5 to 6 weeks. Patients followed protocol instructions which included no restrictions on food or alcohol intake. On-demand dosing was the discretionary administration of tadalafil 20 mg prior to potential sexual activity at a maximum frequency of one dose per day. The 3 times/week dosing was the administration of tadalafil 20 mg on Monday, Wednesday, and Friday (subgroup A) or on Tuesday, Thursday, and Saturday (subgroup B) at a similar time each day, independent of sexual activity. Patients were randomized to receive both regimens, on demand and 3 times/week, in a crossover fashion. Patients selected the treatment regimen for the extension phase which began at the last visit of the treatment phase and was expected to last at least 2 weeks.

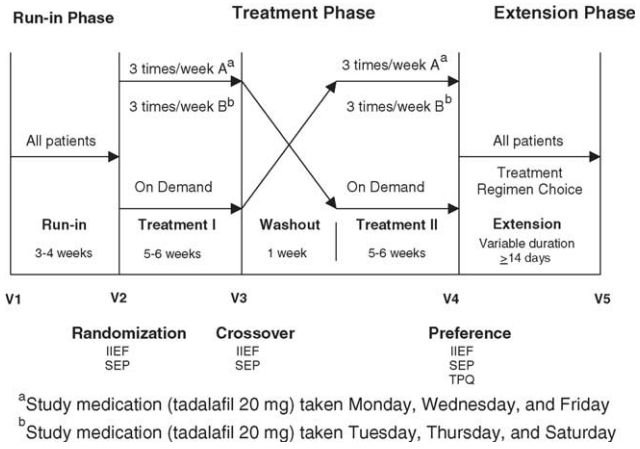

Fig. 1. Study design.

International Index of Erectile Function (IIEF) [5] and Sexual Encounter Profile (SEP) data were collected at baseline and for each 5 to 6 week treatment period. Data from the TPQ were collected after the last 5 to 6 week treatment period.

2.2. Patient population

Study participants were male patients at least 18 years of age and had at least a three month history of ED of any severity (mild, moderate, or severe) or etiology (psychogenic, organic, or mixed). Patients were to have the same female sexual partner during the study for recording responses to efficacy questionnaires. Patients agreed not to use any other erectile dysfunction treatment during the run-in period (before receiving the initial dose of study medication), during the treatment phase of the study, and for 96 hours after the final study visit. Key exclusion criteria for this study were patients receiving treatment with nitrates, cancer chemotherapy, or anti-androgens, or with symptomatic congestive heart failure. Patients who previously used another commercially available PDE5 inhibitor were not excluded form this study.

2.3. Measures

2.3.1. Preference

The primary endpoint in this study was the treatment preference question (TPQ). At the end of the second treatment period, all patients were assessed using the TPQ: ''Which treatment regimen did you prefer?'' The options were on demand or scheduled (3 times/week).

2.3.2. Efficacy

The secondary endpoints were efficacy measures IIEF and SEP. IIEF is a validated, multidimensional, self-administered questionnaire commonly employed to assess therapeutic efficacy of erectile dysfunction therapy [6]. It is a questionnaire of 15 questions arranged into five domains. The erectile function (EF) domain includes questions 1 to 5 and 15.

The SEP diary was used for assessing individual sexual encounters for the run-in, treatment-free period and during treatment. The patient was asked to record responses to 5 questions on the outcome of each sexual attempt with his female sexual study partner.