The Efficacy and Safety of Udenafil, a New Selective Phosphodiesterase Type 5 Inhibitor, in Patients with Erectile Dysfunction

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DOI: 10.1111/j.1743-6109.2007.00723.x

ABSTRACT

Introduction. Udenafil is a potent selective phosphodiesterase type 5 (PDE5) inhibitor newly developed for the treatment of erectile dysfunction (ED).

Aim. This study was performed to evaluate the efficacy and safety of udenafil therapy in patients with ED.

Methods. In this multicenter, double-blind, placebo-controlled, fixed-dose, parallel-group phase III trial, 167 patients with ED of diverse origin and severity were randomized to take placebo or udenafil at fixed doses of 100 or 200 mg as needed for 12 weeks.

Main Outcome Measures. Primary efficacy variable was change from baseline in erectile function (EF) domain scores of the International Index of Erectile Dysfunction (IIEF) questionnaire. Secondary efficacy variables include change from baseline in scores on the IIEF Questions 3 and 4 (IIEF Q3 and Q4), change from baseline in all domain scores of the IIEF, patients' responses to questions 2 and 3 of the Sexual Encounter Profile (SEP2 and SEP3), and patients' responses to the Global Assessment Question (GAQ). Any adverse events were also recorded during the trial.

Results. After 12 weeks of treatment, the patients treated with udenafil showed significantly greater change from baseline in the IIEF-EF domain score compared with placebo (placebo, 0.20; 100-mg udenafil, 7.52; and 200-mg udenafil, 9.93, respectively) ($P < 0.0001$). Compared with placebo, udenafil significantly enhanced the rates of successful penetration (SEP Q2) and maintenance of erection (SEP Q3) ($P < 0.0001$). Furthermore, significantly greater proportions of udenafil treatment groups responded positively to the GAQ compared with the placebo group (GAQ: placebo, 25.9%; 100-mg udenafil, 81.5%; and 200-mg udenafil, 88.5%, respectively) ($P < 0.0001$). Treatment-related adverse events were generally mild to moderate with facial flushing and headache being the most common.

Conclusions. Udenafil is an effective and well-tolerated therapy for ED of broad-spectrum etiology and severity.

Paick J-S, Kim SW, Yang DY, Kim JJ, Lee SW, Ahn TY, Choi HK, Suh J-K, and Kim SC. The efficacy and safety of udenafil, a new selective phosphodiesterase type 5 inhibitor, in patients with erectile dysfunction. J Sex Med 2008;5:946–953.

Key Words. Erectile Dysfunction; PDE5; Udenafil; Clinical Trial

Introduction

Management of erectile dysfunction (ED) has undergone dramatic advances since the successful introduction of sildenafil (Viagra, Pfizer, New York, NY, USA) [1]. As widely known, the cyclic nucleotide signaling pathway mediates the smooth muscle-relaxing effects of nitric oxide necessary for normal erectile function (EF). Accordingly, selective inhibition of phosphodiesterase type 5 (PDE5), which catalyzes the degradation of cyclic guanosine monophosphate (cGMP), is the essential mechanism underlying the action of sildenafil (Viagra). Currently, two other PDE5 inhibitors, vardenafil (Levitra, Bayer HealthCare, Leverkusen, Germany) and tadalafil (Cialis, Lilly ICOS LLC, Indianapolis, IN, USA), are also available as potent and effective treatment options for ED with reported response rates of 60–80% [2]. The advent of these PDE5 inhibitors and other potential agents now in clinical development may well assist clinicians in tailoring treatment regimens to the unique needs of each patient with ED.

Meanwhile, udenafil (Zydena, Dong-A, Seoul, Korea) is a newly developed, potent, selective PDE5 inhibitor that can also inhibit cGMP hydrolysis [3]. Its pharmacokinetic profiles include a Tmax of 1.0–1.5 hours and a $T_{1/2}$ of 11–13 hours, which would confer unique clinical properties of both relatively rapid onset and long duration of action [4]. In addition, the isoenzyme selectivity profile of udenafil is similar to that of sildenafil. On the other hand, unlike tadalafil, it does not inhibit PDE11. Furthermore, the promising results of phase I and phase II studies demonstrated that udenafil was effective and well tolerated at daily doses of up to 400 mg [5]. Thus, we investigated the efficacy and safety of oral udenafil treatment, taken as needed over a period of 12 weeks, in Korean men with ED of broad-spectrum etiology and severity.

Methods

Study Design

This was a multicenter, double-blind, randomized, placebo-controlled, parallel-group study conducted at nine different centers located in Korea in accordance with the Good Clinical Practice and the International Conference on Harmonization guidelines, and in conformity with the ethical principles of the Declaration of Helsinki. A written informed consent was obtained from each patient prior to randomization. Initially, eligible patients had a 4-week, treatment-free run-in period during which time patients must have attempted intercourse on at least four separate days and must have been unsuccessful in at least half of these attempts. Subsequently, the patients were randomly assigned to receive either placebo or 100 or 200 mg of udenafil. Based upon the results of phase I and II trials on udenafil, the patients were allowed to take investigational products (udenafil or placebo), when necessary, with water 30 minutes to 8 hours prior to sexual intercourse, but not to exceed one dose per day in this trial [4,5]. During the 12-week treatment, patients' response to and tolerance of the study drug were assessed by the investigator every 4 weeks, and a follow-up contact was also made 6 or 7 days after the 12-week treatment phase to assess for any additional adverse events.

Subjects

Men aged 19 to 70 years with at least a 6-month history of ED of organic, psycogenic, or mixed etiology, and in a stable monogamous relationship with a female sexual partner, were recruited.

Men with the following conditions were excluded from the study: penile anatomical defects; spinal cord injury, radical prostatectomy, and radical pelvic surgery; a primary diagnosis of another sexual disorder; hyperprolactinemia; a low level of total testosterone; poorly controlled diabetes or proliferative diabetic retinopathy; a major uncontrolled psychiatric disorder; a history of active peptic ulcer disease within 1 year of screening; a history of major hematological, renal, or hepatic abnormalities; a recent (within the previous 6 months) history of cardiovascular disease, stroke or myocardial infarction, cardiac failure, unstable angina, and life-threatening arrhythmia; or a history of alcoholism or substance abuse. The patients were also ineligible if they were receiving regular treatment of nitrates, anticoagulants (except low-dose aspirin), androgens, antiandrogens, or trazodone. Prior use of other PDE5 inhibitors was allowed, but patients who had not responded to them were excluded from this study. Concomitant use of other therapies for ED was absolutely prohibited. Erythromycin, cimetidine, ketoconazole, indinavir, and grapefruit juice were avoided during the study to minimize possible drug interaction.

Efficacy Outcome Variables

Primary efficacy variable was change from baseline in EF domain scores of the International Index of