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

Jae-Seung Paick, MD, PhD,* Sae Woong Kim, MD, PhD,[†] Dae Yeol Yang, MD, PhD,[‡]
Ja Jong Kim, MD, PhD,[§] Sung Won Lee, MD, PhD,[¶] Tai Young Ahn, MD, PhD,[††]
Hyung Ki Choi, MD, PhD,[‡‡] Jun-Kyu Suh, MD, PhD,[§§] and Sae Chul Kim, MD, PhD[¶¶]

*Department of Urology, Seoul National University Hospital, Seoul, Korea; [†]Department of Urology, St Mary's Hospital, Seoul, Korea; [‡]Department of Urology, Hallym Medical Center, Seoul, Korea; [§]Department of Urology, Korea University Hospital, Seoul, Korea; [¶]Department of Urology, Samsung Medical Center, Seoul, Korea; [††]Department of Urology, Asan Medical Center, Seoul, Korea; [‡‡]Department of Urology, Youngdong Severance Hospital, Seoul, Korea; [§§]Department of Urology, Inha University Hospital, Incheon, Korea; [¶¶]Department of Urology, Chung-Ang University Medical Center, Seoul, Korea

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

Erectile Dysfunction (IIEF) questionnaire. It was calculated from comparing the sums of scores from questions 1–5 and 15 from the IIEF questionnaire assessed at baseline and after 12 weeks of udenafil or placebo treatment [6–8].

Secondary efficacy variables included change from baseline in scores on the IIEF Question 3 (Q3: When you attempted sexual intercourse, how often were you able to penetrate [enter] your partner?) and Question 4 (Q4: During sexual intercourse, how often were you able to maintain your erection after you had penetrated [entered] your partner?), along with change from baseline in all domain scores of the IIEF. Additional secondary efficacy measures were the patients' responses to questions 2 and 3 of the Sexual Encounter Profile (SEP2: Were you able to insert your penis into your partner's vagina?; SEP3: Did your erection last long enough for you to complete intercourse with ejaculation?), which were assessed after each attempt at intercourse with udenafil or placebo therapy. Comparative analyses were performed among the three treatment groups regarding the efficacy variables assessed. Patients' responses to the Global Assessment Question (GAQ: Has the treatment you have been taking over the past study interval improved your erections?) was also assessed after 12 weeks of treatment. The percentage of patients exhibiting "shift to normal" (i.e., the proportion of patients in whom IIEF-EF domain score was improved to 26 or greater after 12 weeks of treatment period) was also analyzed.

Adverse Events and Safety

All adverse events were monitored and recorded during the course of the study. For each adverse event, the investigator assessed its seriousness, intensity (mild, moderate, or severe), and relationship to study drug (definite, probable, possible, improbable, none, or impossible evaluation). Vital signs (blood pressure and pulse—sitting and standing position) and clinical laboratory parameters (hematology, blood chemistry, and urinalysis) were evaluated at all visits. The 12-lead electrocardiogram was performed at screening and at the 12th week.

Statistical Methods

All efficacy analyses were performed using the data from the intention-to-treat (ITT) population that included all the randomized patients who have received at least one dose of study drug and at least one valid postbaseline evaluation. The comparison of continuous variables was performed by analysis of variance (ANOVA) or Kruskal–Wallis test. Categorical variables were compared using a contingency table method. If there were confounding variables present, analysis of covariance (ANCOVA) was performed to adjust for heterogeneity among treatment groups. All comparisons were performed at a two-sided alpha level of 0.05. Assuming a standard deviation of 6.57 for change from baseline in EF domain scores, it was concluded that approximately 45 patients per treatment group were required in order for the study to have a 95% power to detect a response difference of 5 between the udenafil dose group and the placebo. Allowance of a 10% dropout rate required 50 randomized patients per group for efficacy analysis.

Primary efficacy variable of changes from baseline in IIEF-EF domain score was tabulated, followed by ANCOVA with baseline value as a covariate. Missing values of EF domain were imputed using the last observation carried forward method to account for patient dropouts. IIEF Q3 and Q4, evaluation for each domain of IIEF, SEP, GAQ, and the percentage of patients exhibiting shift to normal were measured as secondary efficacy variables of the study, and were analyzed using the following. IIEF Q3 and Q4 were analyzed using repeated measures analysis of covariance (RM ANCOVA) method. For each of the four domains of the IIEF questions (orgasmic function, sexual desire, intercourse satisfaction, and overall satisfaction), the intergroup differences were analyzed using the RM ANCOVA method with the covariates adjusted. The intergroup differences in the proportion of "yes" responses to SEP Q2 and Q3 (i.e., the success rate) were analyzed using the RM ANCOVA method with the covariates adjusted or the contingency table method. The response rate of the GAQ and the percentage of patients exhibiting shift to normal were assessed by chi-square test.

Safety analysis included all subjects who received at least one dose of study drug. For safety analysis, 90% confidence intervals were used in listing the number of adverse events that occurred and the rate of patients to experience the adverse events. Also, comparison of intergroup was performed using chi-square test or Fisher's exact test. Continuous laboratory data were analyzed using RM ANOVA, and the change from normal to abnormal of laboratory was analyzed per group using McNemar's test.

Results

Subjects

Initially, a total of 167 patients were randomized and were eligible for the safety population: 54 in the placebo group, and 57 and 56 in 100-mg and 200-mg udenafil dose groups, respectively. Of the 167, three patients did not receive a postbaseline efficacy evaluation, leaving the 164 in the ITT population with 54 in the placebo group, and 56 and 54 in the 100-mg and 200-mg udenafil dose groups, respectively. Of the 167 randomized patients, seven discontinued the study prior to completion: two withdrew the consents, two withdrew because of adverse events, two were terminated because of violation of the protocol, and one was lost to follow-up.

At baseline, there were no statistically significant differences among the treatment groups with respect to any demographic or clinical characteristics (Table 1). Most patients in each treatment group had ED of organic or mixed etiology. Of all the patients enrolled in this study, the IIEF-EF domain score at baseline was ≥11 in 72.22%, 82.46%, and 82.14% of patients with placebo, 100-mg, and 200-mg udenafil groups, respectively. More than 70% of patients had previous PDE5 inhibitor experience before entering this study. Among the concomitant illnesses, hypertension was the most common, with diabetes being the second.

Primary Efficacy Variable

Analysis of intervisit differences in each group revealed that all groups, except for the placebo group, showed statistically significant improvements regarding change from baseline in EF domain scores of the IIEF ($P < 0.0001$). When the difference from the baseline value was compared between visits, statistically significant improvements were observed in the 100-mg and 200-mg udenafil treatment groups (Table 2, $P < 0.0001$), but no significant improvements were observed in the placebo group.

After 12 weeks of treatment with on demand udenafil, mean changes from baseline in EF domain of the IIEF were 7.52 ± 0.87 for the 100-mg group and 9.93 ± 0.94 for the 200-mg group, which were significantly greater than the placebo group (0.20 ± 0.87, $P < 0.0001$) (Figure 1). Final IIEF-EF domain scores reached 13.1 for placebo, 22.2 for 100-mg udenafil, and 24.2 for 200-mg udenafil, of a possible score of 30. Meanwhile, no significant difference was observed between the two udenafil groups.

Secondary Efficacy Variable

Mean score at 12 weeks and mean changes from baseline to end point for each domain of the IIEF are listed in Table 2, which showed significant improvements with udenafil treatments compared with placebo ($P < 0.0001$).

Also, the IIEF Q3 and Q4 scores significantly increased over the 12-week period, with mean changes in scores of 1.26 ± 0.19 (Q3) and 1.81 ± 0.22 (Q4) for the 200-mg udenafil group compared with -0.11 ± 0.20 (Q3) and 0.13 ± 0.18 (Q4) for the placebo-treatment patients, respectively (Figure 2).

Table 1 Demographics and baseline parameters for the ITT population

		Udenafil	
	Placebo (N = 54)	100 mg (N = 57)	200 mg (N = 56)
Mean age: years	55.7 (7.4)	53.6 (7.5)	54.6 (7.3)
Height: cm	168.6 (5.6)	170.2 (5.1)	169.0 (4.6)
Weight: kg	71.0 (8.8)	71.0 (9.9)	70.3 (8.4)
History of ED: years	3.2 (2.4)	3.5 (2.7)	3.9 (3.1)
ED etiology: N (%)			
Organic	21 (38.89)	23 (40.35)	24 (42.86)
Psychogenic	5 (9.26)	6 (10.53)	3 (5.36)
Mixed	28 (51.85)	28 (49.12)	29 (51.79)
Severity of ED–EF domain score: N (%)			
Severe (<11)	15 (27.78)	10 (17.54)	10 (17.86)
Moderate (11~16)	29 (53.7)	27 (47.37)	29 (51.79)
Mild to moderate (17~21)	10 (18.52)	18 (31.58)	15 (26.79)
Mild (22~25)	0 (0)	2 (3.51)	2 (3.57)
Prior other PDE5 inhibitor users: N (%)	40 (74.07)	43 (75.44)	46 (82.14)
Medical history: N (%)			
Hypertension	15 (27.78)	13 (22.81)	16 (28.57)
Diabetes	13 (24.07)	10 (17.54)	7 (12.50)

Values are expressed means (standard deviation).
ITT = intention-to-treat; ED = erectile dysfunction; EF = erectile function; PDE5 = phosphodiesterase type 5.

Table 2 Mean change from baseline in the International Index of Erectile Function (IIEF) domain score

IIEF domains		Placebo (N = 54)	Dose of udenafil	
			100 mg (N = 56)	200 mg (N = 54)
Erectile function	Response (12 weeks)	13.13 ± 0.84	22.2 ± 0.88	24.19 ± 0.85
	Change from baseline	0.20 ± 0.87	7.52 ± 0.87*	9.93 ± 0.94*
Intercourse satisfaction	Response (12 weeks)	7.04 ± 0.35	10.71 ± 0.37	11.37 ± 0.41
	Change from baseline	1.35 ± 0.39	4.16 ± 0.34*	5.11 ± 0.46*
Orgasmic function	Response (12 weeks)	4.20 ± 0.32	7.11 ± 0.34	7.96 ± 0.32
	Change from baseline	0.33 ± 0.36	2.32 ± 0.34*	3.19 ± 0.39*
Sexual desire	Response (12 weeks)	3.85 ± 0.29	6.88 ± 0.28	7.37 ± 0.28
	Change from baseline	0.54 ± 0.28	2.86 ± 0.27*	3.48 ± 0.35*
Overall satisfaction	Response (12 weeks)	5.19 ± 0.27	6.64 ± 0.24	7.35 ± 0.25
	Change from baseline	0.50 ± 0.27	1.23 ± 0.29*	2.44 ± 0.29*
Question 3	Response (12 weeks)	2.61 ± 0.19	3.82 ± 0.17	4.13 ± 0.16
	Change from baseline	−0.11 ± 0.20	0.91 ± 0.18*	1.26 ± 0.19*
Question 4	Response (12 weeks)	1.78 ± 0.15	3.54 ± 0.18	3.89 ± 0.18
	Change from baseline	0.13 ± 0.18	1.46 ± 0.19*	1.81 ± 0.22*

All values are expressed as mean ± standard error.
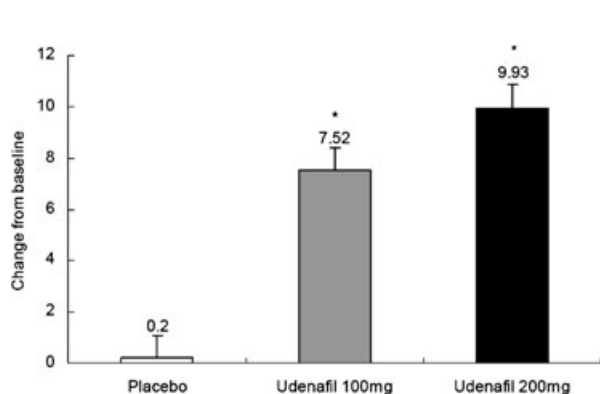*$P < 0.0001$ vs. placebo.

As for SEP, the patients treated with 100-mg and 200-mg udenafil also showed significantly greater improvements in mean per-patient proportions of successful penetration (SEP Q2) and successful intercourse attempts (SEP Q3), than placebo-treated patients. Mean per-patient proportions of successful penetration attempt were 53.4%, 88.8%, and 92.4% for placebo, 100-mg, and 200-mg udenafil group, respectively. Similarly, mean ability of each man to maintain erections until the completion of intercourse was 70.1% with 100-mg udenafil and 75.7% with 200-mg udenafil, compared with 15.4% with placebo (Figure 3).

At 12 weeks, the proportion of "yes" responses to GAQ was 81.5% in the 100-mg udenafil group and 88.5% in the 200-mg udenafil group, being significantly higher than 25.9% in the placebo ($P < 0.0001$) (Figure 4).

As for the percentage of patients reaching normal EF domain scores (≥26), a significantly greater proportion of patients treated with 100-mg udenafil (35.2%) and 200-mg udenafil (48.1%) scored in the no ED range, compared with placebo group (3.7%) ($P < 0.0001$).

Safety and Tolerability

In general, udenafil was well tolerated and exhibited a favorable safety profile. During the study, only two patients in the 200-mg udenafil group discontinued the treatment because of adverse event (one for flushing and headache, and the other for chest pain). Most adverse events were mild or moderate in severity, and no serious adverse events were reported during the study and the follow-up period. The most commonly reported treatment-related adverse events were


Figure 1 Effect of udenafil on mean change from baseline in the International Index of Erectile Function-erectile function domain scores at 12 weeks. *$P < 0.0001$ vs. placebo.
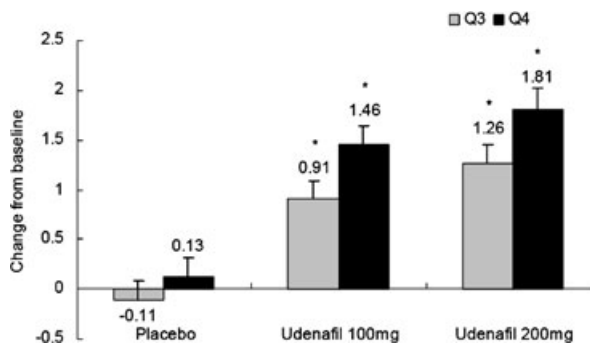
Figure 2 Effect of udenafil on mean change from baseline in the International Index of Erectile Function Q3 (frequency of penetration) and Q4 (frequency of maintaining an erection) score at 12 weeks after the start of treatment. *$P < 0.0001$ vs. placebo.
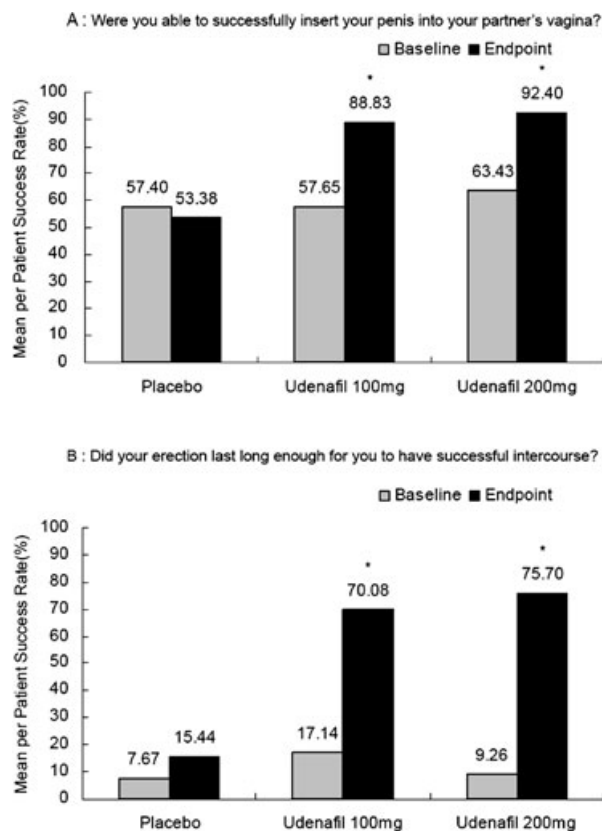
Figure 3 Mean success rates per patient describing the ability to penetrate the partner (A) and maintain erections sufficiently to have successful intercourse (B) at baseline and after 12 weeks. *$P < 0.0001$ vs. placebo.
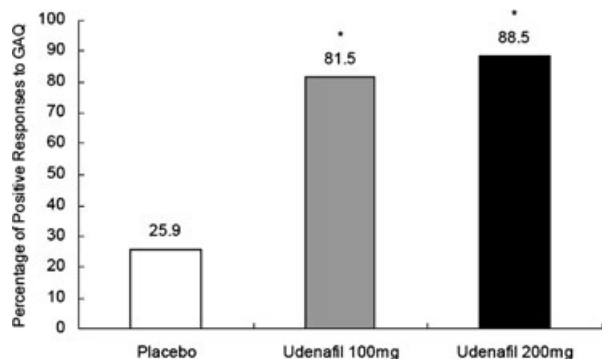
Figure 4 Percentages of patients responding "yes" to the general assessment question "Has the treatment you have been taking over the past 4 weeks improved your erections?" at 12 weeks after the start of treatment. *$P < 0.0001$ vs. placebo.

flushing, nasal congestion, ocular hyperemia, and headache (Table 3). Neither myalgia nor color disturbance in vision was reported. No clinically significant changes in laboratory tests,

electrocardiogram, or blood pressure were observed in all treatment groups.

Discussion

Udenafil is a pyrazolopyrimidinone derivative with a molecular weight of 516.66 [4]. In the phase I study, the drug was shown to be efficacious in 55% of ED patients after 8–12 hours from administration. The phase II, double-blind, placebo-controlled, multicenter, parallel-group clinical trial was also performed in which udenafil treatment produced a highly significant improvement in EF, with up to a 91% vaginal penetration success rate.

In this study, udenafil was shown to provide robust, statistically significant effects across all efficacy variables. IIEF-EF domain score, the primary efficacy variable, showed improvements of 7.52 and 9.93 points following the 12 weeks of 100-mg and 200-mg udenafil treatments, respectively, which were significantly greater compared with the placebo group (0.2 point). With respect to secondary efficacy variables, statistically significant improvements were also observed following udenafil treatments in virtually all of end points. The two udenafil groups demonstrated a significant improvement in the scores from all domains of the IIEF. Furthermore, the findings from evaluating responses to SEP Q2 and Q3, as well as GAQ, were observed to be comparable with those from prior trials with other PDE5 inhibitors [9–11].

Proportions of subjects regaining normal EF based upon changes in the IIEF-EF domain scores have been mentioned by others to be a clinically useful tool in comparing the efficacies of PDE5 inhibitors available [12]. As for udenafil, the proportion of subjects exhibiting normal erection based on the IIEF-EF domain score after the

Table 3 Incidence of treatment-related adverse events (AEs) occurring in ≥5% of all treatment groups

		Dose of udenafil	
AEs (%)	Placebo (N = 54)	100 mg (N = 56)	200 mg (N = 54)
≥1 adverse events	5.6	19.3	37.5
Flushing		10.5	23.2
Nasal congestion		3.5	7.1
Ocular hyperemia		3.5	7.1
Headache		1.8	8.9
Chest discomfort			5.4
Withdrawal due to AEs			3.6

12-week period was 35% and 48% in the 100-mg and 200-mg udenafil treatment groups, respectively, in contrast to 3.7% in the placebo group. Although apparent differences in dosing and/or treatment durations, as well as makeup of study subjects, make a direct objective comparison difficult, the results with udenafil appear to be comparable with those reported on other PDE5 inhibitors [13–15].

As aforementioned, both 100-mg and 200-mg udenafil treatments resulted in significantly greater improvements in all efficacy variables compared with placebo. Meanwhile, the 200-mg udenafil group showed only trends of having greater improvements across all the efficacy variables assessed when compared with the 100-mg group without demonstrating statistical significance. Admittedly, the higher dosage may have resulted in significantly greater efficacy with a larger cohort of subjects.

Adverse events associated with udenafil were similar to those commonly observed in other studies on PDE5 inhibitors. In our study, the most frequently reported adverse events were flushing, headache, ocular hyperemia, and nasal congestion in mild to moderate intensity. Meanwhile, udenafil was not observed to induce myalgia, which was sometimes reported with tadalafil [16]. Also, abnormality in color vision, which was one of the profound side effects of sildenafil, was not observed in the current study with udenafil [17]. Such phenomenon may be because of the fact that the inhibitory concentration of udenafil at the PDE6 receptor (in retinal photoreceptor cells) is 10-fold greater than that for the PDE5 receptor [4]. Only two patients discontinued the treatments because of adverse events, and most of the treatment-related adverse events were attenuated without treatment. Such observed data on adverse events for udenafil may be correlated with favorable pharmacokinetic profiles previously reported including the greater selectivity of udenafil for PDE5 from in vitro studies [3].

As aforementioned, a significant proportion of our subjects had previous PDE5 inhibitor experience. Although we did not provide specific data in the article, no significant differences in the efficacy and adverse events were observed between the patients with previous PDE5 inhibitor experience (prior responders) and the PDE5 inhibitor naïve (presumably a mixture of potential responders and nonresponders) in our study. Such results suggest that exclusion of nonresponders may not have significantly affected the observed outcome in our study, as previously reported on other PDE5 inhibitor [18].

In view of the results evaluated thus far, udenafil treatments in doses of 100 and 200 mg were well tolerated and effective in treating patients with mild to severe ED. Still admittedly, efficacy and safety profiles of udenafil observed in our study were not necessarily overwhelming, but rather similar when compared with those of other existing clinically available PDE5 inhibitors. Fixed dosages and treatment duration applied in our study may have limited the efficacy of udenafil observed. And as our subjects were only enrolled at tertiary-care centers, it can be suggested that the results of our study may only reflect the efficacy of udenafil in a selected group of patients. In addition, no significant differences in the efficacy were observed between the two doses of udenafil in our study. Thus, larger clinical trials with longer treatment duration, applying a flexible dosing of udenafil in a more diverse group of patients, would be needed in the future. As many patients with ED prefer to try all the agents available before deciding which is the most suitable for prolonged continuous use, udenafil will provide a welcome addition to the current management of ED.

Conclusions

Udenafil, in doses of 100 or 200 mg as needed for 12 weeks, resulted in significant improvements in EF as measured by the IIEF, SEP, and GAQ among patients with ED of mild to moderate severity. Moreover, the frequency of adverse events was relatively low, indicating that udenafil is safe and well tolerated. Based upon these data, udenafil may well be another reliable treatment option for broad-spectrum ED.

Corresponding Author: Jae-Seung Paick, MD, PhD, Urology, Seoul National University, 28, Yongon-dong, Chongno-gu, Seoul, 110-744, Korea. Tel: +82-2-2072-2422; Fax: +82-2-762-2428; E-mail: jspaick@snu.ac.kr

Statement of Authorship

Category 1

(a) Conception and Design
   Jae-Seung Paick; Sae Woong Kim; Dae Yeol Yang; Ja Jong Kim; Sung Won Lee; Tai Young Ahn; Hyung Ki Choi; Jun-Kyu Suh; Sae Chul Kim

(b) Acquisition of Data
Jae-Seung Paick; Sae Woong Kim; Dae Yeol Yang; Ja Jong Kim; Sung Won Lee; Tai Young Ahn; Hyung Ki Choi; Jun-Kyu Suh; Sae Chul Kim

(c) Analysis and Interpretation of Data
Jae-Seung Paick; Sae Woong Kim; Dae Yeol Yang; Ja Jong Kim; Sung Won Lee; Tai Young Ahn; Hyung Ki Choi; Jun-Kyu Suh; Sae Chul Kim

Category 2

(a) Drafting the Article
Jae-Seung Paick; Sae Woong Kim; Dae Yeol Yang; Ja Jong Kim; Sung Won Lee; Tai Young Ahn; Hyung Ki Choi; Jun-Kyu Suh; Sae Chul Kim

(b) Revising it for Intellectual Content
Jae-Seung Paick; Sae Woong Kim; Dae Yeol Yang; Ja Jong Kim; Sung Won Lee; Tai Young Ahn; Hyung Ki Choi; Jun-Kyu Suh; Sae Chul Kim

Category 3

(a) Final Approval of the Completed Article
Jae-Seung Paick; Sae Woong Kim; Dae Yeol Yang; Ja Jong Kim; Sung Won Lee; Tai Young Ahn; Hyung Ki Choi; Jun-Kyu Suh; Sae Chul Kim

References

1 Kuan J, Brock G. Selective phosphodiesterase type 5 inhibition using tadalafil for the treatment of erectile dysfunction. Expert Opin Invest Drugs 2002;11:1605–13.

2 Carson CC, Lue TF. Phosphodiesterase type 5 inhibitors for erectile dysfunction. BJU Int 2005;96:257–80.

3 Doh H, Shin CY, Son M, Ko JI, Yoo M, Kim SH, Kim WB. Mechanism of erectogenic effect of the selective phosphodiesterase type 5 inhibitor, DA-8159. Arch Pharm Res 2002;25:873–8.

4 Salem EA, Kendirci M, Hellstrom WJ. Drug evaluation: Udenafil, a long-acting PDE5 inhibitor for erectile dysfunction. Curr Opin Investig Drugs 2006;7:661–9.

5 Amakye D, Ward J, Bryson S, Han K. DA-8159-phase I studies to investigate the safety and pharmacokinetics in healthy male Caucasian subjects. Clin Pharmacol Ther 2004;75:86.

6 Cappelleri JC, Rosen RC, Smith MD, Mishra A, Osterloh IH. Diagnostic evaluation of the erectile function domain of the International Index of Erectile Function. Urology 1999;54:346–51.

7 Rosen RC, Riley A, Wagner G, Osterloh IH, Kirkpatrick J, Mishra A. The International Index of Erectile Function (IIEF): A multidimensional scale for assessment of erectile dysfunction. Urology 1997;49:822–30.

8 Rosen RC, Cappelleri JC, Gendrano N 3rd. The International Index of Erectile Function (IIEF): A state-of-the-science review. Int J Impot Res 2002;14:226–44.

9 Brock GB, McMahon CG, Chen KK, Costigan T, Shen W, Watkins V, Anglin G, Whitaker S. Efficacy and safety of tadalafil for the treatment of erectile dysfunction: Results of integrated analyses. J Urol 2002;168:1332–6.

10 Chen KK, Paick JS, Ishii N, Vardenafil Study Group. The efficacy and safety of vardenafil in East Asian men with erectile dysfunction. J Sex Med 2007;4:753–61.

11 Padma-Nathan H, McMurray JG, Pullman WE, Whitaker JS, Saoud JB, Ferguson KM, Rosen RC, IC351 On-Demand Dosing Study Group. On-demand IC351 (Cialis) enhances erectile function in patients with erectile dysfunction. Int J Impot Res 2001;13:2–9.

12 Mulhall JP. Deciphering erectile dysfunction drug trials. J Urol 2003;170:353–8.

13 Hellstrom WJ, Gittelman M, Karlin G, Segerson T, Thibonnier M, Taylor T, Padma-Nathan H. Vardenafil for treatment of men with erectile dysfunction: Efficacy and safety in a randomized, double-blind, placebo-controlled trial. J Androl 2002;23:763–71.

14 Eardley I, Gentile V, Austoni E, Hackett G, Lembo D, Wang C, Beardsworth A. Efficacy and safety of tadalafil in a Western European population of men with erectile dysfunction. BJU Int 2004;94:871–7.

15 Padma-Nathan H, Montorsi F, Giuliano F, Meuleman E, Auerbach S, Eardley I, McCullough A, Homering M, Segerson T, North American and European Vardenafil Study Group. Vardenafil restores erectile function to normal range in men with erectile dysfunction. J Sex Med 2007;4:152–61.

16 Porst H. Erectile dysfunction. New drugs with special consideration of the PDE5 inhibitors. Urologe A 2004;43:820–8.

17 No authors listed. Ocular adverse effects of sildenafil. Prescrire Int 2003;12:98–9.

18 Broderick GA, Donatucci CF, Hatzichristou D, Torres LO, Valiquette L, Zhao Y, Loughney K, Sides GD, Ahuja S. Efficacy of tadalafil in men with erectile dysfunction naive to phosphodiesterase 5 inhibitor therapy compared with prior responders to sildenafil citrate. J Sex Med 2006;3:668–75.