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## Sexual Medicine

# Efficacy and Safety of Once-Daily Dosing of Udenafil in the Treatment of Erectile Dysfunction: Results of a Multicenter, Randomized, Double-Blind, Placebo-Controlled Trial

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## Abstract

**Background:** A once-daily dosing regimen with a phosphodiesterase type 5 inhibitor is needed for the treatment of erectile dysfunction (ED), in part because of the behavioral complexities associated with sexual intimacy. Many patients prefer spontaneous rather than scheduled sexual activities or they anticipate frequent sexual encounters. The pharmacokinetic profiles of udenafil with a time of maximal concentration of 1.0–1.5 h and a terminal half-life of 11–13 h make udenafil a good candidate for once-daily dosing.

**Objective:** To evaluate the efficacy and safety of once-daily dosing of udenafil in the treatment of ED. **Design, setting, and participants:** This multicenter randomized double-blind, placebo-controlled, fix-dosed clinical trial involved 237 patients with ED. The subjects, who were treated with placebo or udenafil (25 mg, 50 mg, or 75 mg) once daily for 12 wk, were asked to complete the International Index of Erectile Function (IIEF), the Sexual Encounter Profile (SEP) diary, and the Global Assessment Questionnaire (GAQ) during the study.

**Measurements:** The primary outcome parameter was the change from baseline for the IIEF erectile function domain (EFD) score. The secondary outcome parameters were SEP questions 2 and 3, the shift to normal rate (EFD  $\geq 26$ ), and the response to the GAQ.

**Results and limitations:** Compared with placebo, patients who took 50 mg or 75 mg of udenafil had a significantly improved IIEF-EFD score. Similar results were observed in comparing questions 2 and 3 in the SEP diary and the GAQ. Flushing was the most common treatment-related adverse event, which was transient and mild to moderate in severity.

**Conclusions:** Udenafil significantly improved erectile function among ED patients when administered in doses of 50 mg or 75 mg once daily for 12 wk. Daily administration of udenafil (50 mg) may be another treatment option for ED.

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## 1. Introduction

Phosphodiesterase type 5 inhibitors (PDE5-Is) are currently the first-line oral therapy for patients complaining of erectile dysfunction (ED) of any type or etiology [1]. However, on-demand treatment of ED with PDE5-Is can eliminate spontaneity from sexual activity and be burdensome for patients and their partners [2]. Once-daily dosing of a PDE5-I is an alternative for couples who prefer spontaneous rather than scheduled sexual activities or for those who anticipate frequent sexual encounters.

Recent clinical tests have shown that daily dosing of PDE5-Is results in a higher ED treatment effect at a comparatively lower dose than on-demand dosing [3–5]. Long-term administration of PDE5-Is is known to inhibit declining of vascular endothelial cell function, thus accelerating vascular relaxation [6]. Such effects have been reported in human subjects administered sildenafil or vardenafil [7,8]. Thus daily dosing of PDE5-Is may be an ideal treatment for ED.

Udenafil (Zydena; Dong-A, Seoul, Korea) is a selective PDE5-I that was recently developed for the treatment of ED. Based on clinical kinetics data of phase 1 trials involving healthy male subjects, udenafil is rapidly absorbed, reaching peak plasma concentrations at 0.8–1.3 h, then declining monoexponentially with a terminal half-life ( $T_{1/2}$ ) between 7.3 and 12.1 h in the single-dose group [9–11]. Time of maximal concentration ( $T_{max}$ ) of udenafil is similar to that of sildenafil (0.8 h) or vardenafil (0.7 h) and shorter than tadalafil (2 h), implying that the onset of the efficacy would be as fast as that of sildenafil or vardenafil [12]. In a multiple-dose study, the concentration–time profiles on day 7 were comparable with the concentration–time profiles on day 1. The pharmacokinetic parameters showed similar individual values for maximal drug concentration,  $T_{max}$ , area under the curve from time 0 h to infinity, and renal clearance between days 1 and 7 [13]. In various animal models, it has also been confirmed that PDE5 inhibition by udenafil significantly inhibits the decline of vascular

endothelial cell function and inhibits the decrease in endothelial cell and smooth muscle content when administered daily for an extended period of time [14–16]. Given this background, an investigative clinical trial was performed to evaluate the efficacy and safety of a once-daily low dose of udenafil in the treatment of ED and to determine the optimal clinical dose and dosing schedule.

## 2. Materials and methods

### 2.1. Study design

This multicenter, randomized, double-blind, placebo-controlled, fixed-dose study was conducted at 10 centers located in Korea, according to the guidelines of the Good Clinical Practice and International Conference on Harmonization and adhering to the ethical principles of the Declaration of Helsinki. The patients were recruited prospectively and consecutively. Written informed consent was obtained from each patient before study entry.

The duration of the study was 16 wk and consisted of an initial 4-wk run-in period without medications followed by a 12-wk treatment period. One follow-up telephone call was scheduled 6–7 d after the treatment period to assure safety (Fig. 1). Patients were assigned randomly to receive placebo or udenafil (25 mg, 50 mg, or 75 mg once-daily dosing [lower doses compared with the 100 mg or 200 mg on-demand doses]) with an interval of 24 h [9,13].

### 2.2. Subjects

The main inclusion criteria were men with ED, as defined by the National Institutes of Health Consensus Development Panel on Impotence [17], for at least 6 mo; men who preferred spontaneous rather than scheduled sexual activities or who anticipated frequent sexual encounters; and who were >20 yr of age, in a stable heterosexual relationship for at least 6 mo, and making at least four attempts at sexual intercourse on four separate days during the run-in period, of which at least 50% of the attempts were unsuccessful.

Men with the following conditions were excluded: penile anatomic defects; spinal cord injuries; prior radical prostatectomy or radical pelvic surgery; hyperprolactinemia; low level of total testosterone; poorly controlled diabetes (glycosylated hemoglobin >12%) or proliferative

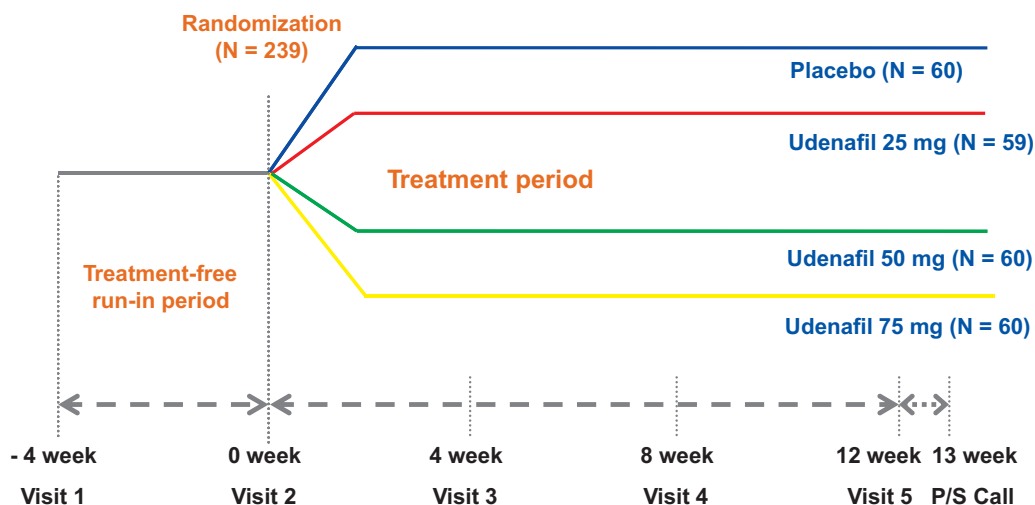


Fig. 1 – Study design and data collection schedule. P/S call = postsurvey call.

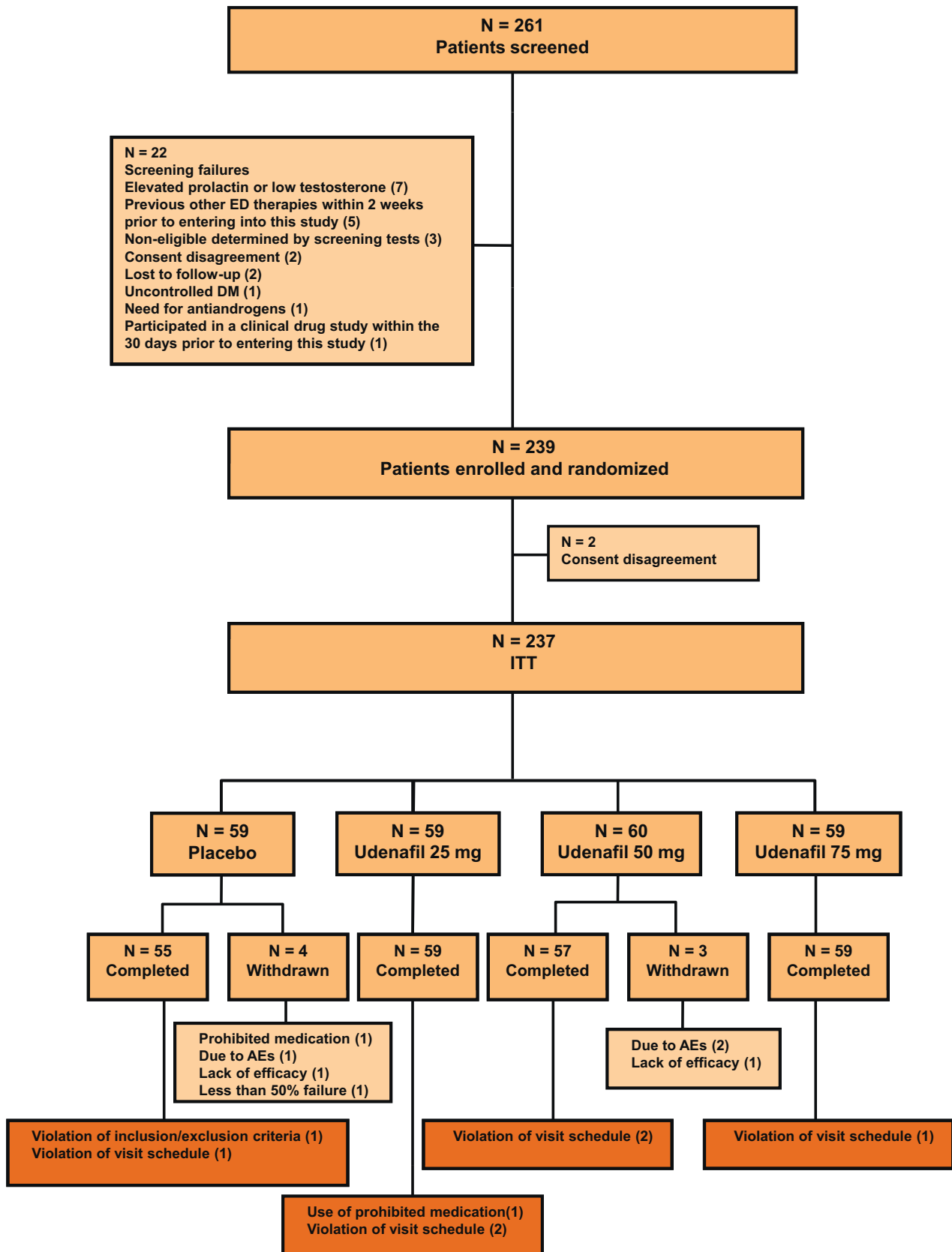


Fig. 2 – Disposition of subjects during the study.

AEs = adverse events; DM = diabetes mellitus; ED = erectile dysfunction; ITT = intention to treat.

diabetic retinopathy; major uncontrolled psychiatric disorder; history of active peptic ulcer disease within 1 yr of screening; history of major hematologic, renal, or hepatic abnormalities; recent (within the previous 6 mo) history of cardiovascular disease, stroke, myocardial infarction, cardiac failure, unstable angina, or a life-threatening arrhythmia; or history of alcoholism or substance abuse. Patients were also ineligible if they were receiving regular treatment with nitrates, anticoagulants (except for aspirin), androgens, antiandrogens, or trazodone. The use of erythromycin, cimetidine, ketoconazole, indinavir, or grapefruit juice was avoided. Prior use of other PDE5-Is was allowed, but patients who had not responded to other PDE5-Is were excluded from this study.

### 2.3. Primary efficacy outcome variable

Changes from baseline of the International Index of Erectile Function-erectile function domain (IIEF-EFD) scores in total or subgroups of patients, classified according to severity of ED or comorbidities, were assessed respectively [18–20].

### 2.4. Secondary efficacy outcome variable

The secondary efficacy variables included the patient responses to Sexual Encounter Profile (SEP) question 2 (“Were you able to insert your penis into your partner’s vagina?”) and question 3 (“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. The patient responses to the Global Assessment Question (GAQ), “Has the treatment you have been taking during the study improved your erections?” were also assessed after 12 wk of treatment. The percentage of patients exhibiting a “shift to normal” (IIEF-EFD score >26) was analyzed.

### 2.5. Adverse events and safety

All adverse events were monitored and recorded. For each adverse event, the investigator assessed the seriousness, intensity (mild, moderate, or severe), and relationship to the study drug (definitely, probably, possibly, probably not, definitely not, or impossible to evaluate). Vital signs were evaluated at each visit, and clinical laboratory parameters and 12-lead electrocardiograms (ECGs) were evaluated at the first, third, and fifth visits.

### 2.6. Statistical analyses

A statistically and clinically significant difference in EFD between the placebo and udenafil group was set at 5, and the standard deviation was set at 7.0. The number of subjects was determined assuming an  $\alpha$  of 0.10 and a power of 90%. Considering an average dropout rate of 10%, 208 patients (52 patients per group) were required.

All efficacy analyses were performed using the data from the intention-to-treat population, which included all of the randomized patients who had received at least one dose of the study drug and at least one valid postbaseline evaluation. The response rate of the GAQ and the percentage of shift to normal patients were assessed by a chi-square test. Other efficacy variables were analyzed using analysis of covariance with severity of ED as a covariate.

For safety analysis, 90% confidence intervals were used in listing the number of adverse events that occurred and the rate of patients who experienced adverse events. An intergroup comparison was also performed using a chi-square test or Fisher exact test.

## 3. Results

### 3.1. Subjects

A total of 237 patients who received at least one dose of double-blind treatment and had adequate data for evaluation were eligible for the safety and efficacy population (59, 59, 60, and 59 patients for placebo and udenafil [25 mg, 50 mg, and 75 mg], respectively; Fig. 2). Table 1 shows the demographic data and baseline characteristics of each group. A total of 79.9% of the patients had previous PDE5-I use before entering the study.

### 3.2. Primary efficacy outcome variable

In the analysis of total patients, the changes of IIEF-EFD score in udenafil groups (50 mg and 75 mg) were significantly greater than the placebo group ( $p < 0.01$ ; Fig. 3). No significant difference existed in the udenafil (25 mg) versus placebo groups.

**Table 1 – Demographic and erectile dysfunction characteristics of study subjects**

	Placebo (n = 60)	Udenafil		
		25 mg (n = 59)	50 mg (n = 60)	75 mg (n = 60)
Age, yr	55.13 ± 9.50	59.71 ± 7.01*	57.62 ± 7.96	56.20 ± 7.51
Height, cm	168.98 ± 6.19	169.93 ± 6.26	169.73 ± 5.35	169.20 ± 5.11
Weight, kg	72.52 ± 9.83	70.54 ± 7.85	72.10 ± 8.91	71.11 ± 8.32
Etiology: n (%)				
Organic	31 (51.7)	36 (61.0)	32 (53.3)	30 (50.0)
Psychogenic	4 (6.7)	0 (0.0)	1 (1.7)	0 (0.0)
Mixed	25 (41.7)	23 (39.0)	27 (45.0)	30 (50.0)
Severity (EFD score): n (%)				
Severe (<11)	7 (11.7)	15 (25.4)	10 (16.7)	5 (8.3)*
Moderate (11–16)	25 (41.7)	20 (33.9)	22 (36.7)	38 (63.3)
Mild to moderate(17–21)	24 (40.0)	19 (32.2)	19 (31.7)	14 (23.3)
Mild (22–25)	4 (6.7)	5 (8.5)	9 (15.0)	3 (5.0)
Prior PDE5-I users: n (%)	43 (71.7)	46 (78.0)	49 (81.7)	53 (88.3)

EFD = erectile function domain; PDE5-I = phosphodiesterase type 5 inhibitor.

Values are mean plus or minus standard deviation;  $p$  values were calculated using chi-square or Fisher exact tests for comparison of subject numbers and analysis of variance for comparison of mean values.

\*  $p < 0.05$ .

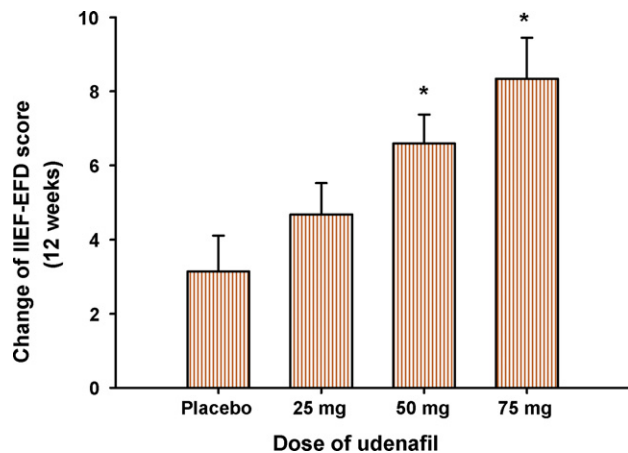


Fig. 3 – Mean changes from baseline to end point at 12 wk for International Index of Erectile Function-erectile function domain (IIEF-EFD) scores (\* $p < 0.01$  vs placebo).

In the analysis of subgroups, udenafil (75 mg) showed higher efficacy in all subgroups except the mild and mild-to-moderate subgroups. Udenafil (50 mg) presented higher efficacy in the mild-to-moderate and hypertension subgroups ( $p < 0.01$ ; Table 2).

### 3.3. Secondary efficacy outcome variables

The changes from baseline in each domain of the IIEF in udenafil (50 mg and 75 mg) groups showed significant changes with the exception of orgasmic function. In the case of the sexual desire domain, all udenafil groups had a significant difference compared with the placebo ( $p < 0.001$ ; Fig. 4).

In comparing the rate of response to SEP question 2, patients treated with 50 mg and 75 mg of udenafil had significantly greater improvement than placebo-treated patients. With respect to the rate of response to SEP question 3, the proportion of “yes” responses to the GAQ, and the percentage of patients achieving normal EFD scores

( $\geq 26$ ), all of the patients in the udenafil groups had a significant difference compared with the patients in the placebo group ( $p < 0.001$ ; Table 3).

### 3.4. Adverse events and safety

In general, udenafil was well tolerated. Most adverse events were mild or moderate in severity. The most commonly reported treatment-related adverse event was flushing (Table 4). There was no significant difference between the udenafil and placebo groups. No clinically significant changes in laboratory tests, ECGs, or blood pressure were observed in the udenafil groups.

## 4. Discussion

For many years, oral PDE5-Is have been prescribed as an on-demand regimen for treating ED. Several studies have reported on the efficacy and safety of such a regimen, with an overall efficacy rate of 60–70% [21]. However, many patients complain of a lack of spontaneity and natural sexual function with on-demand regimens [22]. Planning sexual activity might be anxiety provoking for the man, his partner, and their relationship, causing the sexual encounter to become a stressful event. In 2007, the European Medicines Agency approved low-dose tadalafil to be used as once-daily therapy for ED [23]. Daily dosing or chronic administration of a PDE5-I provides a treatment alternative to on-demand PDE5-Is and more closely approximates natural sexual function [4].

Tadalafil (5 mg) is the only drug currently approved for daily administration in the treatment of ED. The favorable pharmacokinetic profile of tadalafil (5 mg) achieves steady-state concentrations similar to the steady-state concentrations obtained with tadalafil (20 mg twice per week) and avoids the risk of over- and underexposure [24].

Udenafil is a pyrazolopyrimidinone derivative with a molecular weight of 516.66. The pharmacokinetic profile of udenafil includes a time of maximal concentration of 1.0–1.5 h and a  $T_{1/2}$  of 11–13 h, which confers unique

Table 2 – Changes of International Index of Erectile Function-erectile function domain scores in the subgroups

	Placebo	Udenafil			p value <sup>a</sup>
		25 mg	50 mg	75 mg	
Severe (EFD < 11)	3.14 ± 4.56 (n = 7)	8.40 ± 8.59 (n = 15)	10.60 ± 8.33 (n = 10)	17.60 ± 4.72 <sup>†</sup> (n = 5)	0.0201 <sup>†</sup>
Moderate (11 ≤ EFD ≤ 16)	4.04 ± 4.35 (n = 24)	6.30 ± 6.16 (n = 20)	5.41 ± 7.08 (n = 22)	9.24 ± 5.67 <sup>†</sup> (n = 37)	0.006 <sup>†</sup>
Mild to moderate (17 ≤ EFD ≤ 21)	3.63 ± 4.44 (n = 24)	4.79 ± 4.79 (n = 19)	7.47 ± 3.01* (n = 19)	5.86 ± 3.46 (n = 14)	0.0231 <sup>†</sup>
Mild (12 ≤ EFD ≤ 25)	1.75 ± 3.40 (n = 4)	0.80 ± 8.70 (n = 5)	2.89 ± 3.55 (n = 9)	0.67 ± 2.31 (n = 3)	0.6348
Hypertension	2.26 ± 4 (n = 23)	5.69 ± 6.77 (n = 26)	6.26 ± 6.09* (n = 31)	9.5 ± 6.6* (n = 24)	0.0012 <sup>‡</sup>
No hypertension	4.47 ± 4.3 (n = 36)	5.79 ± 7.22 (n = 33)	6.86 ± 6.41 (n = 29)	8.17 ± 5.69* (n = 35)	0.066 <sup>†</sup>
Diabetes	3 ± 5.01 (n = 18)	1.71 ± 6.48 (n = 17)	6.6 ± 5.3 (n = 20)	7.56 ± 6.42* (n = 16)	0.0105 <sup>†</sup>
No diabetes	3.88 ± 3.98 (n = 41)	7.38 ± 6.54* (n = 42)	6.53 ± 6.67 (n = 40)	9.14 ± 5.93* (n = 43)	0.0009 <sup>†</sup>

EFD = erectile function domain.

Values are mean plus or minus standard deviation.

\*  $p < 0.01$ , in comparison with placebo by multiple comparison.

<sup>a</sup> Analysis of variance for intergroup.

<sup>†</sup>  $p < 0.1$ .

<sup>‡</sup>  $p < 0.05$ .

**Table 3 – Changes of secondary efficacy outcome variables after 12 wk**

	Placebo (n = 59)	Udenafil		
		25 mg (n = 59)	50 mg (n = 60)	75 mg (n = 59)
SEP Q2, %	11.95	22.10	27.9*	39.11*
SEP Q3, %	23.46	42.09*	51.41*	73.5*
GAQ, %	35.60	69.5*	75*	88.1*
Shift to normal rate (EFD ≥26), %	13.60	30.5*	40*	44.1*

SEP = sexual encounter profile; Q = question; GAQ = Global Assessment Question; EFD = erectile function domain.

Values are changes of percentage of positive responses from baseline after 12 wk; p values were calculated using chi-square or Fisher exact tests for comparison of subject numbers and analysis of variance for comparison of mean values.

\* p < 0.001.

**Table 4 – Incidence of drug-related adverse events**

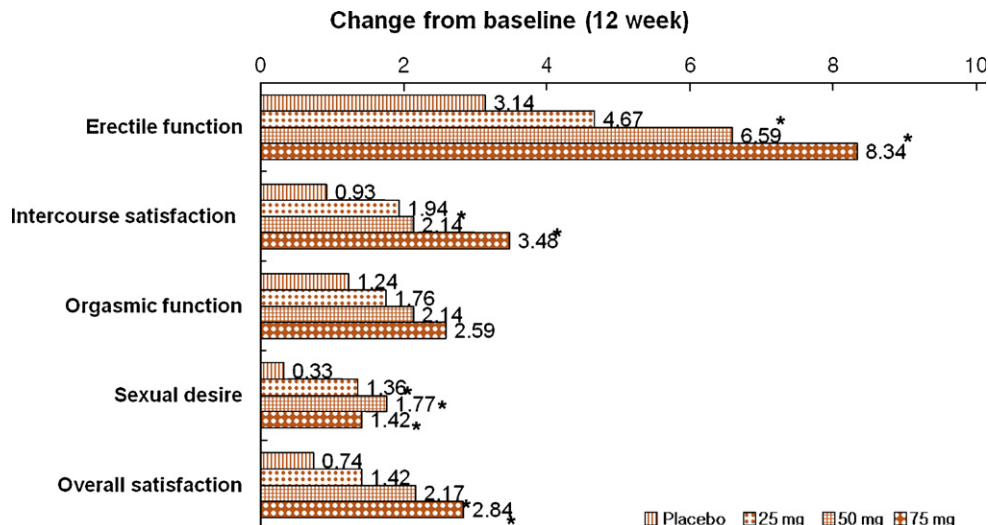
Medical DRA preferred term (%)	Placebo (n = 59)	Udenafil		
		25 mg (n = 59)	50 mg (n = 60)	75 mg (n = 59)
Flushing	1 (1.7)	1 (1.7)	5 (8.3)	4 (6.8)
Headache	–	–	1 (1.7)	2 (3.4)
Vision blurred	–	1 (1.7)	–	–
Nausea	–	–	1 (1.7)	–
Musculoskeletal stiffness	1 (1.7)	–	–	–
Conjunctival hyperemia	–	1 (1.7)	–	–
Nasal congestion	–	–	–	1 (1.7)
Erythema	1 (1.7)	–	–	–
Pruritus	1 (1.7)	–	–	–
Urticaria	–	–	1 (1.7)	–
No. of patients who had experienced at least 1 ADR	2 (3.4)	2 (3.4)	6 (10.0)	6 (10.2)

DRA = drug-related adverse; ADR = adverse drug reaction.

clinical properties (relatively rapid onset and a long duration of action) [9]. There are also small but well-established differences in selectivity of PDE enzymes. Whereas sildenafil has low PDE1 selectivity (selectivity ratio: 41), associated with vasodilation, flushing, and tachycardia, udenafil displayed higher selectivity (selectivity ratio: 1262) than sildenafil. In addition, with regard to PDE11, udenafil (selectivity ratio: 96) displayed much higher selectivity than tadalafil (selectivity ratio: 7.1) [25]. Although its function is not yet clear, PDE11 is widely

distributed in skeletal muscle, testes, heart, prostate, kidney, liver, and pituitary [26]. Therefore, udenafil was found to be safe and well tolerated in human subjects. Compared with once-daily dosing of tadalafil for 12 wk, udenafil also resulted in similar changes in the IIEF-EFD score and in the rate of response to SEP questions 2 and 3 [5,27].

In the present study, udenafil treatment improved the mean sexual desire domain score at 12 wk. In men treated with PDE5-Is, the improved erectile function and sexual



**Fig. 4 – Mean changes from baseline to end point at 12 wk for each domain of the International Index of Erectile Function (\*p < 0.001).**

relationship satisfaction resulted in improvement in confidence, which might increase sexual desire [28].

The adverse events associated with udenafil were similar to the adverse events commonly observed in other studies involving PDE5-Is. In the current study, the most frequently reported adverse events were flushing and headaches. Udenafil did not induce myalgias or abnormalities in color vision, which are profound side effects of tadalafil and sildenafil [29]. The number of patients who received once-daily dosing and experienced at least one adverse drug reaction was significantly less than the on-demand group [13]. Such observed data on adverse events for udenafil may be correlated with favorable pharmacokinetic profiles and the greater selectivity of udenafil for PDE5. A total of 79.9% of the patients had previous PDE5-I use before entering this study, which might have jeopardized the double-blind study design. The effect of daily administration of udenafil on PDE5-I-naïve patients is needed in further study.

## 5. Conclusions

Udenafil in doses of 50 and 75 mg administered once daily for 12 wk significantly improved erectile function among ED patients. The daily administration of udenafil (50 mg) is a promising treatment option for patients with ED.

**Author contributions:** Jong Kwan Park had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

**Study concept and design:** Chen Zhao, Sae Woong Kim, Dae Yul Yang, Je Jong Kim, Nam Cheol Park, Sung Won Lee, Jae Seung Paick, Tai Young Ahn, Kweon Sik Min, Kwangsung Park, Jong Kwan Park.

**Acquisition of data:** Chen Zhao, Jong Kwan Park.

**Analysis and interpretation of data:** Chen Zhao, Jong Kwan Park.

**Drafting of the manuscript:** Chen Zhao, Jong Kwan Park.

**Critical revision of the manuscript for important intellectual content:** Jong Kwan Park.

**Statistical analysis:** Chen Zhao.

**Obtaining funding:** Chen Zhao, Sae Wong Kim, Dae Yul Yang, Je Jong Kim, Nam Cheol Park, Sung Won Lee, Jae Seung Paick, Tai Young Ahn, Kweon Sik Min, Kwangsung Park, Jong Kwan Park.

**Administrative, technical, or material support:** Chen Zhao, Jong Kwan Park.

**Supervision:** Jong Kwan Park.

**Other (specify):** None.

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## References

- [1] Hatzimouratidis K, Amar E, Eardley I, et al. Guidelines on male sexual dysfunction: erectile dysfunction and premature ejaculation. *Eur Urol* 2010;57:804–14.
- [2] Hanson-Divers C, Jackson SE, Lue TF, Crawford SY, Rosen RC. Health outcomes variables important to patients in the treatment of erectile dysfunction. *J Urol* 1998;159:1541–7.
- [3] Bella AJ, DeYoung LX, al-Numi M, Brock GB. Daily administration of phosphodiesterase type 5 inhibitors for urological and nonurological indications. *Eur Urol* 2007;52:990–1005.
- [4] McMahon C. Efficacy and safety of daily tadalafil in men with erectile dysfunction previously unresponsive to on-demand tadalafil. *J Sex Med* 2004;1:292–300.
- [5] Porst H, Giuliano F, Glina S, et al. Evaluation of the efficacy and safety of once-a-day dosing of tadalafil 5 mg and 10 mg in the treatment of erectile dysfunction: results of a multicenter, randomized, double-blind, placebo-controlled trial. *Eur Urol* 2006;50:351–9.
- [6] Kimura M, Higashi Y, Hara K, et al. PDE5 inhibitor sildenafil citrate augments endothelium-dependent vasodilation in smokers. *Hypertension* 2003;41:1106–10.
- [7] De Young L, Yu D, Freeman D, Brock GB. Effect of PDE5 inhibition combined with free oxygen radical scavenger therapy on erectile function in a diabetic animal model. *Int J Impot Res* 2003;15:347–54.
- [8] Schwartz EJ, Wong P, Graydon RJ. Sildenafil preserves intracorporeal smooth muscle after radical retropubic prostatectomy. *J Urol* 2004;171:771–4.
- [9] Salem EA, Kendirci M, Hellstrom WJ. Udenafil, a long-acting PDE5 inhibitor for erectile dysfunction. *Curr Opin Investig Drugs* 2006;7:661–9.
- [10] Paick JS, Kim SW, Yang DY, et al. The efficacy and safety of udenafil, a new selective phosphodiesterase type 5 inhibitor, in patients with erectile dysfunction. *J Sex Med* 2008;5:946–53.
- [11] Park HJ, Park JK, Park K, Min K, Park NC. Efficacy of udenafil for the treatment of erectile dysfunction up to 12 hours after dosing: a randomized placebo-controlled trial. *J Sex Med* 2010;7:2209–16.
- [12] Corbin JD, Francis SH. Pharmacology of phosphodiesterase-5 inhibitor. *Int J Clin Pract* 2002;56:453–9.
- [13] Kim BH, Lim HS, Chung JY, et al. Safety, tolerability and pharmacokinetics of udenafil, a novel PDE-5 inhibitor, in healthy young Korean subjects. *Br J Clin Pharmacol* 2008;65:848–54.
- [14] Ahn GJ, Yu JY, Choi SM, et al. Chronic administration of phosphodiesterase 5 inhibitor improves erectile and endothelial function in a rat model of diabetes. *Int J Androl* 2005;28:260–6.
- [15] Kang KK, Yu JY, Yoo M, Kwon JW. The effect of DA-8159, a novel PDE5 inhibitor, on erectile function in the rat model of hypercholesterolemic erectile dysfunction. *Int J Impot Res* 2005;17:409–16.
- [16] Lee CH, Shin JH, Ahn GJ, Kang KK, Ahn BO, Yoo M. Udenafil enhances the recovery of erectile function and ameliorates the pathophysiological consequences of cavernous nerve resection. *J Sex Med* 2010;7:2564–71.
- [17] NIH Consensus Conference. Impotence. NIH Consensus Development Panel on Impotence. *JAMA* 1993;270:83–90.
- [18] 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.
- [19] 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.
- [20] Rosen RC, Cappelleri JC, Gendrano 3rd N. The International Index of Erectile Function (IIEF): a state-of-the-science review. *Int J Impot Res* 2002;14:226–44.
- [21] Hatzichristou D, Rosen RC, Broderick G, et al. Clinical evaluation and management strategy for sexual dysfunction in men and women. *J Sex Med* 2004;1:49–57.
- [22] Hackett GI. Patient preferences in treatment of erectile dysfunction: the continuing importance of patient education. *Clin Cornerstone* 2005;7:57–65.

- [23] Washington 3rd SL, Shindel AW. A once-daily dose of tadalafil for erectile dysfunction: compliance and efficacy. *Drug Des Devel Ther* 2010;4:159–71.
- [24] Fusco F, Razzoli E, Imbimbo C, Rossi A, Verze P, Mirone V. A new era in the treatment of erectile dysfunction: chronic phosphodiesterase type 5 inhibition. *BJU Int* 2010;105:1634–9.
- [25] Kouvelas D, Goulas A, Papazisis G, Sardeli C, Pourzitaki C. PDE5 inhibitors: in vitro and in vivo pharmacological profile. *Curr Pharm Des* 2009;15:3464–75.
- [26] Makhlouf A, Kshirsagar A, Niederberger C. Phosphodiesterase 11: a brief review of structure, expression and function. *Int J Impot Res* 2006;18:501–9.
- [27] Porst H, Rajfer J, Casabé A, et al. Long-term safety and efficacy of tadalafil 5 mg dosed once daily in men with erectile dysfunction. *J Sex Med* 2008;5:2160–9.
- [28] Althof SE, Berner MM, Goldstein I, et al. Interrelationship of sildenafil treatment effects on the physiological and psychosocial aspects of erectile dysfunction of mixed or organic etiology. *J Sex Med* 2010;7:3170–8.
- [29] Mirone V, Fusco F, Rossi A, Sicuteri R, Montorsi F. Tadalafil and vardenafil vs sildenafil: a review of patient-preference studies. *BJU Int* 2009;103:1212–7.

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