THE JOURNAL OF
SEXUAL MEDICINE

PHARMACOTHERAPY

A Phase 3 Study to Evaluate the 1-Year Efficacy and Safety of Udenafil 75 mg Once Daily in Patients With Erectile Dysfunction

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ABSTRACT

Introduction: Once-daily administration of phosphodiesterase type 5 inhibitors has been shown to correct erectile dysfunction (ED).

Aim: To evaluate the long-term efficacy and safety after once-daily oral administration of udenafil 75 mg in men with ED.

Methods: This clinical trial was an open-label, fixed-dose, 24-week extension study (DA8159_EDDL_III) of a 24-week double-blinded efficacy and safety study of once-daily udenafil (parent study: DA8159_EDD_III). Subjects received udenafil 75 mg once daily for 24 weeks during this extension study, and the follow-up visit occurred during the 4-week ED treatment-free period.

Main Outcome Measures: Subjects were asked to complete the International Index of Erectile Function questionnaire and the Global Assessment Questionnaire at the 24-week extension and after the 4-week ED treatment-free period, and the development of adverse drug reactions was investigated.

Results: In total, 302 subjects were enrolled in this extension study. Improvement was shown with an increased erectile function (EF) domain score compared with baseline (14.60 ± 4.57) at extension week 48 (23.98 ± 5.44) and a slight increase in EF domain score compared with the last time point (week 24) of the parent study ($P < .001$). The Global Assessment Questionnaire showed a high improvement rate of 95.4% at the extension 48-week time point. For shift to normal, almost half the subjects (45.1%) recovered "normal" EF, and 14.2% of subjects reported normal erections after the 4-week ED treatment-free period. The occurrence rate of adverse drug reactions was 8%, which consisted mainly of flushing and headache.

Conclusion: Once-daily dosing of udenafil 75 mg showed excellent efficacy and safety with long-term administration and allowed a more spontaneous sexual life.

J Sex Med 2016;13:1263–1269.

Key Words: Erectile Dysfunction; Phosphodiesterase Type 5 Inhibitors; Udenafil; Long Term

Received March 7, 2016. Accepted May 27, 2016.

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http://dx.doi.org/10.1016/j.jsxm.2016.05.011

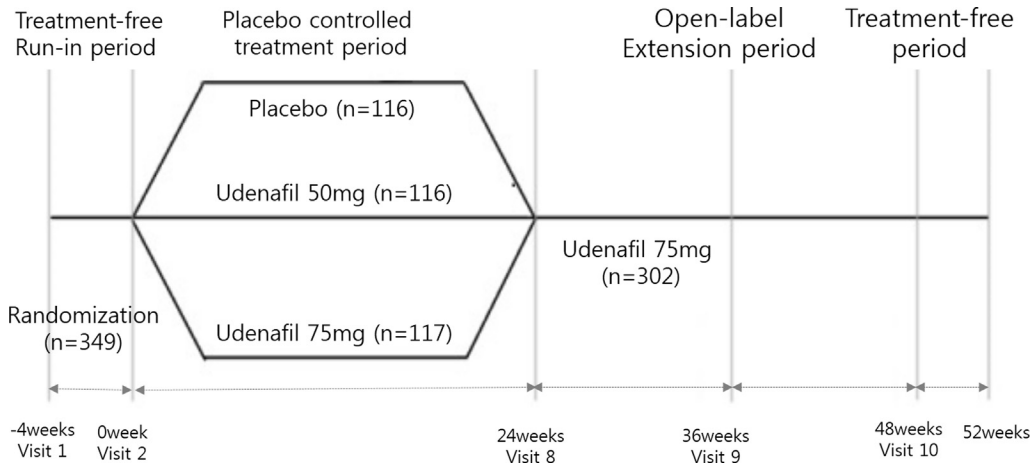

Figure 1. Study design and data collection schedule.

INTRODUCTION

Udenafil is a selective phosphodiesterase type 5 inhibitor (PDE5-I) and an "on-demand" form of oral medication indicated for men with erectile dysfunction (ED).[1] Recent clinical tests have reported that daily dosing of PDE5-I shows some advantage in treatment effect at a comparatively lower dose than on-demand dosing.[2–5] This is theoretically based on the treatment of refractory ED accompanied by conditions such as diabetes, prostatectomy, and spinal injury, achieving a more natural erection, and maintaining consistent sexual function rather than the limited erection induced by the on-demand administration of drugs.[2] In fact, many recent clinical studies have reported that once-daily treatment with PDE5-Is significantly improves erectile function (EF) in men with mild and mild to moderate impairments in EF after on-demand PDE5-I treatment.[2–5] Long-term administration of PDE5-Is inhibits the decrease of vascular endothelial cell function, thus accelerating vascular relaxation,[6] inhibits the decrease in endothelial cell and smooth muscle contents, and prevents their fibrosis within the penile corpus cavernosum.[7–10]

Udenafil also has shown the ability to significantly inhibit the decrease of vascular endothelial cell function and inhibit the decrease in endothelial cell and smooth muscle contents, thus preventing their fibrosis within the penile corpus cavernosum in diabetic or hyperlipidemic animal models when administered once daily for a long period.[11–13] Based on these findings and those of a clinical trial in patients with ED using a low dose of udenafil (25, 50, and 75 mg) once daily in addition to taking the drug on demand, udenafil 50 mg has been shown to be safe and effective, leading to its market approval for once-daily administration.[14] Recently, we reported on the efficacy and safety of udenafil 50 and 75 mg once daily for 24 weeks in a therapeutic confirmatory clinical trial (parent study: DA8159_EDD_III),[15] and the present clinical trial was conducted to evaluate the long-term safety (to 48 weeks) of administering udenafil 75 mg once daily.

METHODS

Study Design

This clinical trial was conducted as an open-label, fixed-dose, 24-week extension study. This long-term safety study was conducted at 13 centers in Korea according to guidelines of Good Clinical Practice and the International Conference on Harmonization and adhered to the ethical principles of the Declaration of Helsinki. This clinical study protocol was reviewed and approved by the institutional review board of each study center after approval by the Korean Ministry of Food and Drug Safety. Figure 1 shows the design and data collection schedules for this study. This clinical trial was an open-label, fixed-dose, 6-month extension study of the 24-week double-blinded efficacy and safety study of once-daily udenafil (parent study).[15] The patients who agreed to participate in this extension study were enrolled at the last visit (week 24) of the parent study. Subjects received udenafil 75 mg once daily for 24weeks during this extension study. After the last visit (extension visit 10), the follow-up visit occurred during the 4-week ED treatment-free period. Subjects visited their respective study center according to the schedule after enrollment, and phone contact was performed to evaluate adverse events after 4 weeks at extension visit 8 (at week 28). All baseline safety and efficacy evaluations were considered the results measured after completion of the 4-week treatment-free run-in period (week 0) of the parent study.[14]

Subjects

The inclusion criteria of the parent study were a history of ED for a minimum of 6 months, which was defined as greater than 50% failure at sexual intercourse (minimum of four attempts at 4 different days during the 4-week treatment-free run-in period), and a score below 25 on the EF domain of the International Index of Erectile Function (IIEF) questionnaire, which was estimated from baseline (week 0). The inclusion criteria of the parent study were adult men at least 20 years old with ED for longer than 6 months, who had a stable relationship with one