ORIGINAL RESEARCH—ED PHARMACOTHERAPY

The POTENT I Randomized Trial: Efficacy and Safety of an Orodispersible Vardenafil Formulation for the Treatment of Erectile Dysfunction

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ABSTRACT

Introduction. Orodispersible tablet (ODT) formulations offer improved convenience over film-coated formulations and are preferred by many patients.

Aim. To investigate the efficacy and safety of an ODT formulation of 10 mg vardenafil administered on demand vs. placebo in a general population of men with erectile dysfunction (ED).

Methods. This was a 16-week, double-blind, multicenter, randomized, parallel-group, placebo-controlled study conducted at 40 centers across Europe and South Africa. Eligible participants were men aged ≥18 years with ED for at least 6 months, in a stable heterosexual relationship for at least 6 months, highly motivated to obtain ED treatment, and making at least four attempts at sexual intercourse on four separate days, of which at least half were unsuccessful. Subjects were randomized to receive 12 weeks of treatment with either 10 mg vardenafil ODT on demand or placebo, and each treatment group was stratified such that approximately half of the subjects were aged ≥65 years.

Main Outcome Measures. Primary measures were the erectile function domain of the International Index of Erectile Function (IIEF-EF) and the Sexual Encounter Profile questions 2 and 3 (SEP2, SEP3). Secondary measures included SEP diary questions 1, 4, 5, and 6; the Treatment Satisfaction Scale; and the Global Assessment Question.

Results. Of the 409 men enrolled (54.8% aged ≥65 years), 355 were included in the intent-to-treat population (vardenafil ODT, N = 183; placebo, N = 172). Vardenafil ODT therapy was statistically significantly superior to placebo for all primary (IIEF-EF, SEP2, SEP3) and secondary efficacy measures (all $P < 0.0001$). The incidence and type of treatment-related adverse events with vardenafil 10 mg ODT were comparable with those of the film-coated tablet formulation.

Conclusions. Treatment with 10 mg vardenafil ODT, taken on demand, significantly improved erectile function and was well tolerated in a broad population of men with ED. **Sperling H, Debruyne F, Boermans A, Beneke M, Ulbrich E, and Ewald S. The POTENT I randomized trial: Efficacy and safety of an orodispersible vardenafil formulation for the treatment of erectile dysfunction. J Sex Med 2010;7:1497–1507.**

Key Words. Vardenafil; Orodispersible; On Demand; Erectile Dysfunction; Elderly; Phosphodiesterase Type 5 Inhibitor

Introduction

Erectile dysfunction (ED), defined as "the persistent inability to attain and maintain a penile erection sufficient to permit satisfactory sexual intercourse" [1] is a common condition in men. The Men's Attitudes to Life Events and Sexuality (MALES) study found the self-reported prevalence of ED was 16% in a general population of men aged 16–75 years [2]. The Cologne Study

of Male Sexual Health recorded a similar prevalence of 19.2% in a European cohort of men aged 30–80 years [3]. ED prevalence increases linearly with age [4], affecting 30–74% of men aged 60 years or older [2,5]. After the age of 60, this increase occurs independently of underlying conditions that can predispose to ED, such as diabetes, hypertension, or heart disease [6]. Furthermore, data from a study of 1,626 men aged 40–70 years showed that more severe forms of ED occur more frequently in older individuals [7].

Endothelial dysfunction, thought to play a role in the origin of organic ED, becomes more common with age because of the cumulative effects of oxidative stress and alterations to vasoactive mediators in the corpus cavernosum [8–10]. Moreover, ED in elderly men is exacerbated by age-related underlying conditions. Certain concomitant medications that are used to treat such conditions, such as diuretics, anti-arrythmics, and lipid-lowering drugs, may also themselves negatively affect erectile function [11,12].

Oral phosphodiesterase type 5 (PDE5) inhibitors are recommended as first-line therapy for the treatment of ED [13,14]. The efficacy and safety of the PDE5 inhibitor, vardenafil, has been widely demonstrated in numerous clinical trials [15–25]. Extensive analysis has shown that men would prefer a more convenient method of taking PDE5 inhibitors (Bayer Schering Pharma, data on file). To address this preference, an orodispersible tablet (ODT) formulation of vardenafil has been developed, which dissolves in the subject's mouth. Vardenafil ODT has a 1.21-to-1.44-fold higher bioavailability than the film-coated tablet formulation (as measured by the area under the plasma concentration vs. time curve [AUC]), and maximum concentrations in plasma after a single dose (C_{max}) are comparable between the two formulations. The bioavailability and C_{max} of vardenafil ODT are not significantly affected by intake with food: mean AUC and C_{max} are 39.4 μg*h/L and 10.9 μg/L, or 38.5 μg*h/L and 7.2 μg/L, respectively, for subjects taking vardenafil ODT in the fasting state, or with a standardized high-fat, high-calorie meal containing 42.0 g protein, 67.0 g carbohydrates, and 63.6 g fat (1,051 kcal total). Vardenafil ODT should be taken without water. If swallowed with water, C_{max} is unchanged (10.7 μg/L) and the bioavailability (AUC) of vardenafil ODT decreases to 28.1 μg*h/L, which is equivalent to that of the existing film-coated tablet formulation. There are no discernable effects on tolerability. Onset and duration of action have not been assessed for vardenafil ODT, but are expected to be comparable with those of the film-coated tablet formulation, based on similar plasma concentration vs. time profiles (R. Heinig et al., manuscript submitted).

The primary objective of POTENT I (Pivotal phase III trial to investigate the efficacy and safety of an Orodispersible Tablet vardenafil vs. placebo in the treatment of men with Erectile dysfunction: a fixed-dose, double-blind, raNdomized, multicenter Trial) was to compare the efficacy and safety of on-demand 10 mg vardenafil ODT with placebo after 12 weeks of treatment or last observation carried forward (LOCF) in a general population of men with ED. To allow for a detailed investigation of the safety of vardenafil ODT in the older population, approximately 50% of the men on active treatment were ≥65 years of age.

Methods

Study Design

POTENT I was a double-blind, multicenter, randomized, parallel-group, placebo-controlled study conducted at 40 centers in Belgium, France, Germany, the Netherlands, Spain, and South Africa. Blinding was maintained until completion of the study. All patients provided written, informed consent, and the study was conducted according to the International Conference on Harmonization/Good Clinical Practice guidelines and the principles detailed in the Declaration of Helsinki.

The main inclusion criteria were men with ED (as defined by the National Institutes of Health [NIH] Consensus Development Panel on Impotence [1]) for at least 6 months, aged ≥18 years, in a stable heterosexual relationship for at least 6 months, highly motivated to obtain treatment for ED, and making at least four attempts at sexual intercourse on four separate days, of which at least half were unsuccessful.

The main exclusion criteria were the presence of any underlying cardiovascular condition that precludes sexual activity, according to the NIH consensus report [1]; history of severe cardiovascular disorder within 6 months prior to first visit; history of prostatectomy because of prostate cancer; spinal cord injury; and confirmed phenylketonuria. Furthermore, patients were excluded if they had underlying conditions, or were taking concomitant medications that are listed in the contraindications or safety warnings of the vardenafil film-coated tablet product labeling.