Vardenafil Improved Erectile Function in a "Real-Life" Broad Population Study of Men with Moderate to Severe Erectile Dysfunction in Australia and New Zealand

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ABSTRACT

Introduction. Phosphodiesterase type 5 inhibitor drugs produce vasodilatation by inhibiting the breakdown of cyclic guanosine monophosphate and have proven efficacy in treating erectile dysfunction (ED).

Aim. To evaluate the efficacy, safety, and tolerability of vardenafil in men with moderate to severe ED of broad etiology.

Main Outcome Measures. The erectile function (EF) domain score, the response to Questions 13 and 14 of the International Index of Erectile Function (IIEF) questionnaire, and the proportion of "yes" responses to questions 2 and 3 of the Sexual Encounter Profile (SEP), a Global Assessment (GAQ), and Global Satisfaction Questions (GSQ) were compared at baseline and at 12 weeks of treatment with as-needed vardenafil.

Methods. A total of 326 subjects with a mean age of 57.6 years and moderate to severe erectile dysfunction of various etiologies received vardenafil (5–20 mg) for 12 weeks in a prospective multicenter, open-label flexible-dose study.

Results. Compared with baseline, vardenafil was superior in all efficacy outcomes. A significant mean improvement of 13.4 ($P < 0.001$) in the EF domain from baseline was obtained at week 12. Subjects who received 5, 10, and 20 mg vardenafil at week 12 experienced improvements of 11.9, 15.1, and 12.9 respectively in the EF domain score. Sexual intercourse was successfully completed (SEP3) in 76.3%, 80.1%, and 74.3% of subjects receiving 5, 10, and 20 mg vardenafil compared with 25.9%, 17.9%, and 19.2% at baseline, respectively. For all doses combined at week 12, the change in SEP3 from baseline was 56.7% ($P < 0.001$). Treatment with vardenafil was well tolerated, and headaches, flushing, nasal congestion, and dyspepsia were the most frequently observed adverse events.

Conclusions. Vardenafil was effective and well tolerated in men with moderate to severe erectile dysfunction. Treatment with vardenafil was associated with a significantly higher IIEF erectile function domain score and completion of successful intercourse rate compared with baseline. **McMahon C, Lording D, Stuckey B, Tan V, Gillman M, White W, Di Natale S, and Bramwell P. Vardenafil improved erectile function in a "real-life" broad population study of men with moderate to severe erectile dysfunction in Australia and New Zealand. J Sex Med 2006;3:892–900.**

Key Words. Oral Vasoactive Agents; Male Erectile Disorder; Vardenafil

Introduction

Erectile dysfunction (ED) is a common and often undertreated condition that is associated with reduced self-esteem and quality of life [1–3]. As many as 152 million men worldwide may be affected by ED, and estimates of the prevalence of ED range from 7% to 52% [1,2,4]. In a community-based study in Australia, 3% of men aged 40–49 years, 42% of men aged 60–69 years, and

64% of men aged 70–79 years reported erections inadequate for intercourse [5]. Although advances have been made in the diagnosis and management of ED, as few as 10% of men with ED are treated [6,7].

Erectile dysfunction is commonly associated with advancing age and medical conditions commonly associated with aging, including depression, atherosclerosis, hypertension, and diabetes mellitus [8]. Penile vascular disease is the most common cause of ED, accounting for up to 80% of cases [9,10]. Kaiser et al. reported that subjects with ED and no significant cardiac risk factors or other clinical cardiovascular disease have a peripheral vascular abnormality in the nitric oxide–cyclic guanosine-3′5′-monophosphate (NO–cGMP) pathway, and suggested that ED may be the first clinical manifestation of generalized endothelial dysfunction and cardiovascular disease [11].

Phosphodiesterase type 5 (PDE-5) inhibitor drugs inhibit the breakdown of cGMP producing vasodilatation, improve endothelial cell function, and have proven efficacy in the treatment of ED [12]. The NO–cGMP system is important in producing the arterial dilation and venous occlusion necessary to attain and sustain an erection. Abnormalities of this vasodilator system due to endothelial dysfunction are present in atherosclerosis and play an important role in the pathophysiology of ED [13–15].

Vardenafil is a potent selective inhibitor of PDE-5, which is rapidly absorbed with a median tmax of 1 hour and a terminal half-life of approximately 4 hours [16]. Multicenter international placebo-controlled clinical trials have demonstrated that compared with placebo, vardenafil is well tolerated and significantly improves erections in men with ED of all etiologies and severities, with sexual intercourse completion rates ranging from 71% to 80% [17–19]. Vardenafil significantly improves erectile function in men with diabetes mellitus and in men following a radical prostatectomy [20,21].

This study was an open-label study designed to assess the safety, efficacy, and tolerability of flexible doses of vardenafil in a representative population of men with ED of various etiologies in Australia and New Zealand. The study's flexible dosing reflects the utilization of vardenafil in "real life" clinical practice by offering subjects the opportunity to optimize their dosing based on individual efficacy and tolerability after having commenced on the recommended starting dose.

Materials and Methods

Study Design

The study was a prospective open-label flexible-dose study of the efficacy, safety, and tolerability of vardenafil, and was conducted at 29 sites in Australia and New Zealand. The study comprised three phases: (i) an initial 4-week treatment-free period; (ii) a 12-week open-label treatment period with initial treatment with 10 mg vardenafil for 4 weeks, followed by dose maintenance or titration to 5 or 20 mg at weeks 4 and 8 according to efficacy and tolerability; and (iii) a 24-hour follow-up for continued monitoring of adverse events. The study was conducted with Institutional Review Board/Independent Ethics Committee approval and with signed informed consent from all subjects. The study was sponsored by the manufacturer of vardenafil (Bayer—GlaxoSmithKline).

Inclusion Criteria

Eligible subjects were men 18 years of age or older in a stable heterosexual relationship for more than 6 months, with a 6-month or longer history of ED and with moderate or severe ED according to their erectile function (EF) domain score (Questions 1–5 and 15) of the International Index of Erectile Function (IIEF) questionnaire assessed at baseline (visit 2). To be enrolled in the treatment phase of the study, subjects were required to have made at least four attempts at sexual intercourse on at least four separate occasions during the initial 4-week treatment-free period. The etiology of ED was classified as organic, psychogenic, or mixed organic/psychogenic on the basis of subject history, examination findings, and/or the results of investigations.

Exclusion Criteria

Conditions that precluded study entry included anatomic abnormalities of the penis that could impair erectile function, hypoactive sexual desire, treated or untreated hypogonadism, a history of radical prostatectomy, ED after spinal cord injury, severe chronic liver disease, severe chronic renal failure, retinitis pigmentosa, unstable angina pectoris, uncontrolled atrial tachyarrhythmia, or, within the previous 6 months, a myocardial infarction, cerebrovascular accident, electrocardiographic ischemia, or life-threatening cardiac arrhythmia. Previous sildenafil treatment was allowed. Excluded medications included androgens, trazadone, antiandrogens, nitrates, NO donors, potent inhibitors of cytochrome P450 3A4