Duration of Erection: Does It Really Matter? A Randomized, Double-Blind Clinical Trial to Assess the Impact of Vardenafil ODT on Duration of Erection and Its Correlation with Patients' and Partners' Sexual Quality of Life and Duration of Intercourse: The VADEOPEN Study

Antonio Martin-Morales, MD,* Pedro Gutiérrez-Hernández, MD,† Javier Romero-Otero, MD,‡ José A. Romero-Martín, MD,§ and on behalf of the Vadeopen Study Group

*Hospital Universitario Carlos Haya, Málaga, Spain; †Hospital Universitario de Canarias, Tenerife, Spain; ‡Hospital Universitario 12 de Octubre, Madrid, Spain; §Hospital de Mataró, Barcelona, Spain

DOI: 10.1111/jsm.12496

ABSTRACT

Introduction. Stopwatch-assessed duration of erection has been proposed as an objective and reliable efficacy end point for erectile dysfunction (ED) treatments.

Aim. The aim of this study is to assess vardenafil orodispersible tablets' (ODTs) efficacy in terms of duration of erection and (i) its correlation with other efficacy end points and male and female sexual quality of life (QoL) and (ii) its impact on intercourse duration.

Methods. Randomized, double-blind, placebo-controlled, multicenter study comparing the efficacy and safety of vardenafil ODT 10 mg on-demand over 12 weeks in 127 patients with ED was carried out.

Main Outcome Measures. Primary efficacy end points were stopwatch-assessed duration of erection (min) at any attempt and when leading to successful intercourse, and the erectile function domain of the International Index of Erectile Function (EF-IIEF) score. Secondary end points were sexual encounter profile (SEP) 3 response rate and male sexual QoL. End points in participating women (N = 46) were stopwatch-assessed duration of intercourse and sexual QoL.

Results. At week 12/last observation carried forward, patients taking vardenafil ODT had longer duration of erections (at any attempt or leading to successful intercourse) vs. placebo (least square mean ± standard error 10.2 ± 0.9 minutes vs. 7.9 ± 1.0 minutes, and 10.4 ± 0.8 vs. 8.3 ± 1.0 minutes, respectively), and significant increases in EF-IIEF scores, the SEP-3 response, and all sexual QoL items. An increased duration of intercourse was also observed. Female sexual QoL improved significantly. Both duration end points strongly correlated with EF-IIEF scores, and the three end points correlated well with SEP-3 response. Correlation was good with sexual QoL scores in men and women and with duration of intercourse, with differences between treatment groups only for duration end points. Safety was similar in both groups.

Conclusion. This study provides further evidence for the consistency and reliability of the stopwatch-assessed duration of erection as an efficacy end point for ED treatments, with "duration of erection leading to successful intercourse" showing better properties than duration at any attempt. **Martin-Morales A, Gutiérrez-Hernández P, Romero-Otero J, and Romero-Martín JA. Duration of erection: Does it really matter? A randomized, double-blind clinical trial to assess the impact of vardenafil ODT on duration of erection and its correlation with patients' and partners' sexual quality of life and duration of intercourse: The VADEOPEN study. J Sex Med 2014;11:1527–1538.**

Key Words. Erectile Dysfunction; Duration of Erection; Phosphodiesterase Type 5 Inhibitors; Vardenafil; IIEF; SEP-3; Orodispersible Tablet

Introduction

In research and clinical settings, efficacy assessment of pharmacological treatments for erectile dysfunction (ED), especially phosphodiesterase type 5 inhibitors (PDE5i), has relied on self-report questionnaires, diaries, event logs, and/or interviews. The International Index of Erectile Function (IIEF), particularly its erectile function domain (EF-IIEF) [1,2], and the sexual encounter profile (SEP) questions are the most commonly used self-report questionnaires. Their main focus is assessing erection hardness and performance, which are subjective in nature. The IIEF is widely accepted and has been routinely used in most PDE5i efficacy studies [3]. Although multiple validated versions of the IIEF are available, social and cultural elements may ultimately influence self-perceptions and responses, distorting comparisons between different populations.

In recent years, duration of erection, timed with a stopwatch, has been proposed as an objective, precise, and reliable end point for ED treatment effect [4–7]. Duration of erection has shown to be shorter in men with ED with respect to healthy men, and even shorter in men with ED and comorbidities [4,5]. According to a survey among 256 men with ED, duration of erection is considered a treatment outcome as important as hardness [8]. This end point is probably better understood and "measurable" than the IIEF by patients, and its objectivity reduces possible cultural interferences. Duration of erection is also important for women: penile–vaginal intercourse duration, which is likely to be related to duration of erection, has been shown to be associated to women's likelihood of partnered orgasm [9]. It has been postulated that, because of its significance for both members of the couple affected by ED, improvement of duration of erection may have a positive impact on their sexual quality of life (QoL) [7].

Two randomized, double-blind, multicenter studies in men with ED (the ENDURANCE study, a cross-over study with fixed-dose vardenafil 10 mg 4 weeks, and the "dyslipidemia" study, a 12-week study with on-demand flexible-dose of vardenafil in men with dyslipidemia treated with statins) have proven that treatment with vardenafil yields a significantly longer duration of erection leading to successful intercourse vs. placebo [4–6,10]. Duration of erection has shown to correlate well with traditional subjective measurements such as EF-IIEF and SEP questions 2 and 3 [11]. The relationship with outcome measures such as sexual QoL or its impact on duration of intercourse or female sexual QoL have not been assessed.

Until recently, vardenafil was only available as a film-coated tablet (FCT). A new orodispersible tablet (ODT) formulation of vardenafil that disintegrates in the subject's mouth has been developed. Both formulations share a similar pharmacokinetic profile, with the ODT formulation showing significantly greater bioavailability [12]. Time to onset of action of both formulations is equivalent [13]. Vardenafil ODT has been shown to significantly improve erectile function, the rates of vaginal penetration, and successful sexual intercourse in men with ED, even with underlying conditions [14–16]. Vardenafil FCT has also been shown to significantly improve sexual QoL of men with ED and their female partners [17]. In the present study, efficacy of vardenafil ODT was assessed after 12 weeks of on-demand treatment by means of traditional measurements (EF-IIEF) and of duration of erection with the aim of further analyzing the validity of this latter end point and to assess how it correlates with improvements in sexual QoL. The impact on the duration of intercourse and sexual QoL of women was also assessed in a subgroup of men whose female partners agreed to participate.

Materials and Methods

Study Design

The study design consisted of a phase IIIb, randomized, double-blind, placebo controlled, parallel-group, multicenter study aimed at comparing the efficacy and safety of a fixed-dose vardenafil ODT 10 mg on-demand or placebo over a 12-week treatment period in patients with ED and common cardiovascular comorbidities and/or obesity attending outpatient urology offices. The study was conducted in Spain from April 2010 to August 2011 (Registration number: EudraCT 2009–017686–34). The study was conducted in accordance with the Declaration of Helsinki, the Good Clinical Practice guidelines, and the International Conference on Harmonization. The Clinical Research Ethics Committee of involved research centers approved all documents. All participants gave a written consent prior to participation.

Following an initial screening visit, male participants entered a 4-week unmedicated run-in period after which (baseline visit, V0) eligible men were randomized (simple randomisation) using a computer-generated code to either vardenafil