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First-dose success with vardenafil in men with erectile dysfunction and associated comorbidities: RELY-I

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SUMMARY

First-dose success of phosphodiesterase type 5 (PDE5) inhibitors may be adversely affected in patients with comorbidities. This article reports first-dose success rates for vardenafil 10 mg in men with erectile dysfunction (ED) and associated comorbidities who participated in the challenge phase of the Reliability – Vardenafil for Erectile Dysfunction I study. This study involved an open-label, single-dose, 1-week challenge period where patients who achieved SEP-2 (penetration) success were randomised to vardenafil 10 mg or placebo for 12 weeks in a double-blind manner. The first-dose success rates for SEP-2 and SEP-3 (maintenance of erection to completion of intercourse) were stratified according to comorbidities. Safety was assessed using adverse events (AEs). Of 600 men who received a single 10 mg dose of vardenafil, 32% had hypertension, 16% had diabetes and 19% had dyslipidaemia. Vardenafil demonstrated overall effectiveness, including first-dose SEP-2 and SEP-3 success rates in patients with and without specific comorbidities. Initial overall success rates for SEP-2 and SEP-3 during the challenge phase were 87% and 74% respectively. First-dose SEP-2 and SEP-3 success rates were 84% and 66% in men with hypertension ($n = 191$); 84% and 72% in men with dyslipidaemia ($n = 116$); and 75% and 58% in men with diabetes ($n = 95$). Vardenafil was well tolerated and most AEs, including the most frequently reported flushing (3.5%), were mild to moderate in intensity. Vardenafil 10 mg is generally well tolerated and efficacious, providing first-dose success with a consistently high rate of reliability of penetration and maintenance of erection in men with ED and associated comorbidities.

Keywords: Vardenafil; PDE5 inhibitors; erectile dysfunction; erection; first-dose success; comorbidities

INTRODUCTION

Erectile dysfunction (ED) is a highly prevalent condition that affects millions of men in the United States (1,2) and it is projected to affect 322 million men worldwide by 2025 (3). Even though erectile function does not constitute the most important measure of sexual satisfaction in some men, most men with ED develop mental stress that has potentially detrimental effects on both family and social relationships (2).

Comorbid conditions are associated with impairment of both neurogenic and endothelium-dependent vasodilation mechanisms which lead to circulatory and structural changes in penile tissues (4–6). The resulting arterial insufficiency and defective smooth muscle relaxation are responsible for the increased prevalence of ED in men with comorbidities and serve to complicate interventional therapy. In men with ED, the presence of comorbid conditions, including diabetes mellitus, hypertension, dyslipidaemia, or other cardiovascular conditions, serves to further exacerbate the disease and can complicate its management (7,8). In addition, ED is more severe in these comorbid populations (7,9,10). Patients with hypertension may have an increased risk of ED due to the contributory effects of elevated blood pressure and the impact of antihypertensive agents, such as thiazide diuretics, beta-blockers, calcium channel blockers and

The ND# for vardenafil trials is 57703. There is, however, no corresponding clinicaltrials.gov registration number for the RELY-I trial. The reason for this is that according to the Study Report RELY-I was initiated on 16 June 2003 and completed on 22 June 2004. The trial was therefore already 'completed' before the International Committee of Medical Journal Editors set their 1 July 2005 and 13 September 2005 deadlines for registration of ongoing clinical trials. Additionally, the study design of the RELY-I trial was published previously (22).

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angiotensin-converting enzyme inhibitors on erectile function (11,12).

Recent advances in therapy for ED include the development and introduction of oral phosphodiesterase type 5 (PDE5) inhibitors, including vardenafil. PDE5 inhibitor therapy represents significant clinical progress in the treatment of ED and provides a generally well tolerated, effective and convenient oral pharmacological therapeutic option. PDE5 catalyses the breakdown of cyclic guanosine monophosphate (cGMP) in the penile corpus cavernosum and reverses the cGMP-mediated pathway responsible for physiological changes required for erection. Consequently, the inhibition of this enzyme leads to an improvement in erectile function (13). Vardenafil is a potent, selective PDE5 inhibitor with efficacy and tolerability that has been demonstrated in randomised, double-blind, placebo-controlled trials in men with ED including those with comorbid conditions, such as diabetes mellitus (14), hypertension (15), or postprostatectomy (16), who are difficult-to-treat ED patients (14,16–19).

First-time and long-term continued success or reliability (subsequent response to treatment after an initial positive response to the same treatment) are important criteria for selecting and continuing ED therapy (20). The currently available PDE5 inhibitors have all demonstrated clinical efficacy in patients with ED and comorbid conditions, such as hypertension, diabetes mellitus and dyslipidaemia. However, demonstrating first-time and continued success in these patient populations is often challenging due to the complicating pathophysiology of ED. The reliability of vardenafil has previously been assessed in a retrospective analysis of two clinical trials in which patients with ED made at least four attempts at intercourse on four separate days, with 50% of the attempts unsuccessful (21). Patients who successfully responded to the first dose of vardenafil during a 1-week challenge phase continued to maintain successful response with vardenafil during the 12 weeks of treatment. This analysis showed that vardenafil improved the reliability of penetration as measured by the Sexual Encounter Profile Question-2 (SEP-2) and maintenance of erection (SEP-3) as well as overall satisfaction. Based on this preliminary evidence supporting the long-term reliability of vardenafil, the Reliability – Vardenafil for Erectile Dysfunction I (RELY-I), a prospective, controlled clinical trial, was designed to assess the reliability of vardenafil 10 mg in men with ED. We also investigated the first-time dose response to vardenafil in ED patients with comorbid conditions, such as hypertension, dyslipidaemia and diabetes mellitus.

PATIENTS AND METHODS

The study was conducted in compliance with the human experimentation guidelines of the US Department of Health and Human Services and the Helsinki Declaration 1975, last amendment in Edinburgh, Scotland, 2000.

Study Objectives

The primary objective of this study was to demonstrate that patients who respond the first time to vardenafil 10 mg will continue to respond to the same dose over a 12-week period in a randomised, placebo-controlled clinical trial. The secondary objective was to evaluate the safety and tolerability of vardenafil 10 mg compared with placebo.

Study Design

This 12-week, multicentre, randomised, double-blind, parallel-group, placebo-controlled trial in vardenafil-naïve patients was conducted in 42 centres in Europe, North America, South America and Asia Pacific, and included an open-label challenge phase and a double-blind treatment phase (Figure 1). The study period commenced on 16 June 2003 and was completed on 22 January 2004. At screening, patients were entered into a 4-week, treatment-free, run-in period, and instructed to make at least

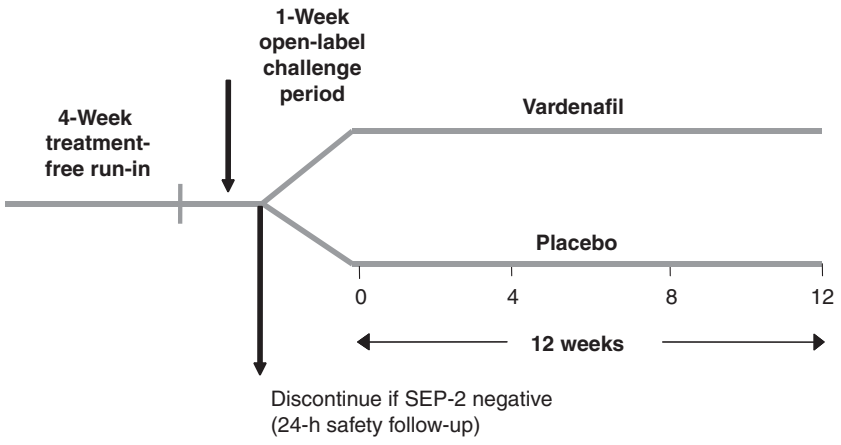

Figure 1 Overview of study design

four attempts at sexual intercourse on four separate days. A diary was provided for patients to record all attempts made at sexual intercourse. The patients who failed at ≥50% of their attempts at intercourse were entered into a 1-week challenge phase. Patients were instructed to make at least one attempt at sexual intercourse within 1 h following administration of a single 10 mg dose of vardenafil. Patients with a positive SEP-2 response, 'Were you able to insert your penis into your partner's vagina?', for attempts made 0.5–6 h post-ingestion of study medication were randomised to receive either vardenafil 10 mg or placebo for 12 weeks. Patients were instructed to take each dose of medication without regard to food, on an as-needed basis, 1 h prior to each attempt at sexual intercourse, with only one dose permitted per day. Patients recorded the date and time of study medication administration, the time of attempt at sexual intercourse, and response to questions regarding success at penetration (SEP-2) and maintenance of erection sufficient enough for completion of intercourse (SEP-3). During the 12-week treatment period, patients were scheduled for study visits at weeks 4, 8 and 12 for assessment of efficacy, safety, tolerability and compliance.

All study medication during the comparative phase of the study was blinded to both the investigator and the patients. Vardenafil 10 mg tablets and placebo tablets were identical in appearance. Study medication was provided to the centres in individual coded bottles. Each bottle had a double-blind label with a unique six-digit container number. The randomisation schedule was not disclosed to the investigator or any other personnel involved in the conduct of the study. The randomised assignment of study medication was done using the Registration and Medication Ordering System (RAMOS).

Patient Population and Demographics

This study included male patients with a diagnosis of ED for >6 months duration, according to the National Institutes of Health Consensus Statement (the inability to attain or maintain penile erection sufficient for satisfactory sexual performance) (2). Patients had to be ≥18 years of age, be in a heterosexual relationship, and have completed written informed consent prior to study entry. For randomisation into the treatment phase patients had to have been unsuccessful in at least 50% of the four attempts made at intercourse during the 4-week treatment-free period. They also had to be successful during the challenge phase that was assessed by the SEP-2 question, 'Were you able to insert your penis into your partner's vagina?', and have an International Index of Erectile Function-Erectile Function (IIEF-EF) domain score ≥5 and <26 at the start of the challenge phase.

Efficacy Assessment

First-dose success rates from the open-label challenge phase for SEP-2 and SEP-3 were stratified according to specific comorbidities with patients stratified into two populations: those with a specific comorbidity and those without that comorbidity. However, this did not preclude patients in the two populations from having other associated comorbidities. In the treatment phase, SEP-2 and SEP-3 success rates through the end of the study were assessed.

Safety Assessment

The safety population included all patients who were administered ≥1 dose(s) of vardenafil therapy or placebo and who had any post-run-in safety data collected. Safety and tolerability were evaluated throughout the study using adverse events (AEs), from the start of the challenge phase to the end of week 12. Clinical chemistry, haematology, urinalysis, complete physical examination, 12-lead electrocardiogram and vital signs were also used as other safety assessments.

Statistical Methods

The primary population for the efficacy analysis was the intent-to-treat (ITT) population, which consisted of randomised patients who took at least one dose of either vardenafil or placebo and had post-randomisation efficacy data collected. Similarly, the primary population for the safety assessment included all randomised patients who took at least one dose of study medication and had any post-run-in safety data collected. The study was designed to detect a clinically meaningful treatment difference in SEP-2 reliability of 15.0 (SD = 35) in the mean proportion of successes at 12 weeks with 96% power and an alpha level of 0.05. It was estimated that 151 patients per treatment arm would be needed to detect a clinically meaningful (15%) difference. The mean proportions of success for each treatment group were compared using an analysis of covariance (ANCOVA) adjusting for baseline values and the least squares (LS) means was calculated for each treatment. Secondary efficacy variables were analysed using ANCOVA or by logistic regression and last observation carried forward (LOCF) was used only for week 12 to account for potential missing values.

RESULTS

Patient Demographics

Patient demographics have been extensively covered in a previous publication (22). Of the 600 men who received a single 10 mg dose of vardenafil in the challenge phase, 32%

had hypertension, 16% had diabetes mellitus and 19% had dyslipidaemia; approximately 8% of the men had both diabetes mellitus and hypertension and about 4% had all three comorbidities concomitantly. In the study, ED-associated comorbidities were identified based on review of patient medical history. Moreover, specific details related to individual comorbidities (e.g. duration of diabetes) were not documented as this would have been beyond the scope of the study objectives. Of the 600 patients who had SEP-2 success following the challenge dose, 260 were randomised to receive vardenafil 10 mg and 263 to receive placebo. The ITT population subsequently consisted of 255 patients randomised to vardenafil and 254 to placebo. Baseline characteristics of the 2 ITT treatment groups were comparable (Table 1). Patients had a mean age of 54 years and a duration of approximately 3.3 years of ED. The majority (83%) of patients used little or no alcohol and the proportion of smokers (51%) to non-smokers (49%) was essentially the same. The mean IIEF-EF domain score which was indicative of moderate ED was similar between vardenafil (14.7) and placebo (14.5). The majority of men in the placebo (75%) and vardenafil (73%) treatment groups had at least one comorbidity at baseline. Patients in the two treatments had a similar prevalence of diabetes mellitus, benign prostatic hyperplasia, and back pain. However, hypertension was more common in the placebo group [34% (87/254) vs. 27% (68/255) for vardenafil] and dyslipidaemia was more common in the vardenafil group [19% (49/255) vs. 13% (33/254) for placebo].

The incidence of prior use of sildenafil and tadalafil was similar between the treatment groups (Table 2). With respect to the number of PDE5 inhibitor-naïve patients, there were 255 in the vardenafil group (166 had previously used sildenafil and 57 used tadalafil, leaving 32 with no prior use of either drug), and 254 in the placebo group (171 previously used sildenafil and 47 used tadalafil, with 36 having no prior use of either drug).

Of the 600 patients challenged with a single dose of vardenafil 10 mg in the RELY-I study, 520 achieved SEP-2 success. Of these patients, 511 along with 12 patients without SEP-2 success (recorded as protocol violations) were randomised to treatment with either vardenafil 10 mg ($n = 260$) or placebo ($n = 263$). Nine of the patients who had SEP-2 success were not randomised for a variety of reasons: AE ($n = 2$), protocol violation ($n = 3$), consent withdrawal ($n = 3$) or insufficient therapeutic effect ($n = 1$). Of the 509 patients in the ITT population, 45 and 41 protocol violations were reported for those patients on vardenafil and placebo respectively. Protocol violations included non-adherence to visit schedule, taking prohibited medication, taking >1 dose of study medication per day and noncompletion of at least one diary entry.

Efficacy

Of the 600 men who received the 10 mg challenge dose of vardenafil, 520 (87%) achieved initial penetration (SEP-2) and 443 (74%) achieved successful completion of intercourse (SEP-3). First-dose success for vardenafil 10 mg was stratified according to specific comorbidities. First-dose SEP-2 and SEP-3 success rates were: 84% and 66% for men with hypertension ($n = 191$), 84% and 72% for men with dyslipidaemia ($n = 116$), and 75% and 58% for men with diabetes mellitus ($n = 95$). When the groups were analysed with their specific comorbidities excluded the first-dose SEP-2 and SEP-3 success rates were: 88% and 77% for men without hypertension ($n = 409$), 87% and 74% for men without dyslipidaemia ($n = 484$), and 89% and 77% for men without diabetes mellitus ($n = 505$). Vardenafil 10 mg was effective in treating ED patients with or without associated comorbidities (Table 3).

At the end of 12 weeks of treatment, patients receiving vardenafil had statistically ($p < 0.001$) and clinically superior reliability of insertion (83%) compared with patients receiving placebo (56%). The increase in reliability was seen within the first 4 weeks of treatment. Subsequent SEP-3 reliability rates were 77% with vardenafil 10 mg and 42% with placebo ($p < 0.001$).

Patients treated with vardenafil had a statistically and clinically significant superiority in the IIEF-EF domain score compared with placebo at each visit ($p < 0.001$). The increase in IIEF-EF domain score in placebo-treated patients between baseline and week 12 was not clinically significant. A significantly larger proportion of patients with an IIEF-EF domain score within the normal range (≥ 26) was observed in the vardenafil group compared with the placebo group at each visit (Table 4; $p < 0.001$).

Safety

Vardenafil was well tolerated with the majority of AEs mild to moderate in intensity. Headache and flushing were the most frequently reported AEs with each reported in approximately 5% of vardenafil-treated patients. An additional 60 patients (10.1%) reported at least one AE during the 1-week challenge period. AEs occurring with an incidence $\geq 2\%$ in either treatment group are presented in Table 5. A total of 112 patients (21.4%), 40 (15.2%) in the placebo group and 72 (27.7%) in the vardenafil group reported at least one treatment-emergent AE.

DISCUSSION

The objective of the RELY-I study was to evaluate the reliability, efficacy, safety and tolerability of vardenafil 10 mg in men with ED who reported a first-dose success of vaginal

Table 1 Baseline data showing patient characteristics, ED severity and comorbidities in the ITT population

Demographic characteristic	*Placebo (n = 254)*	*Vardenafil (n = 255)*	*Total (n = 509)*
Age (years)			
Mean (SD)	54.5 (11.1)	53.2 (10.9)	53.8 (11.0)
Range	23–79	20–27	20–79
Race, *n* (%)			
Caucasian	194 (76)	198 (78)	392 (77)
Asian	34 (13)	31 (12)	65 (13)
Black	11 (4)	15 (6)	26 (5)
Hispanic	13 (5)	10 (4)	23 (5)
Other	2 (< 1)	1 (< 1)	3 (< 1)
Weight (kg)			
Mean (SD)	82.3 (14.4)	84.3 (15.6)	83.3 (15.1)
Range	53–129	55–140	53–140
Body mass index (kg/m^2)			
Mean (SD)	26.9 (3.9)	27.4 (4.4)	27.1 (4.1)
Range	18–42	18–48	18–48
Height (cm)			
Mean (SD)	174.7 (7.6)	175.3 (7.9)	175.0 (7.7)
Range	140–196	154–210	140–210
Alcohol use, *n* (%)			
Abstinent	83 (33)	88 (35)	171 (34)
Light	129 (51)	123 (48)	252 (50)
Moderate	42 (17)	42 (16)	84 (17)
Heavy	0	2 (< 1)	2 (< 1)
Smoking status, *n* (%)			
Smoker	128 (50)	131 (51)	259 (51)
Non-smoker	125 (49)	122 (48)	247 (49)
Passive smoker	1 (< 1)	2 (< 1)	3 (< 1)
Aetiology, *n* (%)			
Organic	113 (44)	106 (42)	219 (43)
Psychogenic	38 (15)	44 (17)	82 (16)
Mixed	103 (41)	105 (41)	208 (41)
Time since ED diagnosis (years)			
Mean (SD)	3.3 (3.8)	3.4 (3.4)	3.3 (3.6)
Range	0–26	0–20	0–26
Time since ED first noticed (years)			
Mean (SD)	5.5 (5.4)	5.8 (5.0)	5.6 (5.2)
Range	1–41	1–29	1–41
ED severity, *n* (%)			
No attempt (≤5)	3 (1)	3 (1)	6 (1)
Severe (6–10)	59 (23)	62 (24)	121 (24)
Moderate (11–16)	96 (38)	89 (35)	185 (36)
Mild-Moderate (17–21)	76 (30)	82 (32)	158 (31)
Mild (22–25)	19 (7)	18 (7)	37 (7)
No ED/normal (> 25)	1 (< 1)	1 (< 1)	2 (< 1)
Baseline IIEF-EF domain score			
Mean (SD)	14.5 (5.0)	14.7 (5.0)	14.6 (5.0)
Range	5–27	1–26	1–27
Comorbidities, *n* (%)			
Hypertension	87 (34)	68 (27)	155 (30)
Diabetes mellitus*	37 (15)	35 (14)	72 (14)
Benign prostatic hyperplasia	36 (14)	33 (13)	69 (14)
Dyslipidaemia†	33 (13)	49 (19)	82 (16)
Back pain	13 (5)	12 (5)	25 (5)
Any concomitant medication, *n* (%)	155 (61)	154 (60)	309 (61)

Table 1 (contd)

Demographic characteristic	*Placebo (n = 254)*	*Vardenafil (n = 255)*	*Total (n = 509)*
Antihypertensive medication			
Amlodipine	10 (4)	8 (3)	18 (4)
Hydrochlorothiazide	5 (2)	6 (2)	11 (2)
Lisinopril	4 (2)	5 (2)	9 (2)
Enalapril	1 (< 1)	6 (2)	7 (1)
Dyslipidaemia medication			
Lipitor	15 (6)	18 (7)	33 (6)
Simvastatin	5 (2)	10 (4)	15 (3)
Atorvastatin calcium	4 (2)	3 (1)	7 (1)
Diabetes medication			
Metformin	7 (3)	5 (2)	12 (2)
Metformin hydrochloride	5 (2)	5 (2)	10 (2)
Amaryl	4 (2)	3 (1)	7 (1)
Pioglitazone	4 (2)	3 (1)	7 (1)

ITT, intent-to-treat; SD, standard deviation; ED, erectile dysfunction; IIEF-EF, International Index of Erectile Function-Erectile Function; PDE5, phosphodiesterase type 5. *Diabetes mellitus includes both insulin dependent and non-dependent. †Dyslipidaemia includes dyslipidaemia, hyperlipidaemia and hypercholesterolaemia.

Table 2 Prior PDE5 inhibitor use at screening

	Vardenafil (n = 255)	*Placebo (n = 254)*	*Total (n = 509)*
Used sildenafil	255	254	509
Yes	166 (65)	171 (67)	337 (66)
No	89 (35)	83 (33)	172 (34)
Sildenafil stopped due to insufficient effect	165	170	335
Yes	30 (18)	23 (14)	53 (16)
No	135 (82)	147 (86)	282 (84)
Sildenafil stopped due to side effects	165	170	335
Yes	19 (12)	15 (9)	34 (10)
No	146 (88)	155 (91)	301 (90)
Used tadalafil	255	254	509
Yes	57 (22)	47 (19)	104 (20)
No	198 (78)	207 (81)	405 (80)
Tadalafil stopped due to insufficient effect	57	46	103
Yes	6 (11)	7 (15)	13 (13)
No	51 (89)	39 (85)	90 (87)
Tadalafil stopped due to side effects	57	46	103
Yes	2 (4)	1 (2)	3 (3)
No	55 (96)	45 (98)	100 (97)

Values are expressed as *n* (%).

penetration. Based on a review of published literature, this placebo-controlled trial is the first non-retrospective study to evaluate first-dose success and reliability of a PDE5 inhibitor on key erectile function parameters.

Results from this study showed that vardenafil 10 mg was highly successful as first-dose therapy for patients with ED. First-dose success and reliability are important for patient confidence and treatment compliance. It is accepted knowledge that men with ED may be reluctant to seek medical attention due largely to the embarrassment of bringing up the topic (23). However, once patients are willing to seek medical attention, it is important that they are given a drug that is effective from the first time it is used and continues to be effective each and every time thereafter. The presence of comorbid conditions, such as diabetes mellitus, hypertension or other cardiovascular conditions, in men with ED serves to further aggravate the disease and can complicate its management (4–6).

Open-label results from this study showed that of the men who took the recommended starting dose of vardenafil for the first time, 87% achieved successful vaginal penetration (SEP-2). Irrespective of the high prevalence of comorbidities in the men in the challenge phase, first-time success for vardenafil 10 mg dose was achieved in men both with and without comorbidities. The overall first-dose success rates for SEP-2 and SEP-3 with vardenafil 10 mg in the subgroup of patients with comorbidities in this study are consistent with those seen in previous vardenafil studies (21,24–26). Additionally, when taking variables such as comorbidities and ED severity into consideration, the first-time successful intercourse and reliability rates with vardenafil were similar to data reported with sildenafil and tadalafil in *post hoc* analyses of data collected from randomised, double-blind, placebo-controlled trials (27,28).

It is important to note that vardenafil was effective across all efficacy measures evaluated regardless of race, age, weight or ED aetiology. Of those men who entered the challenge phase, 74% achieved initial intercourse completion (SEP-3). In addition, the reliability of maintenance in those patients with first-time success with both SEP-2 and SEP-3 was clinically and statistically significantly superior to placebo over

Table 3 First-dose success rates for SEP-2 and SEP-3, stratified according to the presence or absence of a specific comorbidity

*Comorbidity subgroup**			*Subgroup without specific comorbidity**		
	SEP-2 (%)	*SEP-3 (%)*		*SEP-2 (%)*	*SEP-3 (%)*
Hypertension ($n = 191$)	84	66	No hypertension ($n = 409$)	88	77
Dyslipidaemia ($n = 116$)	84	72	No dyslipidaemia ($n = 484$)	87	74
Diabetes mellitus ($n = 95$)	75	58	No diabetes mellitus ($n = 505$)	89	77

SEP-2, Sexual Encounter Profile Question-2; SEP-3, Sexual Encounter Profile Question-3. *Presence or absence of a specific comorbidity did not preclude patients from having other associated comorbidities.

Table 4 IIEF-EF domain score data (actual values and return to normal rates)

	Vardenafil 10 mg	*Placebo*
IIEF-EF domain scores (LS mean)		
Baseline	14.76	14.53
LOCF	23.46*	15.81
IIEF-EF return to normal rates with vardenafil 10 mg vs. placebo		
Week 4	47%	15%
Week 8	52%	18%
Week 12	50%	16%
LOCF	50%	15%

IIEF-EF, International Index of Erectile Function-Erectile Function; LS, least squared; LOCF, last observation carried forward. $p < 0.001$ vs. placebo at every visit. *$p < 0.001$ vs. placebo.

Table 5 Number of patients with most frequent adverse events (≥2%) reported during the double-blind treatment phase

Adverse event	*Placebo ($n = 263$)*	*Vardenafil ($n = 260$)*
Headache	5 (1.9)	13 (5.0)
Flushing	2 (0.8)	14 (5.4)
Dyspepsia	1 (0.4)	6 (2.3)

Values are expressed as *n* (%).

the 12 weeks of treatment ($p < 0.001$) (22). This clinically and statistically significant superiority with respect to the reliability of vardenafil was seen as early as the 0- to 4-week time point, and continued at each of the time intervals investigated over the 12-week treatment period. The consistent improvement in erectile function parameters for up to 12 weeks is consistent with earlier vardenafil studies (18). The lack of investigator and patient blinding during the open-label challenge phase needs to be considered when reviewing the study results. Additionally, the open-label administration of vardenafil during the single-dose challenge phase of the study may have had an impact on any positive efficacy effects on patients in the placebo treatment group. Efficacy data reported in this study were not stratified according to pre-study use of PDE5 inhibitor therapy, although clearly a majority of patients in this study were not PDE5-inhibitor naïve. Vardenafil 10 mg was generally well tolerated in patients with and without comorbidities. The AEs reported during the study are consistent with those seen with PDE5 inhibitors (22).

CONCLUSIONS

Throughout the open-label, challenge phase and the subsequent 12-week double-blind treatment period, vardenafil 10 mg provided a high rate of first-dose SEP-2 success (87%) followed by subsequent success over time when compared with placebo. First-dose success was similar for ED patients with and without specific comorbidities, showing the high level of effectiveness of vardenafil in this patient population. Vardenafil was well tolerated over the 12 weeks of treatment in men with a first-dose response. These results have important clinical implications. Men with ED are more likely to have confidence in a drug that demonstrates first-dose and continued subsequent success, and leads to overall improved clinical outcomes.

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CONFLICTS OF INTEREST

Drs Valiquette and Montorsi are investigators for, and are on, the speaker's bureau of GlaxoSmithKline and Bayer. Dr Auerbach has worked as a clinical investigator and consultant to GlaxoSmithKline.

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