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REVIEW

Vardenafil for the treatment of erectile dysfunction: an overview of the clinical evidence

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Abstract: Many men with erectile dysfunction (ED) also have associated underlying cardiovascular and metabolic conditions, for which they are likely to be taking medication. Therefore, cardiovascular safety and potential drug interactions are two of the major concerns when using PDE-5 inhibitors in these patients. The PDE-5 inhibitor, vardenafil, is characterized by a rapid onset of action, increased duration of erection, high rates of first-dose success and reliable efficacy that can be maintained with continued use. In both clinical trials and real-life observational studies, vardenafil has demonstrated a favorable efficacy and safety profile in men with ED, including those with associated underlying conditions such as diabetes, hypertension and dyslipidemia. Importantly, the concomitant use of medication for these conditions is not associated with any noteworthy changes in the efficacy and safety of vardenafil. The evidence presented in this review supports the use of vardenafil as a first-line treatment for men with ED, including those with underlying conditions.

Keywords: vardenafil, erectile dysfunction, efficacy, safety, underlying conditions

Introduction

Erectile dysfunction (ED) is a common condition affecting an estimated 150 million men worldwide.[1,2] ED is frequently associated with loss of self esteem and can impact significantly on the quality of life and well being of both members of a couple.[3–6] Organic ED and cardiovascular disease share the same risk factors, including diabetes, hypertension, dyslipidemia, obesity and smoking.[7,8] These two conditions also share the same pathophysiology, with endothelial dysfunction, inflammatory and endothelial-prothrombotic activation, and oxidative stress being their common denominators.[9,10] It is increasingly being recognized by researchers that ED may be considered a predictor for the development of cardiovascular disease.[11–13] Biennial screening of a random sample of community-dwelling men (n = 1402) over a 10-year period revealed that the presence of ED was associated with an approximately 80% higher risk of subsequent coronary artery disease (CAD).[14] A study conducted in men with type 2 diabetes who had silent CAD (n = 291) found that patients who experienced major adverse cardiac events over a follow-up period of approximately 4 years were significantly more likely to have ED than those who did not (61% vs 36%, respectively; $P < 0.001$).[15] There is evidence that in patients with established CAD, ED symptoms appeared an average of 2 to 5 years earlier than those of CAD itself.[16,17] A diagnosis of ED therefore provides a golden opportunity for clinicians to assess men's cardiovascular health, and intervene at an early stage in the disease pathway.

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The introduction in the late 1990s of highly effective oral pharmacotherapies for ED transformed ED management and led to an increase in the number of men seeking treatment.[18] Nevertheless, the rate of ED sufferers seeking medical help is still low,[19,20] despite the dramatic impact on overall quality of life and the potential as an indicator for cardiovascular prevention. Current guidelines recommend the phosphodiesterase type 5 (PDE-5) inhibitors, vardenafil, sildenafil and tadalafil, as first-line therapy for ED of varying etiologies and severity.[21,22] Vardenafil is a selective PDE-5 inhibitor, with a profile characterized by rapid onset of action, increased duration of erection, high rates of first-dose success and reliable efficacy that can be maintained with continued use.[23–31]

This review examines the epidemiology of ED, in particular, in men with associated underlying conditions, and evaluates the evidence compiled on the clinical efficacy and safety of vardenafil.

Epidemiological evidence demonstrating the association between ED and underlying conditions

Large-scale epidemiological studies have found the prevalence of ED in the general population of men aged 18 to 64 years to be 10% to 16%.[20,32] The prevalence and severity of ED increases with age.[18,33–35] In the Epidemiologia de la Disfuncion Erectil Masculina (EDEM) study, ED prevalence rates were 3.9% in the 25- to 39-year age group, rising to 32.3% in those men aged 50 to 70 years.[34] The Massachusetts Male Aging Study (MMAS) found that between the age of 40 and 70 years, the probability of having complete ED increased 3-fold from 5% to 15%, with a corresponding 2-fold increase from 17% to 34% in the probability of having moderate ED.[18]

Numerous studies have explored the close association between ED and cardiovascular disease. Evidence shows that cardiovascular risk factors (CRFs) are present in the majority of men with ED, while men with ED are more likely to have CRFs than those with no ED.[20,36,37] A high prevalence of ED has been reported in patients with CAD, with rates ranging from 44% to 75%.[38,39] In men with diabetes, ED prevalence rates can vary between 35% and 90%.[40–42] A prospective cohort study of men over 50 years of age (n = 31,027) found the prevalence of ED in men with diabetes to be almost double that in men without diabetes (46% vs 24%, respectively). ED in men with diabetes is also frequently more severe, compared with the general ED population.[43]

Research has demonstrated a considerable difference in hypertension prevalence rates between patients with and without ED (41% vs 19%, respectively).[37] A correlation has also been observed between increasing hypertension prevalence and increased ED severity.[44] Studies have documented the association between ED and serum lipid levels. An analysis of a nationally representative managed care claims database in the United States found the prevalence rate of hyperlipidemia to be 42% among men with ED.[45] In a study of 215 men with ED and 100 men without ED, the prevalence of hypercholesterolemia (total cholesterol >200 mg/dL or 5.17 mmol/L) was 71% vs 52%, respectively ($P = 0.06$). Both high-density lipoprotein (HDL) cholesterol and total cholesterol/HDL cholesterol ratios were shown to be significant predictors of ED ($P = 0.011$ and $P < 0.0001$, respectively).[46]

The Massachusetts Male Aging Study, a community-based, random sample of men aged 40 to 70 years, found an inverse correlation between age-adjusted probability of ED and levels of HDL cholesterol.[18] In men aged 40 to 55 years, the age-adjusted probability of having moderate ED increased from 7% to 25% with a decrease in HDL cholesterol levels from 90 mg/dL (2.3 mmol/L) to 30 mg/dL (0.9 mmol/L). Similarly, other studies have found correlations between ED and both decreased HDL cholesterol and elevated total cholesterol/HDL cholesterol ratio.[47,48]

The cluster of cardiovascular and metabolic risk factors that are often described as the "metabolic syndrome" include increased abdominal obesity, elevated triglycerides, reduced HDL cholesterol, hypertension, increased fasting plasma glucose and hyperinsulinemia.[49–52] There is a close association between metabolic syndrome, and both ED and hypogonadism.[53,54] In a study of 1086 men with ED, the prevalence of metabolic syndrome was 32% using the National Cholesterol Education Program-Third Adult Treatment Panel (NCEP-ATP III) definition, and 45% using the International Diabetes Federation definition.[50]

Testosterone regulates the formation of cyclic guanosine monophosphate (cGMP), through its effect on nitric oxide synthase expression, and on cGMP catabolism, through its effect on PDE-5 isoenzyme expression. Hypogonadism is believed to play a major role in the pathophysiology of ED, with a minimum threshold testosterone level required for normal erectile function.[55] Prevalence rates of hypogonadism in men with ED range from 2% to 35%.[56,57] The close association between testosterone deficiency, ED and underlying conditions may contribute to a decline in men's overall health, if left untreated.[52]

Efficacy of vardenafil in men with ED

Clinical efficacy

Diabetes

The trend towards the onset of diabetes at a younger age within the general population, combined with a higher prevalence of childhood type 2 diabetes, is expected to lead to an increase in men developing diabetes-related ED.[58] Management of ED in patients with diabetes can be challenging, since ED is often more severe and resistant to long-term treatment in this patient group.[43,59] Furthermore, worsening glycemic control is associated with greater impairment of erectile function.[60]

Favorable efficacy of vardenafil in men with diabetes has been demonstrated in a number of clinical trials. A double-blind, placebo-controlled trial in men with type 1 or type 2 diabetes (n = 452) demonstrated significant improvements in the erectile function domain of the International Index of Erectile Function (IIEF-EF) scores and Sexual Encounter Profile question 2 (SEP2: "Were you able to insert your penis into your partner's vagina?") and 3 (SEP3: "Did your erection last long enough for you to have successful intercourse?") success rates following 12 weeks of treatment with 10 mg or 20 mg vardenafil compared with placebo (all $P < 0.0001$). After 12 weeks, changes from baseline in IIEF-EF scores were 5.9 and 7.8 for 10 mg and 20 mg vardenafil, respectively, compared with 1.4 for placebo ($P < 0.0001$).[61] No relationship between response to vardenafil and level of glycemic control (defined as level of glycosylated hemoglobin [HbA_{1c}]) was observed. For men with ED and good-to-moderate ($HbA_{1c} > 6$ but $< 8\%$; n = 64) or poor ($HbA_{1c} \geq 8\%$; n = 71) glycemic control, SEP3 success rates were 50% and 54%, respectively, in those taking 20 mg vardenafil, compared with 20% (n = 56) and 23% (n = 77) for placebo-treated men. SEP3 responses were significantly superior to placebo for both 10 mg and 20 mg vardenafil in all glycemic control subgroups.

Similar findings were reported in a randomized, double-blind, placebo-controlled trial in Japan in men with diabetes (defined as levels of $HbA_{1c} > 6.5\%$ or receiving hypoglycemic drug treatment).[62] IIEF-EF scores improved significantly from 13.6 and 13.9 at baseline to 21.8 and 22.9 at last observation carried forward (LOCF) in the 10 mg and 20 mg vardenafil groups, respectively, compared with an increase from 13.7 to 16.3 for placebo ($P < 0.0001$).

Hypertension

The number of patients with hypertension has risen considerably in recent years.[63] Accordingly, given the close association between ED and hypertension, the need to determine the efficacy and safety of PDE-5 inhibitors for ED therapy in this patient group has assumed greater importance. A 12-week, multicenter, randomized, double-blind, placebo-controlled trial conducted in Germany investigated the efficacy of flexible-dose vardenafil in men with ED and arterial hypertension, which was adequately controlled with at least one antihypertensive medication.[64] Compared with placebo, vardenafil significantly improved SEP2 and SEP3 success rates over the study period ($P < 0.0001$). In vardenafil-treated patients, average SEP2 success rates increased from 50% at baseline to 84% at week 12, compared with a corresponding increase from 49% to 59% in the placebo group. SEP3 rates increased from 18% at baseline to 68% at week 12 in the vardenafil group, compared with an increase from 18% to 35% for placebo. Improved erections (measured by the Global Assessment Question: "Has the treatment you have taken over the past 4 weeks improved your erections?") were reported by 80% of patients receiving vardenafil versus 40% of those on placebo.

Shabsigh et al conducted a meta-analysis of 8 randomized, double-blind, placebo-controlled, flexible-dose trials of vardenafil in men with ED (n = 2427), where 839 patients (35%) had self-reported hypertension.[44] After 12 weeks of vardenafil treatment, statistically significant and clinically meaningful improvements were observed in all primary outcome measures (IIEF-EF, SEP2, SEP3), compared with placebo. IIEF-EF scores increased by an average of 8.9 points, while SEP2 and SEP3 success rates increased by an average of 32.4% and 38.0%, respectively. A comparison of men with and without hypertension showed no significant differences in any of the three outcome measures, suggesting that vardenafil is equally efficacious for the treatment of ED in both patient groups.

Dyslipidemia

Dyslipidemia is believed to be a causal factor in the endothelial damage thought to underlie many cases of organic ED.[59] It has been demonstrated that statin therapy to correct lipid levels improves penile rigidity in men with ED and hypercholesterolemia.[65] There are few studies evaluating the efficacy of PDE-5 inhibitors in men with ED and dyslipidemia. A 12-week, double-blind, placebo-controlled study investigated the efficacy of flexible-dose vardenafil in men with ED and dyslipidemia on stable statin therapy.[28] In addition to dyslipidemia, 61% of subjects had hypertension and 40% had diabetes. Vardenafil treatment was associated with significant

improvements in IIEF-EF scores and SEP2 and SEP3 success rates compared with placebo ($P < 0.001$). After 12 weeks of treatment, least squares (LS) mean IIEF-EF scores using LOCF were 22.0 vs 14.8 for vardenafil vs placebo, while LS adjusted mean success rates for vardenafil vs placebo were: SEP2, 79.1% vs 51.9% and SEP3, 66.7% vs 33.8%.

Efficacy of vardenafil in patients with ED taking concomitant medications

A recent pooled analysis was conducted on individual patient data from 13 randomized, double-blind, placebo-controlled trials of flexible-dose vardenafil of at least 12 weeks' duration.[66] Primary efficacy measures were the IIEF-EF, SEP2 and SEP3. Efficacy was assessed in subgroups of patients with ED and co-existing diabetes, hypertension and dyslipidemia according to type of concomitant medication taken. Consistent with the findings of earlier studies, the concomitant use of medications was not associated with any noteworthy changes in the efficacy of vardenafil. Across all subgroups, vardenafil was statistically superior to placebo over 12 weeks of treatment ($P < 0.0001$) (Figures 1 to 6). Further, vardenafil treatment resulted in a significant improvement from baseline in IIEF-EF scores and SEP2 and SEP3 success rates, irrespective of the type of medication used ($P < 0.0001$) (Figures 1 to 6).

Efficacy of vardenafil in aging men

Vardenafil improves erectile function in men with ED, including patients over the age of 65 years, the age group in which ED is most prevalent.[67] A 12-week multicenter, randomized, double-blind, placebo-controlled, at-home study of vardenafil 5, 10 and 20 mg was conducted in men (n = 580) with mild to severe ED. In a subgroup analysis in which patients were split into 4 age groups (<45 years, 45 to 55 years, 56 to 65 years and >65 years), mean IIEF-EF scores across all age groups were significantly greater for vardenafil-treated patients than those treated with placebo ($P < 0.001$). No significant differences in the efficacy of vardenafil were observed between age groups.

Duration of erection: a new clinical efficacy measure for vardenafil

Improving penile hardness in men with ED is commonly believed to be the most important factor contributing to successful sexual intercourse. However, there is a body of evidence suggesting that duration of erection, and hence duration of intercourse, may play a role in achieving a satisfactory sexual experience for the man and his partner.[68,69]

Recent clinical data have demonstrated that vardenafil significantly improves duration of erection in men with ED, including those with underlying conditions. In these studies, a novel efficacy parameter, stopwatch-assessed duration of erection, was employed. A randomized, multicenter, double-blind, placebo-controlled crossover study of fixed-dose vardenafil was conducted in a broad population of men with ED, which included patients with diabetes, hypertension, hyperlipidemia and hypercholesterolemia.[29]

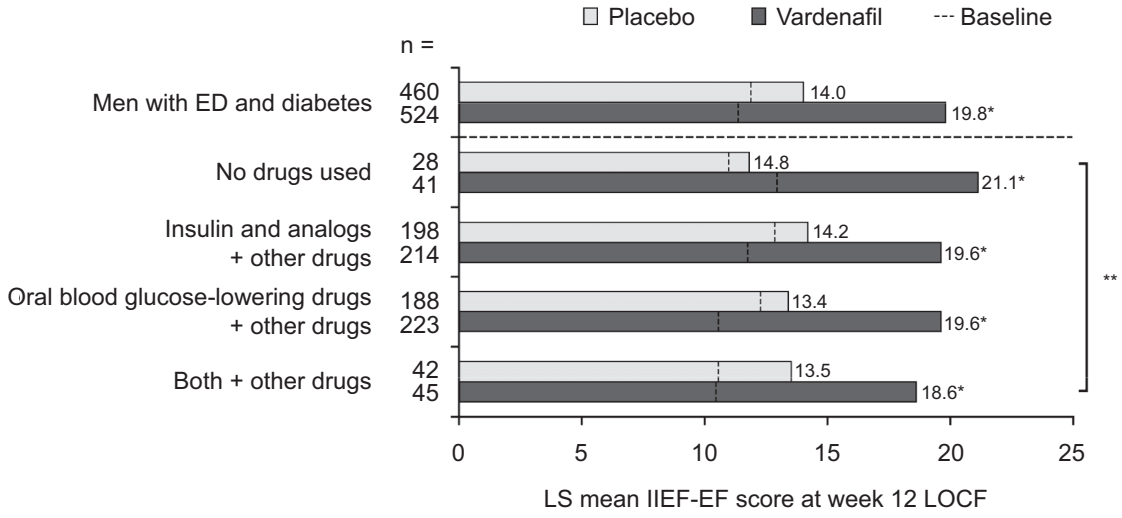

Figure 1 LS mean IIEF-EF scores in patients with ED and diabetes, stratified by type of antidiabetic medication, at baseline and following 12 weeks of treatment with vardenafil or placebo. Reproduced with permission from Eardley I, Lee Jay C, Shabsigh R, et al. Vardenafil improves erectile function in men with erectile dysfunction and associated underlying conditions, irrespective of the use of concomitant medications. *J Sex Med*. 2009.[66] In press. Copyright © 2009 Wiley-Blackwell.
*$P < 0.0001$ for vardenafil vs placebo, **$P = 0.1972$ for comparison of antidiabetic medication subgroups.
Abbreviations: ED, erectile dysfunction; IIEF-EF, erectile function domain of the International Index of Erectile Function; LOCF, last observation carried forward; LS, least squares.

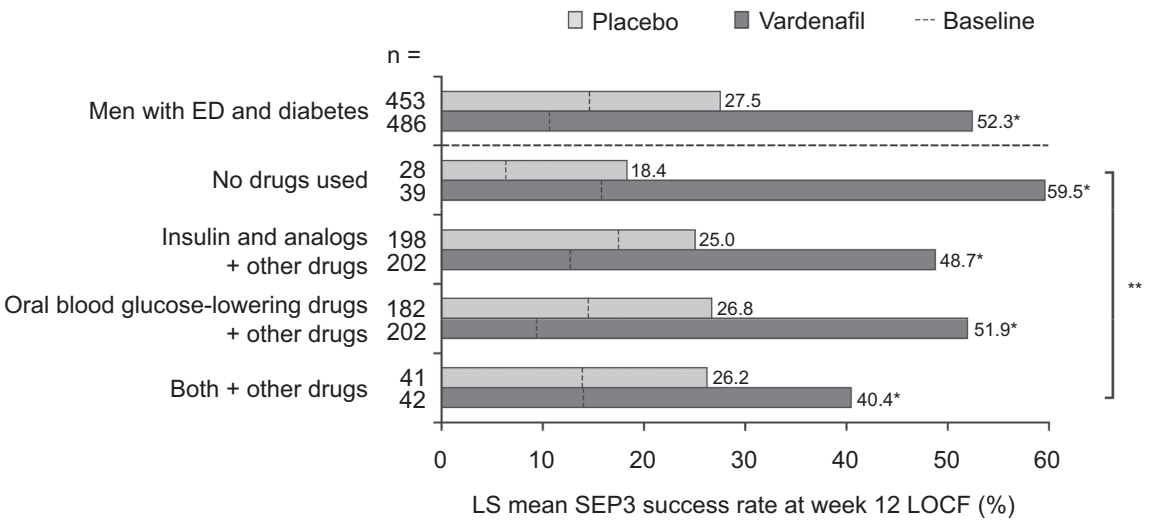

Figure 2 LS mean SEP3 success rates in patients with ED and diabetes, stratified by type of antidiabetic medication, at baseline and following 12 weeks of treatment with vardenafil or placebo. Reproduced with permission from Eardley I, Lee Jay C, Shabsigh R, et al. Vardenafil improves erectile function in men with erectile dysfunction and associated underlying conditions, irrespective of the use of concomitant medications. *J Sex Med*. 2009.[66] In press. Copyright © 2009 Wiley-Blackwell.
*$P < 0.0001$ for vardenafil vs placebo, **$P = 0.0986$ for comparison of antidiabetic medication subgroups.
Abbreviations: ED, erectile dysfunction; LOCF, last observation carried forward; LS, least squares; SEP, sexual encounter profile question.

Over 4 weeks of treatment, vardenafil produced a ~2.3-fold longer duration of erection than placebo ($P < 0.001$). Vardenafil also demonstrated a statistically significant superiority over placebo in IIEF-EF scores and SEP2 and SEP3 success rates (all $P < 0.001$). Duration of erection was also a secondary outcome measure in the study of vardenafil in men with ED and dyslipidemia on stable statin therapy discussed earlier.[28] In this study, vardenafil treatment was associated with a ~3.0-fold longer duration of erection, compared with placebo ($P < 0.001$).

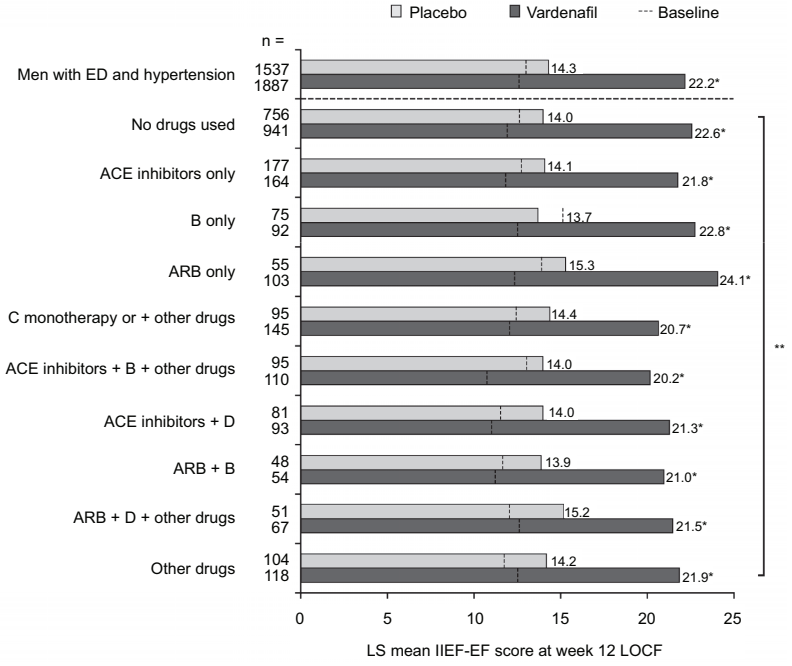

Figure 3 LS mean IIEF-EF scores in patients with ED and hypertension, stratified by type of antihypertensive medication, at baseline and following 12 weeks of treatment with vardenafil or placebo. Reproduced with permission from Eardley I, Lee Jay C, Shabsigh R, et al. Vardenafil improves erectile function in men with erectile dysfunction and associated underlying conditions, irrespective of the use of concomitant medications. *J Sex Med*. 2009.[66] In press. Copyright © 2009 Wiley-Blackwell.
*$P < 0.0001$ for vardenafil vs placebo, **$P = 0.1651$ for comparison of antihypertensive medication subgroups.
Abbreviations: ACE, angiotensin-converting enzyme; ARB, angiotensin II receptor antagonists; B, beta blockers; C, calcium channel antagonists; D, thiazide or thiazide-like diuretics; ED, erectile dysfunction; IIEF-EF, erectile function domain of the International Index of Erectile Function; LOCF, last observation carried forward; LS, least squares.

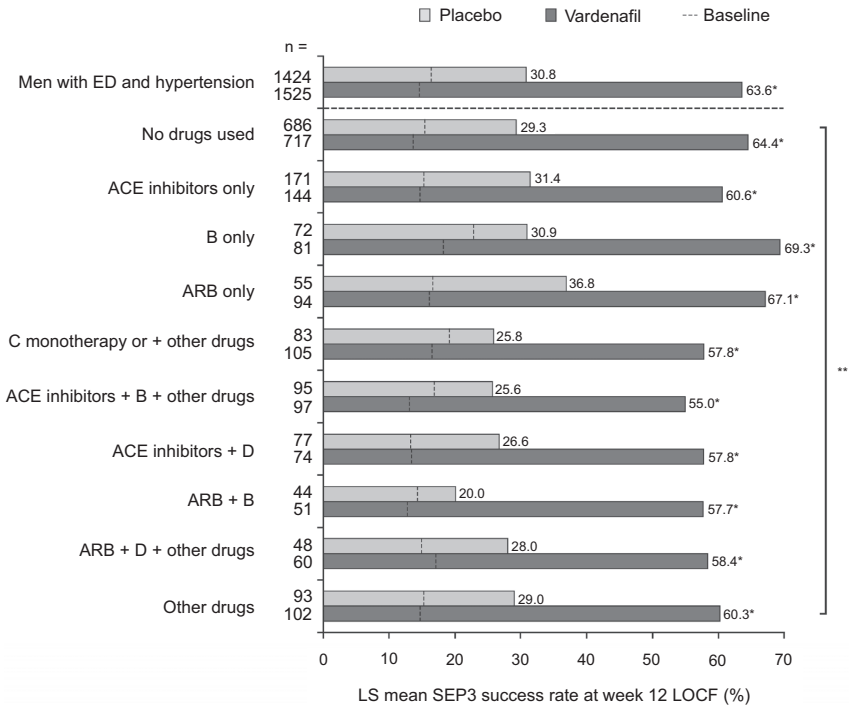

Figure 4 LS mean SEP3 success rates in patients with ED and hypertension, stratified by type of antihypertensive medication, at baseline and following 12 weeks of treatment with vardenafil or placebo. Reproduced with permission from Eardley I, Lee Jay C, Shabsigh R, et al. Vardenafil improves erectile function in men with erectile dysfunction and associated underlying conditions, irrespective of the use of concomitant medications. *J Sex Med*. 2009.[66] In press. Copyright © 2009 Wiley-Blackwell.
*$P < 0.0001$ for vardenafil vs placebo, **$P = 0.7957$ for comparison of antihypertensive medication subgroups.
Abbreviations: ACE, angiotensin-converting enzyme; ARB, angiotensin II receptor antagonists; B, beta blockers; C, calcium channel antagonists; D, thiazide or thiazide-like diuretics; ED, erectile dysfunction; LOCF, last observation carried forward; LS, least squares; SEP, sexual encounter profile question.

Efficacy of vardenafil in a real-life observational study

Numerous controlled clinical trials have demonstrated the efficacy of vardenafil in men with ED, including those with associated underlying conditions. These findings were also confirmed in a large observational, open-label study of vardenafil involving over 100,000 participants worldwide.[70,71] The Real-Life Safety and Efficacy of vardenafil (REALISE) study recruited patients presenting to their physician with ED and involved a follow-up period of

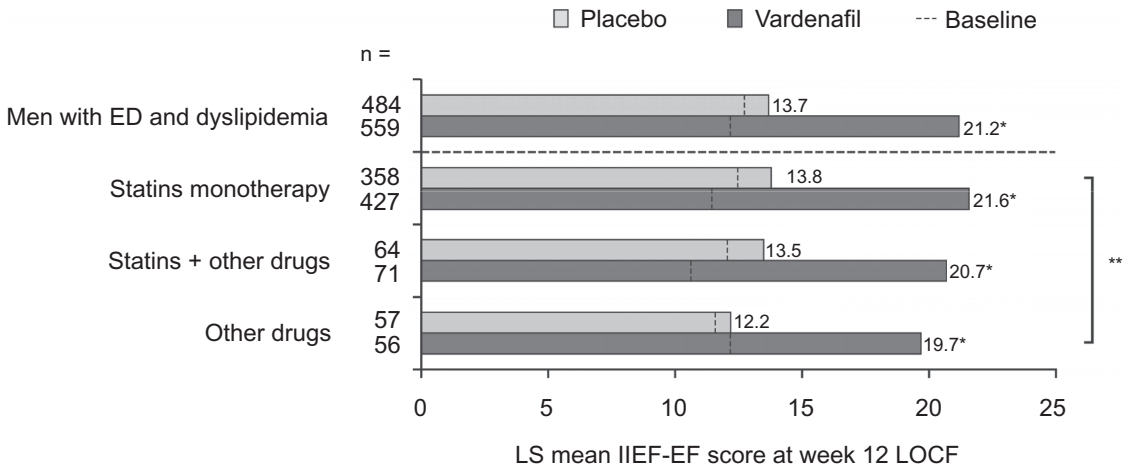

Figure 5 LS mean IIEF-EF scores in patients with ED and dyslipidemia, stratified by type of lipid-lowering medication, at baseline and following 12 weeks of treatment with vardenafil or placebo. Reproduced with permission from Eardley I, Lee Jay C, Shabsigh R, et al. Vardenafil improves erectile function in men with erectile dysfunction and associated underlying conditions, irrespective of the use of concomitant medications. *J Sex Med*. 2009.[66] In press. Copyright © 2009 Wiley-Blackwell.
*$P < 0.0001$ for vardenafil vs placebo, **$P = 0.9169$ for comparison of lipid-lowering medication subgroups.
Abbreviations: ED, erectile dysfunction; IIEF-EF, erectile function domain of the International Index of Erectile Function; LOCF, last observation carried forward; LS, least squares.

2 months. An initially prescribed dose of vardenafil could be titrated within the observation period, according to physician recommendation and labeling instructions. Most patients were prescribed vardenafil 10 mg as a starting dose. Treatment outcome was assessed by physician interview; in addition, a voluntary patient questionnaire was used to assess each attempt at sexual intercourse. Although data from REALISE are uncontrolled, they represent real-world experiences with vardenafil, in contrast to rigidly controlled clinical trials.

A pooled analysis of REALISE data from 47 countries in Europe, Asia-Pacific, Latin America and the rest of the world (excluding the United States) has recently been performed (van Ahlen et al in preparation). Data were stratified by the presence of diabetes, hypertension or lipid metabolism disorder. In all subgroups, high numbers of patients reported improvements in erectile function (diabetes, 92.6%; hypertension, 93.6%; lipid metabolism disorder, 94.7%). A large proportion of patients also reported being 'satisfied' or 'very satisfied' with the efficacy of vardenafil (hypertension 92.0%; diabetes 90.9%; lipid metabolism disorder 93.4%), and stated their intention to continue vardenafil use after the end of the study period.

Safety and tolerability of vardenafil in men with ED and underlying conditions

Interactions between food/alcohol and vardenafil

Vardenafil is rapidly absorbed after the administration of a single oral dose. Absorption is unaffected when taken in conjunction with a meal containing a moderate amount of fat; however, very high fat meals (ie, meals in which more than 57% of the calories come from fat) can affect the rate, but not the extent, of absorption.[72] The simultaneous administration of vardenafil and alcohol does not result in any clinically relevant pharmacokinetic or pharmacodynamic interactions.[73]

Adverse events

The side-effect profile of vardenafil is typical of PDE-5 inhibitors. Commonly reported adverse events in patients receiving vardenafil include headache, rhinitis, flushing and dyspepsia.[74,75] Most men with concomitant cardiovascular disease, including heart failure and stable arrhythmias, can be safely treated for ED with vardenafil or other PDE-5 inhibitors.[76] Eardley et al's previously described analysis,[66] conducted upon data from a large pool of patients with ED and underlying conditions, showed that the use of concomitant medications did not affect the safety or tolerability of vardenafil in patients with diabetes, hypertension or dyslipidemia. The number and type of the most frequent treatment-emergent adverse events were comparable with those of other studies of PDE-5 inhibitors in these patient groups.

Contraindications

Like other PDE-5 inhibitors, vardenafil is contraindicated in patients taking organic nitrates (eg, nitroglycerin, isosorbide mono- or dinitrate), nitrate preparations used to treat angina, amyl nitrate or amyl nitrite.[21,77] This is thought to be due to a stimulation of soluble guanylate cyclase by nitric oxide,

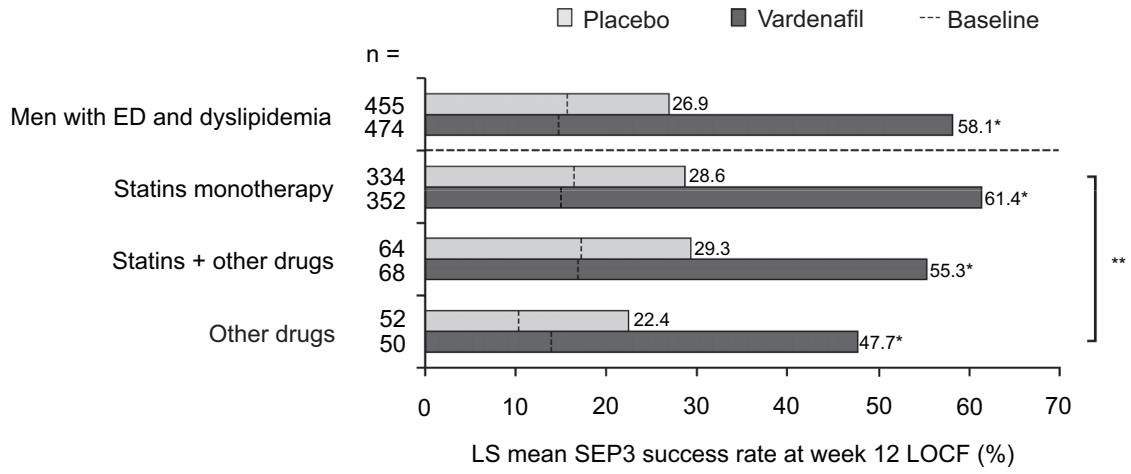

Figure 6 LS mean SEP3 success rates in patients with ED and dyslipidemia, stratified by type of lipid-lowering medication, at baseline and following 12 weeks of treatment with vardenafil or placebo. Reproduced with permission from Eardley I, Lee Jay C, Shabsigh R, et al. Vardenafil improves erectile function in men with erectile dysfunction and associated underlying conditions, irrespective of the use of concomitant medications. *J Sex Med*. 2009.[66] In press. Copyright © 2009 Wiley-Blackwell.
*$P < 0.0001$ for vardenafil vs placebo, **$P = 0.3536$ for comparison of lipid-lowering medication subgroups.
Abbreviations: ED, erectile dysfunction; LOCF, last observation carried forward; LS, least squares; SEP, sexual encounter profile question.

resulting in a large cGMP accumulation which in turn and through a cascade of events leads to smooth muscle relaxation, and thus to a decrease in blood pressure. In patients taking alpha blockers (for the treatment of hypertension and/or benign prostatic hyperplasia), vardenafil should be used with caution and patients' blood pressure carefully monitored. Caution is also recommended with the use of vardenafil in the presence of cytochrome P450, family 3, subfamily A (CYP3A) inhibitors, such as azole antifungal agents, antiretroviral protease inhibitors, macrolid antibiotics, or grapefruit juice.[78]

Expert opinion

The introduction onto the market of the first PDE-5 inhibitor more than a decade ago profoundly revolutionized medical perceptions of ED, and opened the way to oral pharmacological therapy for this condition. For a long time, experts had denied that there was an underlying organic cause of ED, and almost invariably, patients suffering from ED were referred for counselling to address psychological issues. Improvements in our knowledge and understanding of erectile function were triggered in the late 1980s, with the introduction of intracavernosal injections of vasoactive drugs, followed by therapy with oral agents to safely and effectively treat ED. Risk factors for ED and associated underlying conditions have now been identified, and it is widely accepted that a man presenting with ED in the physician's office warrants a thorough evaluation of his metabolic and cardiovascular status, in addition to a comprehensive psycho-social-sexual history.

PDE-5 inhibitors constitute the first-line treatment option for men affected by ED, to be combined with counseling on lifestyle, diet, exercise and weight control, if required. A major concern when using PDE-5 inhibitors in men presenting with ED and associated underlying conditions has been cardiovascular safety and potential drug interactions. Apart from the well established absolute contraindication of concomitant use with nitrates or nitric oxide donors, PDE-5 inhibitors have demonstrated excellent safety and efficacy profiles over time.

The data provided in this review demonstrate the efficacy, safety, effectiveness and satisfaction of vardenafil in two different sample populations: men presenting with ED and associated underlying conditions enrolled in clinical trials, and men presenting with ED without contraindications for vardenafil use, enrolled in a large observational study. Efficacy data are derived from clinical trials, effectiveness and satisfaction data are derived from real-life scenarios, and safety data are derived from all the studies reviewed. Physicians should be confident about safety when prescribing vardenafil to patients with ED and associated underlying conditions. Men with underlying conditions are more likely to suffer from ED, which is generally of greater severity. Taking into consideration overall efficacy, patients' responses to vardenafil treatment are significantly superior compared with placebo, regardless of underlying clinical condition or outcome measure/instrument used (ie, the conventional SEP2, SEP3 and IIEF parameters, or the newly proposed duration of erection measure). This response is also consistent with data obtained from real-life situations, where a high patient satisfaction rate was also demonstrated. Together, this evidence supports the use of vardenafil as a first-line efficacious treatment option for men presenting with ED and underlying conditions.

Conclusion

In light of the evidence that many men with ED also have associated underlying cardiovascular and metabolic conditions, it is important to evaluate the efficacy and safety of PDE-5 inhibitors for ED therapy in these patient groups. There is a significant body of evidence demonstrating the favorable efficacy and safety profile of vardenafil in men with ED and associated underlying conditions including diabetes, hypertension and dyslipidemia. Importantly, the concomitant use of medications, including antihypertensive agents, is not associated with any decreases in efficacy or safety.

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Author contributions

Drafting of the article: AMM, VM, JD, PC.

Revision of the intellectual content of the article: AMM, VM, JD, PC.

Final approval of the version for publication: AMM, VM, JD, PC.

Disclosures

All of the authors have acted as speakers, investigators and/or paid consultants for Bayer Schering Pharma.

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