Effectiveness of Tadalafil 5 mg Once Daily in the Treatment of Men with Lower Urinary Tract Symptoms Suggestive to Benign Prostatic Hyperplasia With or Without Erectile Dysfunction: Results from Naturalistic Observational TadaLutsEd Study

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ABSTRACT

Introduction. Naturalistic clinical trials provide data on the effectiveness of drugs in nonexperimental and everyday situations and are extremely helpful for decision-making purposes and for confirming experimental findings in clinical trials. No data have been published from naturalistic studies performed in patients with lower urinary tract symptoms suggestive of benign prostatic hyperplasia (LUTS/BPH) with or without erectile dysfunction (ED) and treated with phosphodiesterase type 5 inhibitors.

Aim. The aim of this study (TadaLutsEd Study) was to assess, in the context of medical practice, the effectiveness of tadalafil 5 mg once daily in patients with LUTS/BPH with or without erectile dysfunction.

Methods. The study was a 6-week uncontrolled, prospective, open-label, multicentric, observational study. The patient population involved sexually active males aged ≥50 years, diagnosed with LUTS/BPH with or without concomitant ED, and treated with tadalafil 5 mg daily in accordance with standard urological practice.

Main Outcome Measures. Effectiveness was assessed through the self-administered International Prostate Symptom Score (IPSS) questionnaire; quality of life was evaluated through the IPSS quality of life section (IPSS-QoL). The patients were also evaluated with the International Index of Erectile Function (IIEF-5). Adverse events were recorded. Statistical analyses using paired data samples was applied (Wilcoxon signed-ranks test).

Results. Sixty-two patients (mean age 62.2 years) completed the treatment, of whom 85.5% showed improvement in their urinary symptoms. Pre- and post-treatment differences in the IPSS, IPSS-QoL, and IIEF-5 scores were statistically significant at 4.4, 1, and 5.4 points, respectively (P < 0.0001). Tadalafil was well tolerated, and adverse events were mild, with a discontinuation rate of 1.6%.

Conclusion. According to study results, the use of tadalafil 5 mg once daily in a nonselected patient population with LUTS/BPH with or without ED led to improvements in terms of symptoms and quality of life and exhibited a safety profile similar to that obtained in controlled tadalafil clinical trials. Bechara A, Casabe A, Rodriguez Baigorri G, and Cobreros C. Effectiveness of tadalafil 5 mg once daily in the treatment of men with lower urinary tract symptoms suggestive to benign prostatic hyperplasia with or without erectile dysfunction: Results from naturalistic observational TadaLutsEd Study. J Sex Med 2014;11:498–505.

Key Words. Benign Prostatic Hyperplasia; Erectile Dysfunction; Lower Urinary Tract Symptoms; Phosphodiesterase 5 Inhibitor; Tadalafil; IIEF; IPSS
Introduction

Various epidemiological studies have revealed a high prevalence of lower urinary tract symptoms secondary to benign prostatic hyperplasia (LUTS/BPH) and their impact on the quality of life of patients [1–5]. Treatment approaches are aimed at improving symptoms and quality of life, stopping BPH progression, and avoiding BPH-related complications [6,7].

Drugs such as alpha blockers and 5-alpha reductase inhibitors have proven to be very effective both in controlled clinical trials and in clinical practice [8–14]. Recently, tadalafil—a phosphodiesterase type 5 inhibitor of proven efficacy in the treatment of erectile dysfunction (ED)—was proven to be effective in several controlled clinical trials including patients with LUTS/BPH with or without ED. This has led to its approval as a therapeutic product for this population of patients [15–19].

Controlled clinical trials are experimental and provide safety and efficacy data related to a given intervention obtained under exclusively experimental circumstances in a concrete and homogeneous population representative of the general population, though this is not always possible; supplementary data are also needed for application across the general population. Naturalistic clinical trials provide data on the effectiveness of drugs under nonexperimental everyday situations and have proven to be extremely useful for decision-making purposes as well as for confirming the experimental findings of clinical trials [20–23].

Clinical trials are designed to assess efficacy (whether a drug is fit to produce the effects proposed in Phase II studies) and efficiency (comparative efficacy between the new drug and a known drug—Phase III studies). However, effectiveness is assessed vis-à-vis a comparator drug of proven efficiency and efficacy in a population of regular patients. It is for this reason that our study intends to assess effectiveness in terms of improvement in symptoms and quality of life.

We were unable to find data in the literature on studies of this nature performed on patients with LUTS/BPH with or without ED treated with phosphodiesterase type 5 inhibitors such as tadalafil.

As a result, our objective has been to carry out a naturalistic and observational study (TadaLutsEd Study) in order to evaluate the effectiveness of tadalafil 5 mg once daily in the treatment of LUTS/BPH with or without ED.

Aim

The primary objective of this study is to assess the effectiveness of tadalafil 5 mg once daily in the improvement of LUTS, in the context of standard urological practice, in patients with LUTS/BPH with or without concomitant ED. The secondary objective is to assess treatment effectiveness in terms of quality of life and drug safety.

Materials and Methods

This study was a 6-week uncontrolled (naturalistic), prospective, open-label, multicentric, longitudinal, observational study.

In accordance with the design of naturalistic observational studies, diagnosis and treatment type were based on the universal criteria accepted in standard practice; therefore, assessments and treatment were not conditioned in any way. All patients completed questionnaires related to sexual health, urinary symptoms, and quality of life, both before and after treatment.

Based on medical history and the opinion of the intervening physician, the study’s inclusion criteria accepted sexually active male patients of 50 years or more who complained of symptoms of LUTS, ED, or both, and who had been prescribed tadalafil 5 mg daily in accordance with standard urological practice. The exclusion criteria excluded patients with contraindications for tadalafil therapy as established by the drug’s package insert.

Prostate adenoma diagnosis was performed through a physical examination, and the presence and severity of LUTS/BPH and ED were evaluated through a series of self-administered questionnaires (International Prostate Symptom Score [IPSS] and International Index of Erectile Function -5 [IIEF-5]) [24–27]. Quality of life (IPSS-QoL) was also determined.

The severity of LUTS was classified according to IPSS as mild (0–7), moderate (8–19), or severe (20–35). The severity of ED was classified according to IIEF-5 score as mild (17–21), mild to moderate (12–16), moderate (8–11), or severe (5–7).

Treatment satisfaction was evaluated by means of a visual analogue scale ranging from 1 (very bad) to 10 (very good) [28,29].

Patients completing at least 4 weeks of treatment were taken into consideration for effectiveness analysis purposes, and adverse events were recorded.

A statistical analysis of paired sample data (Wilcoxon signed-ranks test) was performed, and the mean change was assessed, consisting in the difference between the first and the last visit.

Besides general efficacy variables, variables related to age and severity of LUTS and ED were also analyzed, as well as prostate-specific antigen (PSA) values, comorbidities, and body mass index (BMI).

A $P$ value $< 0.05$ was considered significant for all the analyses.

The study was performed in accordance with good clinical practice and the ethical principles set forth in the Declaration of Helsinki, and was approved by a Research Ethics Central Committee.

**Results**

Of the total population of 67 treated patients, only 62 (92.5%) had their data analyzed, as 5 were lost to follow-up.

All the patients included in this study had LUTS (62/62), and 59 also had ED (95.2%). None of the patients had ED alone. The patients’ mean age was 62.2 years (range 50–80), and the average BMI was 28.1 (range 20.9–40). A majority (78.7%) had associated risk factors (14 diabetes, 31 hypertension, 8 dyslipidemia, 2 depression). Five patients (8.1%) were on alpha blockers.

Mean prostatic volume as measured by ultrasound was 47.2 mL (range 30–90). The mean PSA value was 2.3 ng/mL (0.1–6.95), with maximal urine flow rate ($Q_{\text{max}}$) at 11.8 mL/second (7−18 mL/second) and postvoiding residual urine volume at 43.8 mL (0–110 mL).

The severity of LUTS was as follows: mild in 10 patients (16.1%), moderate in 37 patients (59.7%), and severe in 15 patients (24.2%).

The severity of ED was as follows: severe in 5 patients (8.1%), moderate in 10 patients (16.1%), mild to moderate in 28 patients (45.2%), and mild in 16 patients (25.8%). Three patients (4.8%) had no ED symptoms.

In 85.5% of patients (53/62), the IPSS score decreased 4.4 points on average; 5 patients (8.1%) did not exhibit any changes, and 4 (6.4%) exhibited a worsened score. Of the patients whose score remained the same, 4 had mild symptoms and 1 had severe symptoms; in the case of those whose score worsened, 3 had mild LUTS and 1 moderate.

| Table 1 Changes from baseline until end of treatment for IPSS, IPSS-QoL, IIEF-5, VAS LUTS, and VAS ED |
|---------------------------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| Pre- | Post- | MD $\pm$ SE (95% CI) | $P$* |
| treatment | treatment | |
| IPSS | 15.0 | 10.6 | $-4.4 \pm 0.6$ (3.3–5.5) | $< 0.0001$ |
| IPSS-QoL | 3.1 | 2.1 | $-1.0 \pm 0.7$ (0.7–1.4) | $< 0.0001$ |
| IIEF-5 | 14.1 | 19.5 | $5.4 \pm 0.5$ (4.1–6.1) | $< 0.0001$ |
| VAS LUTS | 5.1 | 6.8 | $1.7 \pm 0.3$ (0.9–2.1) | $< 0.0001$ |
| VAS ED | 4.6 | 6.8 | $2.2 \pm 0.4$ (1.2–3.8) | $< 0.0001$ |

*Wilcoxon matched-pairs signed-ranks test.
IPSS = International Prostate Symptom Score; IPSS-QoL = International Prostate Symptom Score—Quality of Life; IIEF-5 = International Index of Erectile Function-5; VAS LUTS = visual analog scale lower urinary tract symptom score; VAS ED = visual analog scale erectile dysfunction score

Pre- and post-treatment differences in the IPSS, IPSS-QoL, and IIEF5 scores were statistically significant: 4.4, 1, and 5.4, respectively ($P < 0.0001$ (Table 1).

There were no statistically significant differences when the following variables were compared: BMI (Tukey–Kramer multiple comparisons test), presence of diabetes (Mann–Whitney test), hypertension (Mann–Whitney test), PSA value (Mann–Whitney test), and age (Kruskal–Wallis test).

The efficacy results as measured through changes in the IPSS score, which is designed to assess LUTS severity, were as follows: severe, 26.3 to 18.3; moderate, 13.6 to 9.8; and mild, 6.4 to 4.5 ($P < 0.05$). The efficacy results as measured through changes in the IIEF-5 score, which is designed to assess ED, were as follows: severe, 5.3 to 17.8; moderate, 10.3 to 15.6; mild to moderate, 13.9 to 19.3; and mild, 17.9 to 21.8 ($P < 0.05$ (Table 2).

The five patients treated with alpha-blocking con-meds improved on the IPSS and the IPSS-QoL scores by 4 and 1.4 points, respectively.

Sixteen patients (25.8%) reported mild adverse events that were not a reason for therapy discontinuation; 1 patient discontinued therapy in month 1 due to an adverse event (headache) (Table 3).

**Discussion**

Drug effectiveness is assessed together with efficacy and efficiency parameters in the context of controlled clinical trials performed in a population of regular patients. For this reason our study has been designed to assess effectiveness in terms of symptom improvement and quality of life.

Nowadays it is clear that efficacy data (i.e., the results obtained with a drug under ideal, controlled, and experimental conditions) must be
supplemented with effectiveness data (i.e., the results obtained under actual conditions and as part of everyday medical practice) whenever the goal is to discover the actual and final effects of drugs on a given condition and the patients’ health and well-being [20].

Effectiveness or naturalistic studies lack a standard design and may be prospective, observational (basically cohort studies), randomized (pragmatic clinical trials), and/or retrospective, and are chiefly performed by means of databases involving computerized medical records.

Observational studies exhibit a high level of external validity and can be applied across the entire population, as they include all types of patients and assess the effectiveness of actual clinical practice, although there is always a high chance that the groups being compared are not completely homogeneous in terms of social and demographic status, associated comorbidities, and prognostic factors.

Therefore, these trials should be performed based on extremely accurate scientific standards, as well as using techniques enabling greater uniformity across study groups. Provided these studies are carried out following high quality standards, the results obtained will be fairly similar to those that can be drawn from clinical trials, and importantly, they will serve to complement them [21,22]. In addition, observational studies enable detection of adverse events that may otherwise not have been found in clinical trials, and thus allow consideration of their actual impact [23].

Saraim et al., cited by Gacci et al., were the first to suggest that PDE5 inhibitors could be useful for treating LUTS in male patients who sought medical consultation due to ED: this was subsequently confirmed by Mulhall [30]. McVary et al. were able to conclusively demonstrate the emerging role of PDE5 inhibitors as an effective and well-tolerated treatment for LUTS with or without ED [31]. Over the following years, controlled clinical trials designed to assess the efficacy and safety of tadalafil 5 mg once daily in men with LUTS/BPH with or without ED showed a significant improvement in IPSS as compared with placebo, thus enabling the recent approval of this drug for the treatment of these conditions [16,17].

PDE5 inhibitors lead to symptom improvement in patients with LUTS/BPH due to several mechanisms of action elucidated in basic research and subsequently demonstrated in clinical trials. The enhanced nitric oxide/cyclic guanosine monophosphate activity produced by PDE5 inhibitors reduces sympathetic system activity, inhibits RhoA kinase activity and inflammatory markers, and improves pelvic circulation. Together, these phenomena reduce prostate tissue tension, contraction, and proliferation, as well as bladder hyperactivity and inflammation, and increase vesicoprostatic blood perfusion [32].

Porst et al. showed that tadalafil 5 mg/day reduced urinary symptoms by 5.6 points as measured by the IPSS and increased quality of life by 1 point in 164 patients, as compared with improvements of 3.6 and 0.7 points in the placebo arm with 161 patients. As regards erectile function, the IIEF score and quality of life increased 6.7 and 2 points, respectively. Even though changes in the IPSS score were evident from the first week of treatment, they became significant (5.3 vs. 3.5) from the fourth week onwards, although no tests were conducted between the first and fourth weeks [15].

Table 2 Changes in the IIEF-5 score and IPSS in accordance with severity of ED and LUTS from baseline until end of treatment

<table>
<thead>
<tr>
<th>ED</th>
<th>IIEF Pre treatment</th>
<th>IIEF Post treatment</th>
<th>LUTS Pre treatment</th>
<th>LUTS Post treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe</td>
<td>5.3</td>
<td>17.8*</td>
<td>Severe</td>
<td>26.3</td>
</tr>
<tr>
<td>Moderate</td>
<td>10.3</td>
<td>15.6*</td>
<td>Moderate</td>
<td>13.6</td>
</tr>
<tr>
<td>Mild to moderate</td>
<td>13.9</td>
<td>19.3*</td>
<td>Mild</td>
<td>6.4</td>
</tr>
<tr>
<td>Mild</td>
<td>17.9</td>
<td>21.8*</td>
<td></td>
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</tbody>
</table>

*P < 0.05 vs. pre-treatment (Wilcoxon rank test).

IIEF-5 = International Index of Erectile Function; IPSS = International Prostate Symptom Score; ED = erectile dysfunction; LUTS = lower urinary tract symptoms

Table 3 Adverse events

<table>
<thead>
<tr>
<th>Adverse event</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dyspepsia</td>
<td>6.4</td>
</tr>
<tr>
<td>Headache</td>
<td>6.4</td>
</tr>
<tr>
<td>Backache</td>
<td>4.3</td>
</tr>
<tr>
<td>Palpitations</td>
<td>2.1</td>
</tr>
<tr>
<td>Interruption due to adverse event</td>
<td>1.6</td>
</tr>
<tr>
<td>More than one adverse event</td>
<td>0</td>
</tr>
<tr>
<td>Serious adverse events</td>
<td>0</td>
</tr>
</tbody>
</table>
Egerdie et al. found that tadalafil 5 mg/day decreased the urinary symptoms score by 6.1 points in 208 patients, compared with 3.8 points in the placebo arm with 200 patients. As regards erectile function, tadalafil 5 mg/day increased the IIEF score by 6.5 points vs. 1.8 points in the placebo arm [18]. The efficacy of tadalafil for urinary symptoms was independent of whether ED was present or not [33]. Similar results were obtained by Porst et al. in a pooled analysis of four randomized multinational studies including sexually active males over 45 years of age with LUTS/BPH and ED [34].

In our design, we considered a maximum of 6 weeks of treatment for the assessment, and we chose patients who had completed at least 4 weeks, based on data from controlled trials evidencing significant changes starting from the fourth week [15,19]. All but one of our patients (98.4%; 61/62) completed all 6 weeks of therapy. The remaining patient discontinued treatment due to adverse events 1 month after having started therapy, and he was taken into consideration in the analysis, as he had completed at least 4 weeks of treatment.

The demographic data and baseline characteristics of the population in the study are similar to those of populations in controlled clinical trials notwithstanding the fact that our patients were nonselected; this could be an indication of a profile similar to that of patients experiencing LUTS/BPH in the general population (Table 4).

In this regard, it should be noted that 74.2% of patients consulting for LUTS/BPH experienced ED, and all patients with ED experienced a certain degree of LUTS/BPH. The high prevalence of these associated urological factors, already reported by other authors, suggests that it will be possible to identify concomitant symptoms both in patients consulting for LUTS and in those consulting for ED and, in this way, prevent the potential development of both conditions; furthermore, concurrent symptom detection may enable patients to be started on treatments that will prevent further deterioration of their quality of life [35–37].

Likewise, the fact that our results are comparable with the efficacy and safety results obtained from various controlled Phase II and Phase III clinical trials (Table 5) shows that we have attained our intended goals.

However, it is very important to point out that whenever a study’s inclusion and exclusion criteria are too strict, results cannot be generalized to a great extent. Thus, the results arising from the same intervention in nonselected population samples, as is the case in everyday practice, may differ, and therefore our results justify additional research in naturalistic conditions.

As mentioned by Gacci et al., further studies will be necessary to assess long-term safety and efficacy, as well as effects on disease progression and the cost-effectiveness of PDE5 inhibitors as applied to this condition [30].

Even though the decrease in IPSS and the increase in the IIEF5 score, though significant, were lower than in controlled trials, it should be noted that in the latter the active treatment schedule generally lasted 12 weeks; this is twice as long

**Table 4** Baseline characteristics compared with controlled clinical trials

<table>
<thead>
<tr>
<th></th>
<th>Controlled</th>
<th>Naturalistic</th>
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<tbody>
<tr>
<td></td>
<td>Porst et al. [15]</td>
<td>Egerdie et al. [18]</td>
</tr>
<tr>
<td>N</td>
<td>161</td>
<td>208</td>
</tr>
<tr>
<td>Age (years)</td>
<td>65.1</td>
<td>62.5</td>
</tr>
<tr>
<td>BMI</td>
<td>27.1</td>
<td>28</td>
</tr>
<tr>
<td>IPSS</td>
<td>17.1</td>
<td>16.5</td>
</tr>
<tr>
<td>IIEF-5 score</td>
<td>—</td>
<td>18.5</td>
</tr>
<tr>
<td>Qmax (mL/sec)</td>
<td>11.7</td>
<td>10.3</td>
</tr>
<tr>
<td>PVR (mL)</td>
<td>44.9</td>
<td>—</td>
</tr>
<tr>
<td>PSA (ng/mL)</td>
<td>2</td>
<td>1.9</td>
</tr>
<tr>
<td>ED (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mild (%)</td>
<td>30.4</td>
<td>47.6</td>
</tr>
<tr>
<td>Moderate (%)</td>
<td>54.5</td>
<td>26</td>
</tr>
<tr>
<td>Severe (%)</td>
<td>15.2</td>
<td>26.4</td>
</tr>
<tr>
<td>LUTS (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mild (%)</td>
<td>6.2</td>
<td>—</td>
</tr>
<tr>
<td>Moderate (%)</td>
<td>55.9</td>
<td>59.6</td>
</tr>
<tr>
<td>Severe (%)</td>
<td>37.9</td>
<td>40.4</td>
</tr>
</tbody>
</table>

BMI = body mass index; IPSS = International Prostate Symptom Score; IIEF-5 = International Index of Erectile Function-5; Qmax = maximal urine flow rate; PVR = postvoiding residual urine volume; PSA = prostate-specific antigen; ED = erectile dysfunction; LUTS = lower urinary tract symptoms.
as the treatment our patients received. This may bias end results.

On the other hand, the percentage of patients with mild LUTS—who tend to notice fewer symptom changes (16.2% according to our data)—was significantly higher than that included in most controlled trials (Oelke et al. 1.6% [38], Porst et al. (2011) 6.2% [15], Porst et al. (2013) and Egerdie et al. 0% [34,37]), thus introducing another bias which may have reduced the significance of the final results.

In fact, 5 (55.5%) patients whose IPSS either remained unchanged or worsened had mild symptoms. The exclusion of patients with mild LUTS from our study would have increased the difference in the reduction of the IPSS score from 4.4 to 5.1, that is, a figure closer to the one obtained in controlled trials (Table 5).

Also, the percentage of adverse events does not differ significantly from the percentage observed in controlled trials, even though the occurrence of headache and lower back pain was slightly higher. However, this fact did not modify the comparative percentage of patients who discontinued treatment because of adverse events.

Finally, 5 patients in our series were receiving alpha blockers and continued receiving them throughout the treatment concurrently with tadalafil. These patients improved their IPSS and IPSS-QoL by 4 and 1.4 points, respectively.

As regards combination therapy with tadalafil and alpha blockers, two controlled clinical trials have shown a significant improvement in IPSS as compared with alpha blocker monotherapy. However, Liguori et al. did not find a significant improvement when analyzing a group receiving PDE5 inhibitors alone [39,40].

As regards the effects of alpha blockers and PDE5 inhibitors on sexual performance, recently Giuliano et al. conducted a randomized, double-blind, placebo-controlled trial of tadalafil 5 mg/day over 12 weeks in men with LUTS/BPH, compared with tamsulosin 0.4 mg/day, and proved that tadalafil 5 mg/day significantly improved orgasm and ejaculation, as well as sexual intercourse, general satisfaction, and erectile function. Men on tamsulosin 0.4 mg/day, by contrast, experienced impairments in ejaculatory volume, frequency of orgasms, and general satisfaction vis-à-vis the placebo arm, and experienced no significant effects on erectile function [41].

In an independent study conducted without the industry’s financial support, the figure tends to be lower than the one generally obtained in short-term controlled trials. These two factors may be indicative of two biases; however, we are also aware that the benefits shown in a clinical trial of a drug may not be sustained or evident when they are transferred to daily clinical practice, which involves factors related to medical experience and the patient himself; this is the rationale for studies such as the one that we have conducted. Unfortunately, these studies tend to be scarce and are superseded by trials, leading to evidence-based medicine and current recommendation levels. However, evidence does not necessarily imply accuracy. For this reason, we believe that randomized clinical trials should be complemented by their nonrandomized counterparts, because whenever a decision needs to be made in connection with medical intervention, it is important to consider not only efficacy data, but also effectiveness and efficiency data.

We expect that the results obtained from this observational study performed by independent investigators will provide initial data that may be useful for motivating additional studies involving a larger number of patients and enabling the confirmation of our findings in nonselected populations.

<table>
<thead>
<tr>
<th>Table 5 Comparative data of efficacy measures and adverse events with controlled clinical trials</th>
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<tr>
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<tr>
<td>Changes in IPSS (mean score)</td>
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<tr>
<td>Changes in IPSS-QoL (mean score)</td>
</tr>
<tr>
<td>Total AE (%)</td>
</tr>
<tr>
<td>Headache (%)</td>
</tr>
<tr>
<td>Back pain (%)</td>
</tr>
<tr>
<td>Dyspepsia (%)</td>
</tr>
<tr>
<td>Palpitations (%)</td>
</tr>
<tr>
<td>Nasopharyngitis (%)</td>
</tr>
<tr>
<td>Subjects discontinuing due to AE (%)</td>
</tr>
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</table>

IPSS = International Prostate Symptom Score; IPSS-QoL = International Prostate Symptom Score—Quality of Life; AE = adverse events
Conclusion
According to our results, the use of tadalafil 5 mg once daily in a nonselected patient population with LUTS/BPH with or without ED produced symptom and quality-of-life improvements and a safety profile similar to that obtained in controlled clinical trials.

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Conflict of Interest: Amado Bechara is a speaker and investigator on clinical trials for Lilly, Bayer, Boheringer Ingelheim, and GSK, and sits on the advisory boards of Lilly and Boheringer Ingelheim.

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(c) Analysis and Interpretation of Data
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(b) Revising It for Intellectual Content
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Amado Bechara; Adolfo Casabe; Gustavo Rodríguez Baigorri; Christian Cobreros

References


