# PDE-5 Inhibitors May Relieve Benign Prostatitis

*Combined with alpha-blockers, "you might be able to enhance both sexual function and voiding function."*

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PARIS — Phosphodieterase-5 inhibitors may have a role in the relief of lower urinary tract symptoms, according to two studies presented at the annual congress of the European Association of Urology.

Daily tadalafil (Cialis) therapy significantly improved symptom scores in men with benign prostatic hyperplasia in a placebo-controlled, phase II trial reported by Dr. Kevin T. McVary.

The 12-week, double-blind study enrolled 281 participants. Not unexpectedly, a sexually active subset with erectile dysfunction also experienced significantly improved erectile function with tadalafil.

In the second study, investigators combined sildenafil (Viagra) with alfuzosin (Uroxatral), an alpha$_1$-blocker, for previously untreated lower urinary tract symptoms (LUTS) and erectile dysfunction. Dr. Steven A. Kaplan reported that the combination was more effective than either agent alone in the three-armed study of 62 men who had the two conditions.

Dr. McVary, a professor of surgery at Northwestern University, Chicago, described his results as "somewhat provocative" and the benefits as comparable to others reported on the use of alpha-blockers for LUTS. Patients on tadalafil improved in all end points except for the Qmax measure of urinary peak flow.

"If you give combinations of medications, you might be able to enhance both sexual function and voiding function," said Dr. Kaplan, a professor of urology at Cornell University, New York.

### Daily Tadalafil

Dr. McVary and his colleagues randomly assigned men with benign prostatic hyperplasia to tadalafil (n = 138) or placebo (n = 143). Both groups had an average age in the early 60s (range, 45-82 years).

At baseline, nearly two-thirds of the men had moderate LUTS, defined as International Prostate Symptom Score (IPSS) results below 20. The remainder had severe LUTS, with IPSS results of 20-35. A greater proportion of the tadalafil group had erectile dysfunction (72%), compared with the placebo group (59%).

After wash-out and placebo run-in periods, patients began taking either 5 mg of tadalafil or placebo at week 3. They continued at this daily dose for another 3 weeks, then moved to a 20-mg dose.

Average IPSS results declined by 2.8 points, compared with baseline, for the men on the 5-mg tadalafil dose.

Increasing the dose to 20 mg brought the decline to 3.8 points by the end of the 12-week trial. The placebo group's scores fell by 1.2 points at week 6 and 1.7 points at week 12.

Tadalafil also improved LUTS and International Index of Erectile Function (IIEF) scores for the subset (56%) who were sexually active and had erectile dysfunction, but the correlation was weak.

"There was a disconnect," Dr. McVary said. "There were patients who had improvement in symptom scores for IPSS that did not directly correlate or correspond to changes in sexual function."

He described tadalafil as well tolerated with no serious adverse events. The most frequent treatment-related side effects were increased erection, dyspepsia, back pain, and headache.

Lilly ICOS LLC funded the study.

### Sildenafil Plus Alfuzosin

Dr. Kaplan and his colleagues randomized 62 consecutive men, with an average age of 63 years (range 50-76 years). For 12 weeks, 20 men took 10 mg daily of alfuzosin, an alpha$_1$-blocker that has been shown to relieve LUTS with "minimal sexual and cardiovascular side effects." Another 21 men took 25 mg of sildenafil each day. The other 21 men took both.

All three groups had significant improvements on the IPSS at 12 weeks. Scores fell from 17.8 to 14.6 with alfuzosin alone, from 16.9 to 14.9 with sildenafil alone, and from 17.3 to 13.5 with both.

Alfuzosin significantly improved frequency, nocturia, peak flow rate (Qmax), and postvoid residual urine equally well when used alone or in combination. Sildenafil alone did not have a significant effect.

All arms of the study showed improvement in erectile function, frequency of penetration, and frequency of maintained erections after penetration. Notably, IIEF scores went from 17.4 to 20.3 with alfuzosin alone, from 14.3 to 21.4 with sildenafil alone, and from 16.2 to 25.7 with both agents. These changes reached significance only in the sildenafil arms.

Seven patients dropped out because of dizziness, flushing, or dyspepsia. ■

# Range of Vascular Uses Anticipated for ED Drugs

PARIS — Indications for phosphodiesterase-5 inhibitors will likely go beyond treatment of erectile dysfunction to include a range of vascular disorders, Dr. Peter Hedlund said at the annual congress of the European Association of Urology.

Promising uses include treatment of pulmonary hypertension, digital ischemia, lower urinary tract symptoms in benign prostatic hyperplasia, and female sexual response, according to Dr. Hedlund of the department of clinical and experimental pharmacology at Lund University Hospital in Sweden.

For erectile dysfunction patients, he cited studies showing better outcomes when tadalafil and sildenafil are taken daily as opposed to as needed. Prophylactic treatment with a phosphodiesterase-5 (PDE-5) inhibitor also may improve erectile function after nerve-sparing procedures, Dr. Hedlund added. He emphasized that larger randomized controlled trials are necessary before definitive statements can be made about postprostatectomy patients.

"Endothelial dysfunction is probably the common denominator between erectile dysfunction and vascular disease," Dr. Hedlund said. He noted that endothelial dysfunction is linked to vascular disease and risk factors for vascular disease, such as hypercholesterolemia, diabetes, and hypertension.

All three PDE-5 inhibitors—tadalafil (Cialis), vardenafil (Levitra), and sildenafil (Viagra)—caused pulmonary vasorelaxation in a small study, he noted, but sildenafil was the only one to improve arterial oxygenation.

Sildenafil is the only PDE-5 inhibitor approved for treatment of pulmonary hypertension in the United States and in Europe.

In another presentation at the congress, Dr. Piero Montorsi cited growing evidence that erectile dysfunction is a vascular disorder. Dr. Montorsi of the Institute of Cardiology at the University of Milan spoke at a symposium sponsored by Lilly ICOS LLC, maker of tadalafil.

Outlining the "reconditioning endothelium concept," he suggested that PDE-5 inhibitors may be effective in treating erectile dysfunction because they improve endothelial function.

"The goal of chronic therapy should be to achieve a sustained improvement of both erectile function and systemic vascular function through an improvement of endothelial function," Dr. Montorsi said.

"Beneficial effect of concomitant treatment of risk factors is a crucial step and should always be a part of the [erectile dysfunction] treatment strategy." ■

# *Physician's Attitude Affects Therapy Adherence in Erectile Dysfunction*

PARIS — How a physician responds to a male patient's disclosure of erectile dysfunction can determine whether the patient uses medical treatment, investigators said at the annual congress of the European Association of Urology.

In an eight-country study of nearly 3,000 men with erectile dysfunction, patients who were dissatisfied or extremely dissatisfied with their physician-patient interaction during the disclosure were about half as likely to use a phosphodiesterase-5 (PDE-5) inhibitor more than once, compared with men who were extremely satisfied with their doctors' responses. Men who felt neutral about the discussion were most apt to stop treatment (odds ratio 0.20 for continued use).

**'Men … are looking for some signal from what they consider to be a knowledgeable source that [medical treatment] is a good idea.'**

Patients were less likely to stay on a PDE-5 inhibitor in three other circumstances: if they felt the doctor was not positive (OR 0.24), if they discussed the problem only once (OR 0.33), or if the doctor advised something other than a prescribed treatment (OR 0.53).

"Clearly the perception that you [the physician] are taking me [the patient] seriously, that you are interested in this problem, will make an impact on my continuing with therapy," coinvestigator Michael Sand, R.N., said in an interview after Dr. Raymond C. Rosen reported on the multinational Men's Attitudes to Life Events and Sexuality (MALES) phase II study.

"I am sure part of this is because men are uncomfortable to begin with," Mr. Sand said. "The other key is men are recognizing that their physicians know more about this problem than they do, so they are looking for some signal from what they consider to be a knowledgeable source that this is a good idea."

Mr. Sand, a sexologist, is based in Germany with the Bayer Corporation, maker of vardenafil (Levitra). Dr. Rosen is a psychologist at Robert Wood Johnson Medical School in Piscataway, N.J. Their coauthors were based in Canada and the United Kingdom.

The MALES study recruited 2,912 men, aged 20-75 years, who self-reported erectile dysfunction. This analysis was based on follow-up questions that were posed to 1,907 men who reported discussing erectile dysfunction with their physicians.

Patients were most likely to continue therapy if the doctor prescribed a PDE-5 inhibitor (OR 4.67), but referral to another physician also favored staying on a drug (OR 1.75). All of the differences were statistically significant.

The investigators reported on interviews with 293 female partners of men in the MALES study. Men were more likely to seek treatment if their female partners were concerned about the impact of erectile dysfunction on their sex lives, if they believed that it was caused by a medical condition, and if they believed that the condition could be treated medically.

"If she believes this is a medical problem, [that] it is related to an organic disease, that it is not going away, he is more likely to seek therapy," Mr. Sand said. ■