

AUA: ED Drug May Offer Aid for BPH

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CHICAGO, May 4 -- A drug for erectile dysfunction significantly improved symptoms of benign prostatic hyperplasia (BPH) in a randomized clinical trial reported here.

Once-daily tadalafil (Cialis) improved prostate symptom scores, bladder symptom scores, and quality of life in men with BPH/lower urinary tract symptoms (LUTS), said Gregory Broderick, M.D., of the Mayo Clinic in Jacksonville, Fla.

The improvement occurred irrespective of erectile function status, he said in a presentation at the American Urological Association meeting.

"Once-daily tadalafil demonstrated clinically meaningful and statistically significant improvements in BPH symptoms scores in men with BPH/LUTS," said Dr. Broderick. "Treatment with once-daily tadalafil was associated with consistent improvements in [symptoms] in men with or without erectile dysfunction."

A second report at the AUA meeting showed that tadalafil improved prostate symptoms but did not increase urodynamic parameters in men with BPH and bladder outlet obstruction.

Action Points

* Explain to patients that a drug approved for treatment of erectile dysfunction relieved prostate symptoms in two different studies.

* The drug is not approved for treatment of BPH/LUTS.

* Note that these studies were published as abstracts and presented orally at a conference. These data and conclusions should be considered to be preliminary until published in a peer-reviewed journal.

Tadalafil and other phosphodiesterase type 5 (PDE5) inhibitors have been shown to improve prostate symptom score with increasing flow rate. PDE5 mRNA has been identified in human prostate and bladder tissue, providing plausibility for an effect on BPH/LUTS.

However, the mechanism by which PDE5 inhibitors might relieve BPH/LUTS is unclear, Dr. Broderick said. Moreover, possible relationships between improvements in erectile dysfunction and LUTS continue to be examined.

"We sought to provide evidence that improvements observed in subjects administered once-daily tadalafil for BPH/LUTS symptoms and related quality of life are similar in men with or without coexisting erectile dysfunction," said Dr. Broderick.

Investigators in a multicenter trial randomized 1,054 patients to placebo or to one of four doses of tadalafil (2.5, 5, 10, and 20 mg).

The patients were followed for 12 weeks, and completed symptom evaluations every four weeks: the International Prostate Symptom Scale (IPSS), BPH Impact Index (BII), and IPSS Quality of Life index.

From baseline to end of study, men randomized to any dose of tadalafil had significantly greater improvement in symptoms and quality of life compared with the placebo group.

- * IPSS: placebo --2.2 versus -3.8 to -5.2 for tadalafil
- * BII: -0.8 versus -1.0 to -1.9
- * IPSS Quality of Life: -0.5 versus -0.8 to -0.9 for tadalafil

Stratification by baseline erectile function status showed similar improvement in men with or without erectile dysfunction for all three outcomes.

"In men with erectile dysfunction, improvements in BPH/LUTS were correlated to improvements in erectile function," said Dr. Broderick.

The second AUA report focused on a randomized study designed to assess the effect of tadalafil on urodynamics in men with BPH. Investigators in the U.S. and Canada randomized 200 patients to placebo or to 20 mg of tadalafil daily for 12 weeks.

The primary urodynamic outcome was the effect of tadalafil on the Bladder Outlet Obstruction Index (BOOI), said Roger Dmochowski, M.D., of Vanderbilt University in Nashville, Tenn. The primary efficacy outcome was the change in IPSS from baseline to the end of the study.

At baseline, a third of men in both groups had severe obstruction (BOOI >40), a third had equivocal results (BOOI 20 to 40), and a third had no obstruction (BOOI <20).

Half the men in both groups had more than a three-year history of BPH/LUTS. About two thirds of the men had severe BPH/LUTS (IPSS \geq 20).

At the end of the study, none of the free-flow or pressure-flow assessments differed significantly between the placebo and tadalafil groups. The average BOOI score decreased from 36 at baseline to 35.07 in the placebo group and from 35.57 to 32.75 in the tadalafil group.

Analysis of BOOI category shifts did show an advantage for tadalafil. In the placebo group, the proportion of patients with frank obstruction increased from 33.7% at

baseline to 40.5% at 12 weeks. Most of the upward shift came from the equivocal category.

In the tadalafil group the proportion of patients with frank obstruction decreased from 30.1% at baseline to 27.7%, the equivocal decreased from 36.1% to 32.5%, and the unobstructed category increased from 33.7% to 39.8%.

"Despite the absence of an effect on free flow rates, there is a suggestion that some urodynamic parameters improved numerically," said Dr. Dmochowski. "The changes, while not statistically significant, may be clinically meaningful."

In contrast to the urodynamic results, prostate symptomatology improved significantly in tadalafil-treated patients, including relative improvement in IPSS ($P < 0.001$), obstructive symptoms ($P < 0.001$), and irritative symptoms ($P = 0.006$).

Adverse events occurred in twice as many tadalafil patients (55.6% versus 27.7%), the most common events being dyspepsia, headache, back pain, and gastroesophageal reflux disease.

About a fourth of tadalafil patients had drug-related adverse events. Only two patients in the tadalafil group and one in the placebo group withdrew from the study because of adverse events.

Both studies were sponsored by Eli Lilly.

Dr. Broderick disclosed relationships with Eli Lilly, Ethicon, GlaxoSmithKline, Ortho, Willex, and Vivus. Dr. Dmochowski disclosed relationships with Allergan, Astellas, Eli Lilly, Novartis, Pfizer, and Watson Pharma. Employees of Eli Lilly participated in both studies.

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