URINARY INCONTINENCE

Neurokinin receptor antagonist inferior to tolterodine for OAB

Serlopitant, a neurokinin-1 receptor antagonist, offers no advantage over tolterodine for the treatment of adult overactive bladder (OAB), according to the results of a multicenter randomized controlled trial conducted by Tara Frenkl and colleagues from Merck & Co, Inc. and published in the August issue of *The Journal of Urology*.

Signaling through the neurokinin-1 receptor has been implicated in the micturition reflex, and receptor antagonists have been shown to reduce detrusor overactivity in animal models. Thus, it was hoped that serlopitant would provide effective treatment for patients with OAB while also avoiding the adverse effects of more-commonly used anticholinergic drugs, such as dry mouth, dry eyes and constipation.

557 patients with OAB from 69 centers were enrolled in the trial. OAB was defined as a history of urinary urgency for at least 3 months with 8 or more average daily micturitions and at least 1 daily urge incontinence episode. Patients were

randomized equally to receive 0.25 mg, 1 mg or 4 mg daily of serlopitant, 4 mg of tolterodine extended-release or placebo for a total of 8 weeks after 1 week of single-blind placebo run-in.

The primary outcomes—change from baseline number of micturitions per day, and tolerability—were well met. Serlopitant was tolerated well at all doses; the most common adverse effects were headache (5.7%) and diarrhea (5.2%). Although dry mouth was experienced by 4.5% of patients who took serlopitant, no dose–response effect was seen. This incidence was comparable to that of placebo and much lower than that in the tolterodine group.

The average number of micturitions per day was reduced over the course of the trial in all treatment groups. At week 8, the average daily number of urination episodes was markedly decreased in patients who took 0.25 mg and 4 mg serlopitant, and 4 mg tolterodine, compared to placebo. Unlike tolterodine, no dose of serlopitant had a significant

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effect on secondary outcomes—urgency, total incontinence and urge incontinence episodes—relative to placebo.

Although the results support a role for neurokinin-1 receptor antagonism in OAB treatment, this approach is unlikely to offer clinically meaningful advantages over currently available therapies. Frenkl confirms that development of serlopitant for OAB has been discontinued by Merck.

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Original article Frenkl, T. L. *et al.* A multicenter, double-blind, randomized, placebo controlled trial of a neurokinin-1 receptor antagonist for overactive bladder. *J. Urol.* **184**, 616–622 (2010)