

## IMPACT OF URGE INCONTINENCE SEVERITY ON DRUG TREATMENT EFFICACY

### Aims of Study

Urinary incontinence is often the key symptom associated with assessment of OAB symptom severity and the decision to use drug therapy. Furthermore, patients with more severe symptoms are typically those most likely to seek treatment and it is commonly perceived that such patients are more difficult to treat. However, data on the impact of incontinence severity on antimuscarinic treatment efficacy in patients with OAB are very limited. We therefore evaluated the efficacy of tolterodine extended-release (TER) in OAB patients with severe incontinence.

### Methods

Patients aged  $\geq 18$  years old with urge incontinence ( $\geq 5$  episodes/week), urinary frequency ( $\geq 8$  micturitions/24 hours) and symptoms of OAB for  $\geq 6$  months were enrolled into a multinational, randomized, double-blind, placebo-controlled trial conducted at 159 centers in North America, Europe and Australia/New Zealand. Patients were randomized to receive TER 4 mg once daily or placebo for 12 weeks. Severe incontinence was defined as  $\geq 21$  episodes/week. Changes in the number of incontinence episodes/week and micturition frequency after 12 weeks were compared between treatments with SAS PROC FREQ and StatXact, using generalized Mantel-Haenszel procedures (based on rank scores) to adjust for the variation among baseline severity strata and clinical centers.

### Results

A total of 986 patients were eligible for this post-hoc analysis (TER, n=492; placebo, n=494). After 12 weeks, overall absolute median reductions in weekly incontinence episodes were significantly greater with TER (9.0 episodes/week; 70.8% reduction) than with placebo (5.0 episodes/week; 34.1% reduction;  $p < 0.02$ ). In the subgroup of patients with severe incontinence, the median number of incontinence episodes/week at baseline was similar in both placebo (31.5; n = 210) and TER (34; n = 171) groups. For patients with severe incontinence at baseline, the median reduction in incontinence episodes was significantly ( $p < 0.001$ ) greater with TER (21.0 episodes/week; 68% reduction) than with placebo (9.5 episodes/week; 30% reduction) after 12 weeks ( $p = 0.022$ , adjusted for baseline incontinence severity strata and clinical center). There was also a significantly ( $p < 0.02$ ) greater reduction in micturition frequency with TER (median decrease of 1.9 episodes/24 h; 17.4% reduction) than with placebo (median decreases of 0.4 episodes/24 h; 4.5% reduction) in this severe incontinence patient-subgroup, adjusted for baseline incontinence severity and clinical center. In patients with non-severe incontinence at baseline (5 – 20 incontinence episodes/week), the median reduction in incontinence episodes was also significantly ( $p < 0.03$ ) greater with TER (6 episodes/week; 71% reduction) than with placebo (4 episodes/week; 39% reduction) after 12 weeks of treatment, when adjusted for baseline incontinence severity strata and clinical center. The median reduction in number of incontinence episodes/week increased with baseline severity in both treatment groups, with tolterodine ER more effective than placebo irrespective of symptom severity (Figure 1). Moreover, the median percentage reduction in the number of incontinence episodes/week was comparable across the whole range of baseline severity strata (Figure 2).

### Conclusions

During treatment with TER, patients with severe incontinence at baseline experienced a significant percentage reduction in incontinence episodes similar to that achieved in patients with less severe incontinence. This corresponded to a greater absolute reduction in

incontinence episodes in the severe incontinence subgroup. Therefore, the benefits of antimuscarinic treatment may be greater in these severely incontinent patients than has previously been reported in clinical studies in OAB.

Figure 1. Median absolute change in urge incontinence per week stratified by baseline incontinence severity in patients receiving tolterodine ER or placebo for 12 weeks.

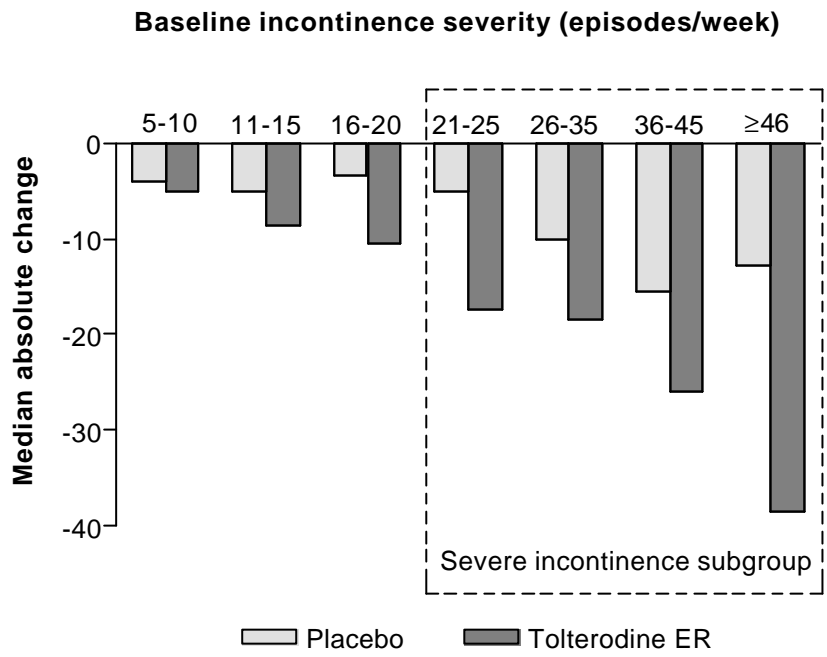


Figure 2. Median percentage change in urge incontinence per week stratified by baseline incontinence severity in patients receiving tolterodine ER or placebo for 12 weeks.

