

## CLINICAL EFFICACY OF TOLTERODINE EXTENDED RELEASE IS MAINTAINED FOR 24 HOURS IN PATIENTS WITH OVERACTIVE BLADDER

### Hypothesis / aims of study

Tolterodine extended release (ER) is indicated for the treatment of overactive bladder (OAB), and is formulated for once-daily dosing. Because of the drug's prolonged release and lower peak serum concentration than the immediate-release (IR) formulation [1], we assessed the 24-hour efficacy of tolterodine ER in patients with OAB and urgency urinary incontinence (UUI).

### Study design, materials and methods

This is a post hoc analysis of a 12-week, randomized, double-blind, placebo-controlled trial of tolterodine ER performed at 167 centers in Australia, Europe, and North America. Eligible patients were  $\geq 18$  years of age with symptoms of urinary frequency ( $\geq 8$  micturitions/24 h) and UUI ( $\geq 5$  episodes/wk) for  $\geq 6$  months. Patients received once-daily treatment with placebo or tolterodine ER (4 mg). Micturition diaries were completed for the 7 days before the baseline visit and again before the last dose of study medication. Patients recorded all micturitions and UUI episodes at the times they occurred, along with volume voided. For this analysis, data for weekly UUI episodes and volume voided per micturition were stratified by the 6-hour time period during which each UUI episode or micturition occurred: 12 AM to 6 AM, 6 AM to 12 PM, 12 PM to 6 PM, and 6 PM to 12 AM. Analysis of median percentage reductions from baseline in weekly UUI episodes between treatment groups was performed by rank analysis of covariance (ANCOVA), and mean numeric changes in volume voided per micturition were compared using ANCOVA. Both statistical models included treatment and country as factors, with baseline value as covariate, using a 5% level of significance.

### Results

1015 patients (508 placebo, 507 tolterodine ER) were included in the intent-to-treat analysis. Baseline UUI episodes and volume voided per micturition for each time period were similar between treatment groups. Results are summarized in the **Table**. Compared with placebo, tolterodine ER significantly reduced weekly UUI episodes and increased volume voided per micturition during each of the 4 time intervals.

### Interpretation of results

Although the peak serum concentration of tolterodine ER is reduced compared with that of the twice-daily IR formulation [1], once-daily tolterodine ER significantly reduced UUI episodes throughout the 24-hour period. Volume voided per micturition was significantly increased in patients receiving tolterodine ER, suggesting increased bladder capacity.

### Concluding message

Clinical efficacy of tolterodine ER was maintained over the full 24-hour period, as demonstrated by time interval analysis of UUI episodes and volume voided per micturition. Tolterodine ER should be effective for OAB symptoms without regard to whether symptoms occur during the day and/or night.

**Table. Efficacy Results: Change From Baseline to Week 12**

	Weekly UUI Episodes			Volume Voided Per Micturition		
	Median Change From Baseline			Mean $\pm$ SD Change From Baseline		
	Placebo	Tolterodine ER	<i>P</i> Value	Placebo	Tolterodine ER	<i>P</i> Value
12 am to 6 am	-36.4	-74.1	0.0001	19.4 $\pm$ 91.0	34.6 $\pm$ 105.8	0.003
6 am to 12 pm	-42.9	-73.3	<0.0001	16.7 $\pm$ 59.3	38.7 $\pm$ 64.6	<0.0001
12 pm to 6 pm	-40.0	-78.8	<0.0001	13.0 $\pm$ 43.8	31.3 $\pm$ 59.4	<0.0001
6 pm to 12 am	-40.8	-83.3	<0.0001	12.8 $\pm$ 51.5	28.9 $\pm$ 57.3	<0.0001
24 hours	-36.7	-71.4	<0.0001	14.8 $\pm$ 42.6	34.3 $\pm$ 50.7	<0.0001

ER=extended release; SD=standard deviation; UUI=urgency urinary incontinence.

Reference

1. Multiple dose pharmacokinetics of a new once daily extended release tolterodine formulation versus immediate release tolterodine. Clin Pharmacokinet. 2001;40(3):227-235.

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