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Abstract Reproduction Form B-1

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Title (type in CAPITAL LETTERS): **A COMPARISON OF THE EFFICACY RESPONSE PROFILE OF TOLTERODINE AND OXYBUTYNIN**

Aims of Study: Antimuscarinic treatment of overactive bladder, while effective, is frequently limited by poor tolerability. Tolterodine is a potent muscarinic receptor antagonist, indicated for the treatment of overactive bladder and its associated symptoms of frequency, urgency and/or urge incontinence, which exhibits a selectivity for the bladder over salivary glands in vivo {1}.

Tolterodine 2 mg BID was compared with oxybutynin 5 mg TID and placebo in 2 separate studies. Efficacy (measured using patient-recorded micturition diaries), safety, and tolerability were evaluated at the end of treatment and during the 12-week treatment period. This analysis investigated the delayed onset to maximum effect that is observed with tolterodine or oxybutynin treatment.

Methods: Both studies were multicenter randomized, double-blind, parallel, placebo- and comparator-controlled trials that enrolled a total of 570 patients (113 placebo, 227 tolterodine 2 mg bid, 230 oxybutynin 5 mg tid). Patients completed a 2-week washout/run-in period. They were then seen at the randomization visit, and 2, 4, 8, and 12 weeks following randomization.

Results: In both studies, the effects of treatment on micturitions and incontinence and volume voided per micturition did not reach a maximum until 8 to 12 weeks after treatment was initiated, irrespective of the treatment group.

Table: Percentage of Maximum Effect on Micturitions and Incontinence and Volume Voided Over Time

Week	Tolterodine Mics/Inc	Oxybutynin Mics/Inc	Tolterodine Volume voided	Oxybutynin Volume voided
0	0	0	0	0
2	62*	67*	90*	84*
4	87*	85*	100*	90*
8	99*	96*	97*	94*
12	100*	100*	97*	100*

Mics/Inc, micturitions and incontinence.
* $p < 0.05$ versus placebo.

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Ref. No. (Page 2) 255

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In these studies, the enhanced bladder selectivity of tolterodine 2 mg BID compared with oxybutynin 5 mg TID was confirmed: while tolterodine and oxybutynin had equivalent efficacy, *tolterodine-treated patients had significantly lower incidence and severity of dry mouth.* Furthermore, significantly more oxybutynin patients required dosage reduction and withdrew as a *result of side effects.*

Studies measuring the urodynamic effects of tolterodine on the bladder show that the effect is immediate and no further increase occurs over time. Therefore, these results suggest that the delay to maximum effect is a function of the condition and not the treatment. Tolterodine- or oxybutynin-treated patients are experiencing the change in bladder control and are modifying their bladder habits to match the new control they experience over the first few weeks of treatment. Approximately 85% of maximum effect on micturitions and incontinence is reached within 4 weeks of initiating treatment. Of further interest is that the placebo effect, brought on at least partially by bladder training introduced with micturition diaries, also takes a period of time to reach maximal effect.

Conclusions: Tolterodine 2 mg BID and oxybutynin 5 mg TID are equivalent dosages with regards to efficacy; however, tolterodine 2 mg BID is significantly better tolerated. Tolterodine and oxybutynin require 8 to 12 weeks of treatment before maximal effect is noted, however, the vast majority of effect (> 85%) is reached within 4 weeks after initiating treatment. Results of this study indicate that while the full pharmacologic effect of tolterodine occurs following the first dose, approximately 4 weeks of treatment may be necessary to allow patients to adjust their bladder habits to the new control they experience.

Reference:

1. *Eur J Pharmacol.* 1997;327:195-207.

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