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ONCE-DAILY TROSPIUM CHLORIDE EXTENDED RELEASE IS EFFECTIVE AND WELL TOLERATED FOR THE TREATMENT OF OVERACTIVE BLADDER: RESULTS FROM A MULTICENTER, PHASE III TRIAL

Hypothesis / aims of study
A once-daily (QD), extended-release formulation of trospium chloride (trospium QD) has recently been studied for the treatment of overactive bladder syndrome (OAB). The purpose of this multicenter trial was to investigate the safety, efficacy, and tolerability of trospium 60 mg QD in subjects with OAB with an urge urinary incontinence (UUI) component.

Study design, materials and methods
Subjects with OAB and UUI were randomized (1:1) to receive trospium 60 mg QD or placebo in this 12-week, multicenter, parallel-group, double-blind, placebo-controlled trial. The primary endpoints were change in the number of toilet voids/day and change in the number of UUI episodes/day. Secondary endpoints included UUI episodes/week, urgency severity associated with voids, volume voided/void, frequency of daily urgency voids, and OAB-Symptom Composite Score. Safety parameters collected during the study included clinical laboratory tests, 12-lead electrocardiograms, spontaneously reported adverse events, and vital signs.

Results
A total of 601 participants were randomized to receive trospium QD (n=298) or placebo (n=303). Trospium QD was associated with statistically significant improvements in both primary efficacy outcomes from as early as Week 1, with progressive improvement to Week 12. Subjects treated with trospium QD experienced a reduction in the mean number of daily voids from 12.8 at baseline to <10 at Week 12 ($p<0.001$). Similarly, subjects treated with trospium QD experienced a reduction in the mean number of daily UUI episodes from 4.1 at baseline to 1.6 at Week 12 ($p<0.01$). These improvements in the primary efficacy outcomes were reflected in the analysis of “normalization” (defined as no UUI episodes and a void frequency of ≤8 voids/day), such that nearly twice as many subjects treated with trospium QD (20.5%) achieved “normalization” at Week 12 ($p<0.01$) compared with those receiving placebo (11.3%). Treatment with trospium QD also resulted in significant benefits compared with placebo in the secondary outcome parameters as early as Week 1 onwards. Trospium QD was well tolerated. Dry mouth was reported in 8.7% versus 3% and constipation in 9.4% versus 1.3% of subjects administered trospium QD versus placebo, respectively. Central nervous system adverse events occurred rarely in both the placebo and trospium QD groups (dizziness, 1.3% vs 0.3%; headache, 2.6% vs 1.0%, respectively).

Interpretation of results
Trospium QD provided early and sustained improvements in the key symptoms of OAB. Typical anticholinergic adverse events, particularly dry mouth, occurred at considerably lower levels with trospium QD than reported previously with twice-daily (BID) trospium, while efficacy was maintained with the new formulation.

Concluding message
These data, coupled with the convenience of a once daily dosing regimen, suggest that this new formulation of trospium chloride is an effective treatment option for patients suffering from OAB. In this study, trospium QD demonstrated the lowest dry mouth rate of any current oral medication for OAB.

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CLINICAL TRIAL REGISTRATION: This clinical trial has not yet been registered in a public clinical trials registry.
HUMAN SUBJECTS: This study was approved by the IRB of first author (multicenter study): Evanston Northwestern Healthcare and followed the Declaration of Helsinki Informed consent was obtained from the patients.