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THE EFFICACY AND TOLERABILITY OF TARAFENACIN, A NEW MUSCARINIC ACETYLCHOLINE RECEPTOR M3 ANTAGONIST IN PATIENTS WITH OVERACTIVE BLADDER; RANDOMIZED, DOUBLE- BLIND, PLACEBO-CONTROLLED PHASE 2 STUDY

Hypothesis / aims of study

To evaluate the dose-response relationship of tarafenacin, an antimuscarinic agent in development phase, for efficacy and safety, at daily doses of 0.2mg and 0.4mg for the treatment of overactive bladder (OAB)

Study design, materials and methods

This multi-center, placebo-controlled, randomized, double-blind, phase 2b study was conducted at 8 centers in Korea. After 2-week single blind placebo run-in period, patients were randomized to one of the 3 treatment groups; tarafenacin 0.2mg, tarafenacin 0.4mg or placebo daily for 12 weeks. Adult patients with symptomatic OAB for at least 6 months, with an average of ≥ 8 micturitions/day and ≥ 3 incontinence episodes or a total of ≥ 6 urgency episodes/3days in the patient diary were enrolled. The primary objective was to compare the mean changes in the number of micturitions/24 hours of the two doses of tarafenacin compared to placebo from baseline to 12 weeks after treatment.

Results

A total of 334 patients were screened, of whom 235 patients were randomized. The mean decrease in the number of micturitions/24 hours from baseline to 12 weeks was statistically higher in the tarafenacin 0.4mg group (-2.43 ± 2.21 times/day, $p=0.0331$) and non-statistically significant in the tarafenacin 0.2mg group (-1.92 ± 2.45 times/day, $p=0.3929$) when compared to the placebo group (-1.77 ± 2.95 times/day). The mean changes in the number of micturitions/24 hours after 4 weeks of treatment showed a statistically higher decrease in both tarafenacin groups with respect to placebo (both $p<0.01$). There were no statistically significant differences in the mean change of urgency episodes/24hours at 12 weeks among 3 groups (tarafenacin 0.4mg: -3.42 ± 3.93 , tarafenacin 0.2mg: -3.08 ± 3.71 , placebo: -2.68 ± 4.00). Like other antimuscarinic drugs, the most common adverse event (AE) was dry mouth (64.2% in tarafenacin 0.4mg, 32.9% in tarafenacin 0.2mg and 16.0% in placebo). The great majority of these AEs were mild.

Interpretation of results

In this phase 2 study, dose-response relationship of tarafenacin 0.2 mg and 0.4 mg was assessed for efficacy and tolerability. The tarafenacin 0.4 mg group was identified to be superior to the placebo group in terms of the primary efficacy endpoint, the mean change at 12 weeks in the number of micturitions per 24 hours from baseline. There were no significant differences in blurred vision and constipation compared to placebo. Interestingly, the incidence rate of constipation was remarkably advanced from the other anti-muscarinic drugs.

Concluding message

Tarafenacin 0.2mg and 0.4mg decreased the number of micturitions in patients with symptomatic OAB after 12 weeks of treatment comparing placebo, and the dose-response relationship of tarafenacin 0.2 mg and 0.4 mg for efficacy and tolerability was confirmed in this study. Both dose levels of tarafenacin were well tolerated.

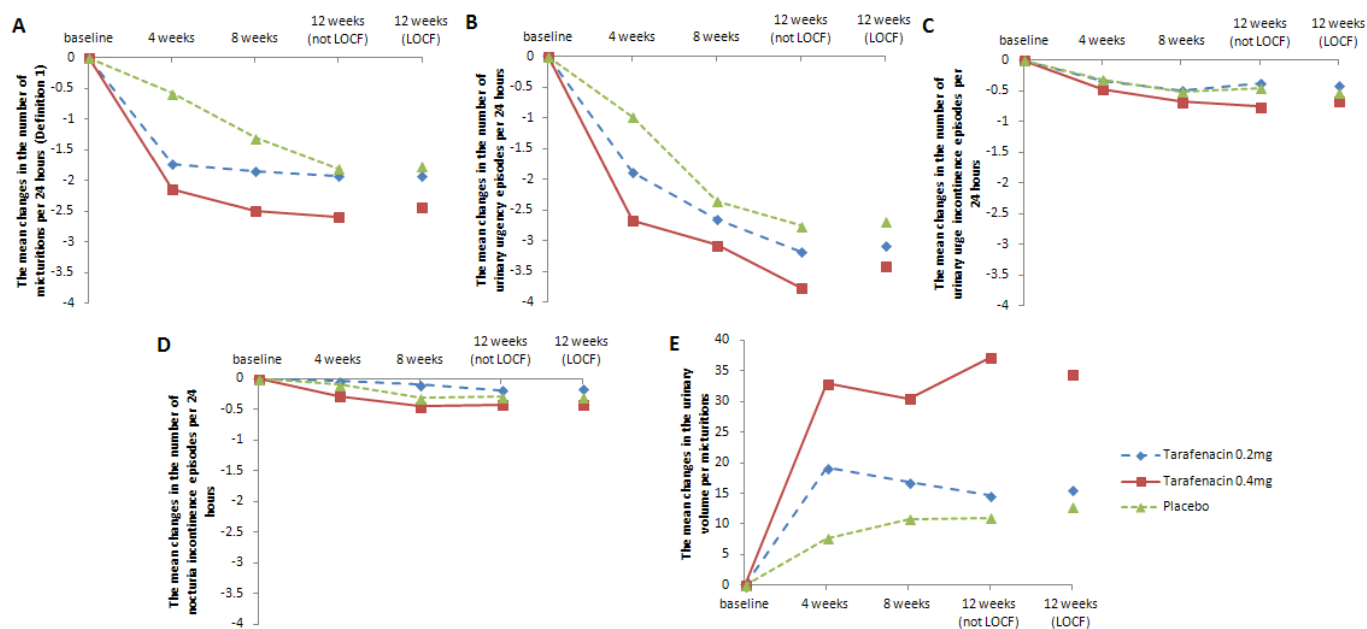


Figure 1. (A) The mean changes in the number of micturitions per 24 hours (B) The mean changes in the number of urinary urgency episodes per 24 hours (C) The mean changes in the number of urinary urge incontinence episodes per 24 hours (D) The mean changes in the number of nocturia incontinence episodes per 24 hours (E) The mean changes in the urinary volume per micturitions

Disclosures

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IRB number 20110513 **RCT:** Yes **Subjects:** HUMAN **Ethics Committee:** Asan **IRB number** 20110513 **Helsinki:** Yes **Informed Consent:** Yes