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CLINICAL EFFICACY AND SAFETY OF A BETA3-ADRENOCEPTOR AGONIST (MIRABEGRON) AND AN ANTIMUSCARINIC AGENT (IMIDAFENACIN) IN FEMALE PATIENTS WITH OVERACTIVE BLADDER: A RANDOMIZED CROSSOVER STUDY.

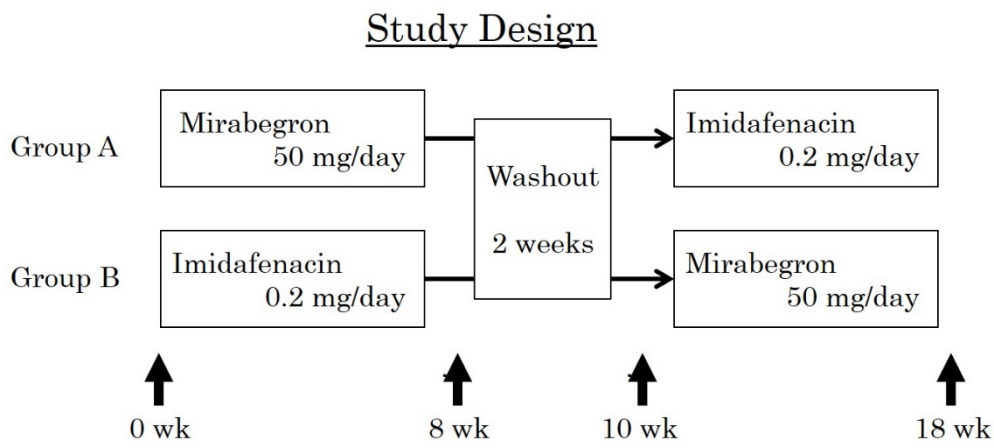
Hypothesis / aims of study
Antimuscarinic agents have been mainly used to treat overactive bladder. A beta-3 adrenoceptor agonist was newly developed and approved by the Ministry of Health, Labour and Welfare in July, 2011. We conducted a randomized crossover multi-institutional study to investigate the clinical efficacy and safety of antimuscarinic agents and a beta-3 adrenoceptor agonist.

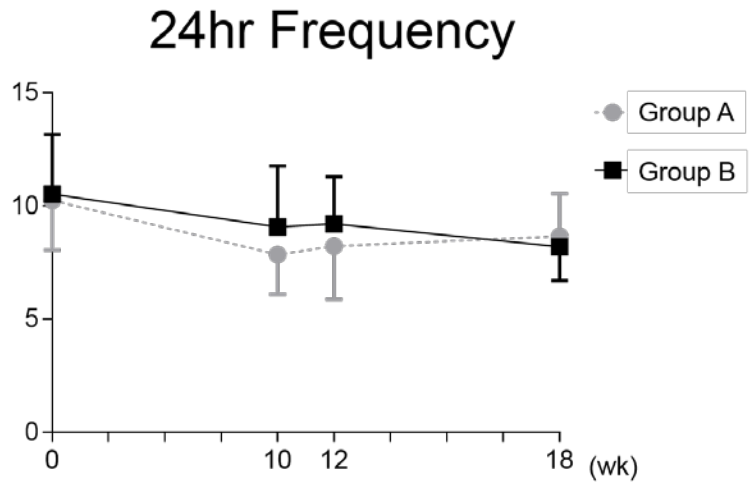
Study design, materials and methods
We included female patients with overactive bladder and randomly divided them into two groups using the enveloped method. In Group A, we administered daily mirabegron (50 mg) for 8 weeks, followed by a 2-week washout period and daily administered imidafenacin (0.2 mg) for another 8 weeks. In Group B, we administered daily imidafenacin (0.2 mg) for 8 weeks, followed by a 2-week washout period and daily mirabegron (50 mg) for a further 8 weeks. Each subject recorded 3-day frequency volume charts and overactive bladder symptom scores (OABSSs) at 0, 8, 10, and 18 weeks after the start of the study. We compared the change from 0 to 8 weeks with the change 10 to 18 weeks and calculated the period effect, carry-over effect, and treatment effect. We compared the change in the first period (0 to 8 weeks) to evaluate treatment effect if either medicine showed a period effect or carry-over effect. In addition, we compared adverse effects of dry mouth, constipation, and misty vision between mirabegron and imidafenacin. We evaluated these adverse effects with the faces scale modified from Faces Pain Rating Scale, comparing the scales before and after administration. All values were expressed mean ± SD. The Mann–Whitney *U* test was used to analyze statistical significance. Differences were considered to be significant at $p < 0.05$.

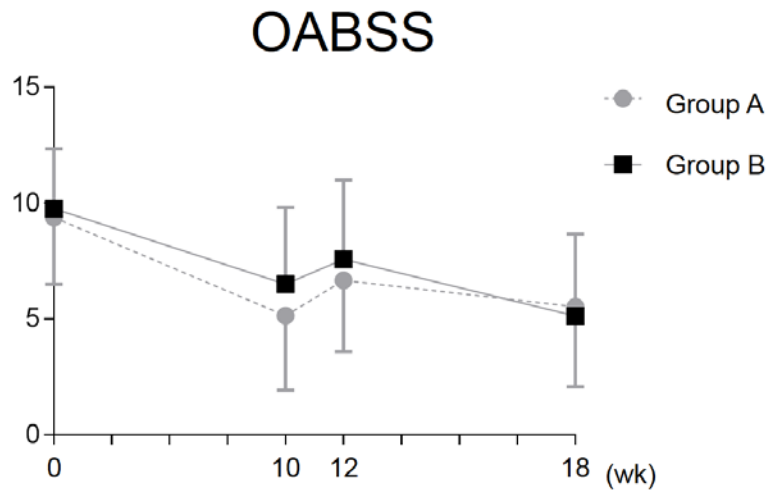
Results
We enrolled 40 subjects whose mean age was 66.0 ± 10.4 in Group A and 40 subjects whose mean age was 68.0±10.2 in Group B. Finally we analyzed the data of 30 subjects in Group A and 34 subjects in Group B. [24-hour frequency] Mirabegron had period effect because the decrease of 24-hour frequency was significantly greater at 0-8 weeks than 10-18 weeks (-2.3 ± 1.9 *vs.* -1.1 ± 1.4, $p = 0.0179$), but no carry-over effect. Imidafenacin had neither period effect nor carry-over effect. Therefore, we compared the change of medicines only in the first period to evaluate treatment effect, demonstrating no difference between the medicines. [OABSS] Both of the medicines had neither period effect nor carry-over effect. Therefore, we compared the change of medicines in the first and second period to evaluate treatment effect, demonstrating no difference between the medicines. [Adverse effects] Imidafenacin significantly increased the rate of dry mouth, but mirabegron did not (0.77 ± 1.48 *vs.* -0.10 ± 1.14, $p = 0.0002$). Age was not correlated with the prevalence of dry mouth at the start of the study and the incidence of dry mouth after medicine administration. Both medicines did not significantly increase the rates of constipation or misty vision.

Interpretation of results
Mirabegron (50 mg/day) was as effective in treating overactive bladder as imidafenacin (0.2 mg/day). Imidafenacin caused dry mouth as part of antimuscarinic effects, but mirabegron did not.

Concluding message
The beta-3 adrenoceptor agonist mirabegron, and the antimuscarinic agent imidafenacin have the same efficacy in female patients with overactive bladder. Imidafenacin causes a higher rate of dry mouth than mirabegron.







Disclosures
Funding: Astellas Pharma Inc. **Clinical Trial:** Yes **Registration Number:** University hospital Medical Information Network (UMIN) Center, UMIN000010060 **RCT:** Yes **Subjects:** HUMAN **Ethics Committee:** Ethics Committee of Nara Medical University **Helsinki:** Yes **Informed Consent:** Yes