A Phase III, Randomized, Double-Blind, Placebo and Active Controlled Study of Once-Daily Mirabegron 50 mg in Patients with Overactive Bladder

Introduction and Objective: Mirabegron is a potent and selective β_3-adrenoceptor agonist for the treatment of overactive bladder (OAB) with a mechanism of action distinct from anti-muscarinics; we report efficacy and tolerability data from a Japanese Phase III trial.

Materials and Methods: This randomized, double-blind, placebo- and tolterodine-controlled, multicenter study enrolled adult patients with OAB symptoms for ≥24 weeks. Patients with ≥8 micturitions/24 h and ≥1 urgency or urgency incontinence episode/24 h were randomized to once-daily placebo, mirabegron 50 mg, tolterodine 4 mg for 12 weeks. Primary endpoint was change from baseline to end of treatment in mean number of micturition episodes/24 h. Secondary endpoints included change from baseline to end of treatment in mean number of urgency episodes/24 h, urinary incontinence episodes/24 h, urgency incontinence episodes/24 h, and QoL domain scores on the King's Health Questionnaire. Safety assessments included adverse events (AEs), laboratory parameters, vital signs, ECG, post void residual volume.

Results: A total of 1139 patients were randomized into 3 groups (placebo: n=381; mirabegron: n=380; tolterodine: n=378 [results not presented]). Demographic and baseline characteristics were similar for all groups. At study end, mirabegron showed significant improvements versus placebo in mean number of: micturitions, urgency episodes, incontinence episodes, and urgency incontinence episodes, and also in volume voided/micturition (Table) and in QoL domain scores. The incidence of AEs in the mirabegron group was similar to the placebo group. Most AEs in the mirabegron group were mild; none were severe. The incidence of individual AEs – including cardiovascular or antimuscarinic AEs – was low and similar to placebo. The incidence of dry mouth was low and similar in the mirabegron (2.6%) and placebo groups (2.9%).

Conclusion: Mirabegron demonstrated significant improvements compared with placebo in OAB symptoms and was well tolerated. Mirabegron provides clinicians with a new approach to treat OAB patients.

Mean change from baseline to end of treatment	**Placebo**	**Mirabegron 50 mg**
Number of micturitions/24 h	–0.86 (2.35)	–1.67 (2.21)*
Number of urgency episodes/24 h	–1.37 (3.19)	–1.85 (2.56)*
Number of incontinence episodes/24 h	–0.66 (1.86)	–1.12 (1.48)*
Number of urgency incontinence episodes/24 h	–0.60 (1.75)	–1.01 (1.34)*
Number of nocturia episodes/24 h	–0.36 (1.06)	–0.44 (0.93)
Mean volume voided/micturition (mL)	9.72 (29.09)	24. 30 (35.48)*
Data are mean (SD). *P<0.05		