Urodynamic Safety of the Potent and Selective β3-adrenoceptor Agonist, Mirabegron, in Males with Lower Urinary Tract Symptoms and Bladder Outlet Obstruction

Introduction and Objectives: Many men with bladder outlet obstruction (BOO) also experience overactive bladder symptoms. Mirabegron selectively enhances storage of urine during bladder filling by stimulating β3-adrenoceptors. This study aimed to evaluate the urodynamic safety of the potent and selective β3-adrenoceptor agonist, mirabegron, in males with lower urinary tract symptoms (LUTS) and BOO.
Materials and Methods: In this multicenter, double-blind, parallel-group, placebo-controlled Phase II study, males ≥45 years with LUTS for ≥3 months, BOO index ≥20, and maximum urinary flow rate (Q_{max}) ≤12 mL/sec with a voided volume of ≥120 mL during free flow were randomized 1:1:1 to receive once-daily oral mirabegron 50 or 100 mg, or placebo for 12 weeks. Primary variables were changed from Baseline to End of Treatment in Q_{max} and detrusor pressure at Q_{max} ($P_{det}Q_{max}$). Non-inferiority of mirabegron to placebo was demonstrated if the two-sided 95% CI lower limit for treatment difference was >–3 mL/sec for Q_{max}, and the upper limit was <15 cmH_2O for $P_{det}Q_{max}$.
Results: There were 200 patients who were randomized and received study drug or placebo. Demographic and baseline characteristics were similar between groups. Both mirabegron doses were non-inferior to placebo in Q_{max} and $P_{det}Q_{max}$. Adjusted mean change (SE; 95% CI for difference from placebo) from Baseline in Q_{max} (mL/sec) was –0.33 (0.370) for placebo, 0.07 (0.366; –0.63, 1.42) for mirabegron 50 mg, and 0.30 (0.388; –0.43, 1.68) for mirabegron 100 mg; $P_{det}Q_{max}$ (cmH_2O) was 2.92 (2.906), –3.03 (2.872; –13.98, 2.09), and 1.53 (3.086; –9.73, 6.96), respectively. Mean change from Baseline in Bladder Contractile Index (BCI) was not significantly different between mirabegron 50 or 100 mg and placebo. At End of Treatment, adjusted mean change in post-void residual volume from Baseline was only significantly different from placebo with mirabegron 100 mg (p=0.0459); however, this was not considered clinically meaningful. Treatment emergent adverse events (TEAEs) occurred in 43.1%, 40.0%, and 52.3% of patients on placebo, mirabegron 50 mg, and 100 mg, respectively. One patient each on placebo (catheterization required) and mirabegron 100 mg (no invasive intervention required) had a urinary retention TEAE; no serious TEAEs or deaths occurred.
Conclusions: Mirabegron did not affect the voiding urodynamics or bladder contractility index after 12 weeks of treatment in a male population with comorbid LUTS/BOO