

## URODYNAMIC EFFICACY AND SAFETY OF MIRABEGRON FOR MALE PATIENTS WITH OVERACTIVE BLADDER: A PROSPECTIVE PRESSURE-FLOW STUDY

### Hypothesis / aims of study

Mirabegron, a new class of agent for treating overactive bladder (OAB), enhances relaxation of the bladder and increases bladder capacity by acting on adrenergic  $\beta_3$  receptor in the bladder. This agent is thought not to impair bladder contraction during voiding. In this study we investigated urodynamic efficacy and safety of mirabegron for male patients with OAB.

### Study design, materials and methods

A prospective study was conducted in consecutive 21 male patients with OAB who had been receiving tamsulosin. OAB was determined by overactive bladder symptom score (OABSS); Q3 (urgency) score  $\geq 2$  and total score of OABSS  $\geq 3$ . Before and 8 weeks after mirabegron (50 mg daily) add-on treatment with preceding tamsulosin, we assessed OABSS, International Prostate Symptom Score (IPSS), free uroflowmetry (UFM), filling cystometry and PFS.

### Results

Mean age and prostatic volume of the study patients were  $76.3 \pm 6.6$  years and  $31 \pm 19$  ml, respectively. Mirabegron significantly improved total score of OABSS (from  $9.0 \pm 2.3$  to  $4.9 \pm 2.6$ ) and each subscore (Q1; urinary frequency, Q2; nocturia, Q3; urgency, Q4; urgency incontinence) of OABSS. IPSS (from  $13.9 \pm 5.0$  to  $9.2 \pm 4.9$ ), voiding symptom subscore (from  $4.7 \pm 3.2$  to  $3.5 \pm 2.5$ ), storage symptom subscore of IPSS (from  $7.8 \pm 2.7$  to  $4.7 \pm 2.0$ ) and QoL index (from  $4.1 \pm 0.9$  to  $2.6 \pm 1.2$ ) were also significantly improved after mirabegron.

On free UFM, mirabegron significantly increased maximum flow rate (from  $10.9 \pm 4.1$  to  $14.0 \pm 7.0$  ml/sec) and average flow rate (from  $5.4 \pm 2.2$  to  $7.3 \pm 3.6$  ml/sec), while postvoid residual urine volume (PVR) (from  $49 \pm 31$  to  $68 \pm 65$  ml) and PVR rate ( $\{PVR / [PVR + voided volume]\} \times 100\%$ ) (from  $27 \pm 14$  to  $27 \pm 22\%$ ) did not change significantly. Voided volume tended to increase from  $134 \pm 49$  to  $176 \pm 108$  ml ( $P=0.06$ ).

Before mirabegron, all study patients had detrusor overactivity (DO) on filling cystometry. After mirabegron, DO disappeared in 4 patients (19%). In the other 17 patients, the decrease in the amplitude of DO (from  $56 \pm 27$  to  $49 \pm 30$  cmH<sub>2</sub>O) did not reach statistical significance, however, bladder capacity at the time of initial DO (from  $94 \pm 75$  to  $134 \pm 82$  ml) significantly increased. Maximum cystometric capacity did not change significantly after mirabegron (from  $166 \pm 90$  to  $200 \pm 88$  ml). On PFS, detrusor pressure at maximum flow rate (from  $73 \pm 30$  to  $64 \pm 18$  cmH<sub>2</sub>O) or bladder contractility index (from  $120 \pm 39$  to  $117 \pm 26$ ) did not change significantly.

### Interpretation of results

Mirabegron significantly improved OAB symptoms in male patients and concurrently improved maximum flow rate possibly through a significant increase in voided volume. Although DO disappeared in some patients, the improvement of storage symptom was not associated with significant change in urodynamic parameters of bladder storage function. No significant changes in PVR, PVR rate, or bladder contractility index after mirabegron imply that this drug does not affect bladder contraction during voiding. However, the study duration was only 8 weeks and we need a further study with long-term treatment.

### Concluding message

Mirabegron can improve storage symptom without impairment of bladder contraction during voiding in male OAB patients treated with alpha blocker.

|  | Before mirabegron | After mirabegron | P value |
|--|-------------------|------------------|---------|
| OABSS  | 9.0±2.3           | 4.9±2.6          | <0.01   |
| IPSS   | 13.9±5.0          | 9.2±4.9          | <0.01   |
| Voiding symptom score  | 4.7±3.2           | 3.5±2.5          | <0.05   |
| Storage symptom score  | 7.8±2.7           | 4.7±2.0          | <0.01   |
| QOL index  | 4.1±0.9           | 2.6±1.2          | <0.01   |
| <b>Free uroflowmetry</b>   |                   |                  |         |
| Voided volume (ml)   | 134±49            | 176±108          | 0.06    |
| Free Qmax (ml/sec)   | 10.9±4.1          | 14.0±7.0         | 0.01    |
| Free Qave (ml/sec)   | 5.4±2.2           | 7.3±3.6          | <0.01   |
| Postvoid residual (ml)   | 49±31             | 68±65            | 0.24    |
| Rate of postvoid residual (%)  | 27±14             | 27±22            | 0.90    |
| <b>Filling cystometry and pressure-flow study</b>  |                   |                  |         |
| Maximum cystometric capacity (ml)  | 166±90            | 200±88           | 0.09    |
| Prevalence of DO (%)   | 100               | 81               | <0.05   |
| Amplitude of DO (cmH <sub>2</sub> O)   | 56±27             | 49±30            | 0.30    |
| Bladder capacity at the time initial DO (ml)   | 94±75             | 134±82           | <0.05   |
| Detrusor pressure at Qmax (cmH <sub>2</sub> O)   | 73±30             | 64±18            | 0.13    |
| Qmax (ml/sec)  | 9.2±3.4           | 10.5±4.2         | 0.06    |
| Bladder contractility index  | 120±39            | 117±26           | 0.70    |
| OABSS: overactive bladder symptom score IPSS: international prostate symptom score                   |                   |                  |         |
| Qmax: maximum flow rate Qave: average flow rate DO: detrusor overactivity                            |                   |                  |         |
| Using the Wilcoxon matched-pairs signet-ranks test except for prevalence of DO using Chi-square test |                   |                  |         |

#### Disclosures

**Funding:** no **Clinical Trial:** No **Subjects:** HUMAN **Ethics Committee:** Ethics committee of Asahikawa Medical University  
**Helsinki:** Yes **Informed Consent:** Yes