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THERAPEUTIC ADDING EFFECT OF MIRABEGRON 50 MG IN ASIAN OAB PATIENTS AFTER INITIAL TREATMENT OF MIRABEGRON 25 MG – A RANDOMIZED CLINICAL TRIAL

Hypothesis / aims of study
Mirabegron is the first β3-adrenoceptor agonist for overactive bladder (OAB) patients in clinical practice, and 50 mg is the most common used daily dose. In contrast to other countries, the suggested initial dose is 25 mg daily in Taiwan. We conducted a randomized trial investigating the therapeutic adding effect of mirabegron 50 mg in OAB patients after initial treatment of mirabegron 25 mg.

Study design, materials and methods
Male patients aged ≥20 years with symptoms of OAB (an average of ≥8 micturitions and an average of ≥1 episode of urgency or urgency incontinence per 24-hours) for at least 12 weeks were enrolled. Patients were randomized into 2 groups. Patients in the first group received mirabegron 25mg once-daily for 4 weeks, and continue the same dose for another 8 weeks. Patients in the second group received mirabegron 25mg once-daily for 4 weeks, and increase the dose to 50mg for another 8 weeks. The treatment results were assessed by using overactive bladder symptom score (OAB-SS), patient perception on intensity of urgency scale (PPIUS), international prostate symptom score (IPSS) storage subscore (IPSS-S), patient perception of bladder condition (PPBC), and quality of life index (QoL-I) at 4 and 12 weeks after treatment. All the adverse events (AEs) were also recorded. Primary end-point was comparison the treatment results between groups. Wilcoxon signed-rank tests were used to compare parameters before and after treatment.

Results
Of the 266 enrolled patients (mean age, 69.0 years), 134 patients were randomized to 25 mg group while 132 patients were randomized to 50 mg group. The demographic and baseline parameters were similar between groups. Table 1 showed parameters before and after mirabegron treatment. The OAB-SS, PPIUS, IPSS-S, PPBC, and QoL-I improved significantly at 4 weeks and 12 weeks after mirabegron treatment in both groups. Further improvement of OAB-SS and IPSS-S from 4 weeks to 12 weeks could only be seen in patients receiving 50 mg mirbegron after initial 25 mg mirabegron. In void diary, the improvement of daily micturition episodes at daytime and urgency episode could be found at 12 weeks after treatment in both groups. There was no significant change of nocturia episodes after treatment. The improvement of daily UUI episode could only be found in patients receiving 50 mg mirabegron. Adding dose to 50 mg could result in further improvement of daily urgency and UUI episodes from 4 to 12 weeks after mirabegron treatment (Figure 1). There were no significant changes of maximum flow rate (Qmax) and post-void residual (PVR) after treatment. Increased voided volume could be found at 4 and 12 weeks after mirabegron treatment in both groups. All the AEs were mild and tolerable. The rate of AEs was similar between groups.

Interpretation of resuls
Our results showed that treatment with 25 mg mirabegron could result in improvement of OAB symptoms in Asian population. Adding dose of mirabegron to 50 mg could further improves daily urgency and UUI episode even patients were satisfied with 25 mg mirabegron. There was no significant difference of rate of AEs and PVR after treatment between groups.

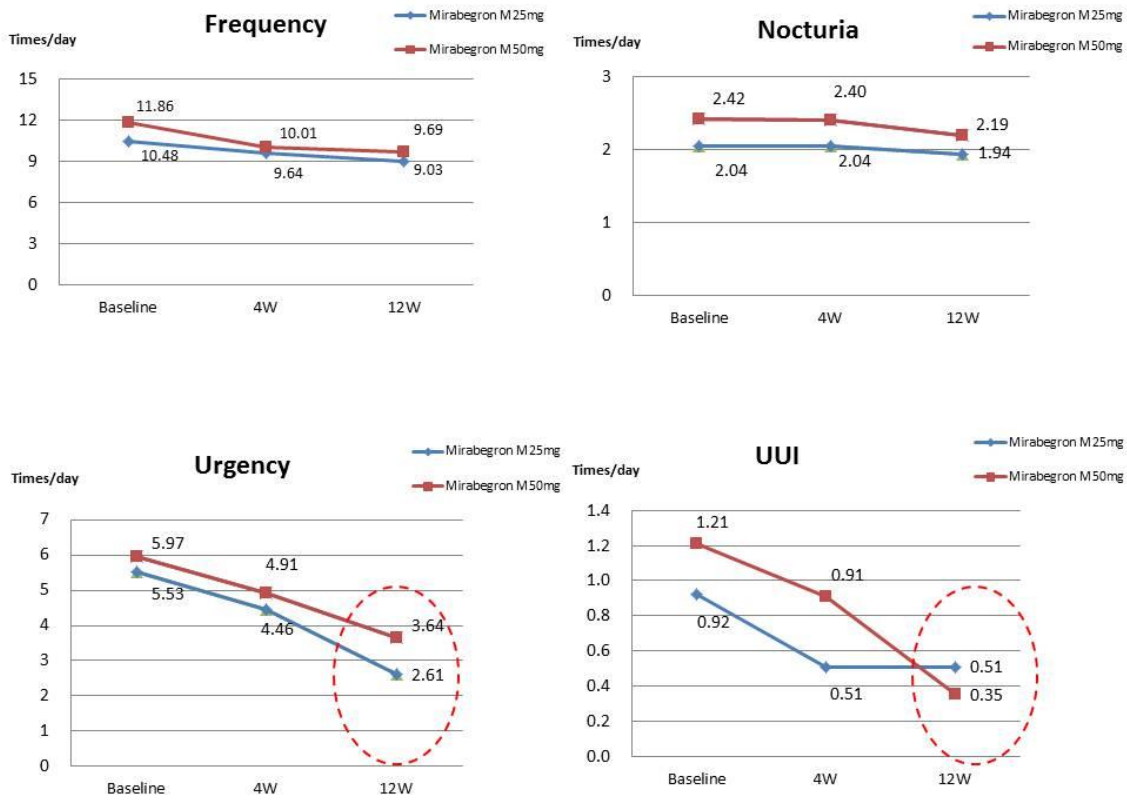
Concluding message
For patients receiving daily 25 mg of mirabegron for 4 weeks, adding dose to 50 mg could result in further improvement of daily urgency and UUI episodes. The safety and tolerability were similar between patients receiving 25 mg and 50 mg mirabegron. We suggested that although 25 mg mirabegron daily is safe and effective for Asian OAB population, 50 mg of mirabegron daily is a more optimal dose for those with severe urgency or UUI episodes.

Table 1 Comparisons of parameters before and after mirabegron treatment

		Baseline	4 weeks	12 weeks
OAB-SS	25 mg	8.7 ± 3.6	6.2 ± 3.3*	5.5 ± 3.1*
	25 mg-50 mg	9.4 ± 3.4	7.1 ± 3.5*	6.2 ± 3.6*#
PPIUS	25 mg	3.0 ± 1.5	2.0 ± 1.6*	1.6 ± 1.7*
	25 mg-50 mg	3.3 ± 1.2	2.1 ± 1.6*	1.8 ± 1.6*
IPSS-S	25 mg	7.8 ± 3.5	5.3 ± 2.6*	5.0 ± 2.6*
	25 mg-50 mg	9.4 ± 3.2	7.0 ± 3.5*	5.4 ± 3.2*#
PPBC	25 mg	2.5 ± 1.6	1.9 ± 1.5*	1.2 ± 1.4*
	25 mg-50 mg	2.8 ± 1.6	1.8 ± 1.7*	1.7 ± 1.7*
QoL-I	25 mg	3.9 ± 1.4	2.2 ± 1.2*	1.7 ± 1.2*
	25 mg-50 mg	4.0 ± 1.5	2.4 ± 1.6*	2.1 ± 1.5*
Daytime/day	25 mg	10.4 ± 4.1	9.6 ± 6.5	9.0 ± 3.8*
	25 mg-50 mg	11.8 ± 4.9	10.1 ± 5.2	9.6 ± 4.1*
Nocturia/day	25 mg	2.0 ± 1.6	2.0 ± 1.8	1.9 ± 1.4
	25 mg-50 mg	2.4 ± 1.7	2.4 ± 2.1	2.1 ± 1.6
Urgency/day	25 mg	5.3 ± 5.8	4.4 ± 2.6	2.6 ± 4.3*
	25 mg-50 mg	5.9 ± 7.2	4.9 ± 6.5	3.6 ± 5.8*#
UUI/day	25 mg	0.9 ± 2.3	0.5 ± 2.3	0.5 ± 1.7
	25 mg-50 mg	1.2 ± 3.7	0.9 ± 0.3	0.3 ± 0.9*#
Qmax	25 mg	14.8 ± 9.5	15.1 ± 10.7	14.0 ± 9.0
	25 mg-50 mg	12.4 ± 8.6	14.1 ± 8.5	14.7 ± 8.6
Volume	25 mg	171.0 ± 128.1	194. 8 ± 136.5*	219.1 ± 146.3*
	25 mg-50 mg	154.9 ± 105.7	194.0 ± 109.0*	201.2 ± 121.9*
PVR	25 mg	40.0 ± 53.8	43.7 ± 54.3	49.2 ± 51.4
	25 mg-50 mg	38.3 ± 40.9	40.3 ± 51.6	42.6 ± 63.5

*P<0.05 when comparison with baseline parameters
#p<0.05 when comparison between parameters at 4 weeks and 12 weeks after treatment

Figure 1. Comparisons of the parameters changed in voiding diary



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