

INVESTIGATION OF AVAILABILITY OF ANTI-CHOLINERGIC DRUG IN FEMALE OVERACTIVE BLADDER PATIENTS WITH INSUFFICIENT EFFECT OF β_3 RECEPTOR AGONIST -SWITCHING STUDY FROM MIRABEGRON TO SOLIFENACIN- WATCH (WOMAN AVAILABILITY TRIAL BY CHANGING FROM MIRABEGRON TO SOLIFENACIN) STUDY

Hypothesis / aims of study

Mirabegron, β_3 receptor agonist with the new mechanism of action, was authorized as a new therapeutic drug for the overactive bladder (OAB) in Japan in 2011. Although the mirabegron has been considered superior in the efficacy as well as the safety since then, insufficient effects among some patients treated by the drug have been also reported frequently. For those patients, the administration of anti-cholinergic drug was empirically considered effective and is currently practiced in general. However, as far as we know, only few studies prospectively examined the efficacy as well as the safety of the treatment.

Thus, we designed an original cohort study to prospectively investigate the efficacy and safety of the treatment of solifenacin (anti-cholinergic drug) for female OAB patients who experienced insufficient effects with the mirabegron as a first line treatment.

Study design, materials and methods

This study is a single arm, multicenter, open label study.

This study was reviewed and approved by central Ethics Committee (NPO Clinical Research Network Fukuoka) and each institutional review board. All patients provided signed informed consent prior to the start of the study.

Female OAB patients who met the following three conditions were the subjects of the study: (1) Overactive Bladder Symptom Score (OABSS) ≥ 3 , (2) urgency score (OABSS) ≥ 2 and (3) QOL score ≥ 4 .

The primary endpoint was the difference of the total OABSS score between the baseline (0w) and the last (12w) observation. To avoid the effects of "the regression to the mean" phenomena, the OABSS was obtained at an examination within 4 weeks before the enrollment (-4w) besides that on the day of enrolment (0w) and the patients who met the three conditions in both examinations were considered eligible.

The results of questionnaires (at -4w, 0w, 4w, 8w and 12w) on OABSS and International Prostate Symptom Score/Quality of Life (IPSS/QOL), frequency volume chart (FVC) (at 0w, 4w and 12w), post-void residual urine (PVR) (at 0w, 4w, 8w and 12w) and adverse event (at 4w, 8w and 12w) were investigated. To avoid possible biases due to drop-out of a few patients before 12w, a generally performed measure so-called LOCF (Last observation carried forward) was applied.

Results

Twenty seven subjects (mean age: 72) were enrolled during Dec, 2013 and Mar, 2015 in five sites. All subjects were considered for the safety but 26 subjects, excluding 1 non-eligible patient, were statistically analysed for the efficacy. The mean (SD) of the Total OABSS at 0w, 4w, 8w and 12w was 8.2 (1.6), 5.8 (2.8), 5.6 (2.7) and 5.4 (2.9), respectively. The mean (SD) of the IPSS-QOL index at 0w, 4w, 8w and 12w were 4.8 (0.7), 2.9 (1.6), 2.7 (1.8) and 2.6 (1.9), respectively. Significant improvements in Total OABSS score and IPSS-QOL index at 4w, 8w and 12w from 0w were confirmed. As for the OABSS sub-scores, significant improvements were observed on the urinary urgency at 4w-12w, nocturia at 8w-12w and urgent urinary incontinence at 12w. The proportion (%) of patients with disease severity was moderate 96% and mild 4% at 0w, moderate 58% and mild 52% at 4w, moderate 58% and mild 42% at 8w and moderate 50% and mild 50% at 12w. According to the results of the OABSS, the proportion of patients with OAB improved was 44% and 47% at 4w and 12w, respectively and those with urgent urinary incontinence (OABSS: Q4 ≥ 1) were 65%, 48% and 42% at 0w, 4w and 12w, respectively. The analysis of FVC revealed significant improvements for the mean daytime urination, urination quantity, urinary urgent frequency and urgent urinary incontinence frequency at 4w and 12w. It is also verified with FVC that the proportion of the patients with urgent urinary incontinence was 46% at 0w, 33% at 4w and 21% at 12w. The residual urine volume after changing to solifenacin was not increased significantly. As for adverse events, the number of subjects (%) of the dry mouth, visual disorder such as blurred vision and constipation were 14 (52%), 6 (22%) and 2 (7%), respectively.

Interpretation of results

The significant improvement effects in total OABSS score were observed immediately from 4 weeks after solifenacin administration and the effect of solifenacin continued after that. It was considered that the effect on urinary urgency greatly contributed to an effect on total OABSS score in female patients.

Concluding message

The change therapy with anti-cholinergic drug (solifenacin) for female OAB patients that improvement effect of β_3 receptor agonist was insufficient was suggested to be the choice that enough efficacies could be expected.

Disclosures

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