
Methods and Materials

• This was a prospective, multicentre, open-label study conducted at 12 sites.

• Registration started in August 2016 and ended in April 2019.

• The study was performed in accordance with the International Conference on Harmonization Good Clinical Practice and the Declaration of Helsinki.

• The study was conducted in accordance with a protocol approved by the institutional ethics committee for clinical trials, and written informed consent was obtained from all patients.

• The total duration of the study was 8 weeks. Participants were recruited from the regular urology patients at each study site.

• Patients meeting the following criteria were included in this study: aged ≥50 years, diagnosed as having lower urinary tract symptoms due to bladder outlet obstruction, and had persistent storage symptoms after treatment with tadalafil (5 mg/day).

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• The treatment was deemed ineffective in patients when the OABSS question 3 score was ≥2 points and a total OABSS of ≥3 points, and an international prostate symptom (IPSS) question 7 score ≥2 points.

• The criteria for withdrawal from the study were as follows: request for withdrawal from the patient, no clinic visit, difficulty in assessing the adverse events or data set, or death or dropout.

• The IPSS is a validated, self-administered questionnaire that assesses lower urinary tract symptoms associated with BPH. It is composed of 7 questions, each scored on a scale of 0–5.

• The maximum possible score is 35, with higher scores indicating more severe symptoms.

• The IPSS voiding score assesses symptoms related to the need to void, such as frequency, urgency, and hesitancy.

• The IPSS storage score assesses symptoms related to bladder fullness, such as nocturia and the need to store urine.

• The IPSS QOL score assesses the impact of lower urinary tract symptoms on quality of life.

• The OAB-q is a validated, self-administered questionnaire that assesses OAB symptoms, including urgency with urinary frequency, nocturia, and sometimes urgency incontinence.

• The N-QOL is a validated, self-administered questionnaire that assesses the impact of lower urinary tract symptoms on quality of life.

• The combination group was defined as patients who received both tadalafil and mirabegron, while the monotherapy group was defined as patients who received tadalafil alone.

• The data were compared using the paired and unpaired t-test and McNemar’s test.

• A limitation of the present study was that efficacy endpoints were based on changes from the baseline. In addition, this study might not be sufficiently large enough to show small differences in outcomes. A placebo-controlled study would be necessary to elucidate the true efficacy profile of mirabegron as an add-on treatment.

References


Figure 1. Patient demographic and other baseline characteristics.

Table 1.

Table 2.

Figure 2. Mean post-void residual (PVR) volume in the two groups during the treatment period: monotherapy, combination.

Figure 3. Mean post-void residual (PVR) volume in the two groups during the treatment period: monotherapy, combination.

Discussion

• The present study was conducted to evaluate the safety and efficacy of add-on treatment with mirabegron (50 mg/day) in patients with BPH who had persistent storage symptoms after treatment with tadalafil (5 mg/day).

• The PDE5-I tadalafil has been approved in many countries for the treatment of BPH, and previous randomized studies have demonstrated that its efficacy is similar to that of the α1-blockers [2]. Nevertheless, currently there is insufficient data on the efficacy and safety of add-on treatment (tadalafil + PDE5-I) with an α1-blocker and β3-adrenergic agonist. β3-adrenergic agonists relax detrusor smooth muscle during the bladder storage phase and increase bladder capacity without negatively affecting voiding parameters, including maximum flow rate, detrusor pressure at maximum flow rate and PVR [3]. Mirabegron was the first β3-adrenergic agonist to be used in clinical practice. Since the mechanism of action of mirabegron is different from that of anticholinergics, it might prove useful in treating patients experiencing intolerable AEs to anticholinergics.

• A limitation of the present study is that efficacy endpoints were based on changes from the baseline. In addition, this study might not be sufficiently large enough to show small differences in outcomes. A placebo-controlled study would be necessary to elucidate the true efficacy profile of mirabegron as an add-on treatment.

Conclusions

• Combination treatment of tadalafil (5 mg/day) with mirabegron (50 mg/day) add-on improved efficacy with comparable safety in BPH patients with persistent storage symptoms after initial tadalafil monotherapy.

• This study indicated that combined treatment with tadalafil and mirabegron additive for therapeutic options and constitutes an improvement in the QOL, as well as decreases the impact of LUTS in patients with OAB caused by BPH.