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MIRABEGRON AS A TREATMENT FOR OVERACTIVE BLADDER SYMPTOMS IN MEN: EFFICACY AND SAFETY RESULTS FROM A MULTICENTER, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED, PARALLEL COMPARISON PHASE IV STUDY (MIRACLE STUDY).

Hypothesis / aims of study

Mirabegron, a β_3 -adrenoreceptor antagonist, may effectively mitigate overactive bladder (OAB) symptoms in males without adverse events. Thus, the present study aims to evaluate the efficacy and safety of mirabegron in males with OAB symptoms.

Study design, materials and methods

A phase IV, randomized, double-blind, placebo-controlled, parallel comparison clinical trial was conducted at 14 institutes in South Korea. The study included males aged ≥ 18 years with OAB symptoms for at least 12 weeks. The sample size of patients in the two groups provided 80% power to detect a significant difference of 0.77 in mean numbers of micturitions per 24 hours (based on the median value of treatment differences from previous studies [1,2]) between placebo and mirabegron group, based on a two-sided t-test with $\alpha = 0.05$ and a standard deviation of 2.52. Assuming post-randomization dropout rates of 10%, 464 patients were to be randomized 1:2 to placebo vs mirabegron 50 mg group (154 vs 308). Change from baseline to 12 weeks of treatment in mean numbers of micturitions per 24 hours was compared between the two groups as the primary end point. Change of overactive bladder symptom score (OABSS) and international prostate symptom score (IPSS) from baseline to 12 weeks of treatment was compared between the two groups as the secondary endpoint; total score, urgency score (question 3), and urgency incontinence score (question 4) from OABSS and storage subscore (sum of question 2, 4, and 7), urgency score (question 4), and quality of life (QoL) score from IPSS were assessed. Safety assessments included treatment-emergent adverse events (TEAEs), blood pressure, pulse rate, postvoid residual (PVR) volume, and maximum urinary flow rate (Qmax). The comparison of continuous variables between the two groups and between baseline and 12 weeks of treatment within each group was performed by using independent t-test and paired t-test, respectively. The categorical variables between the two groups were compared by using chi-square test.

Results

The numbers of micturitions per 24 hours and the scores of the questionnaires assessed in this study were significantly reduced from baseline to 12 weeks of treatment in both groups ($p < 0.001$ in all). The mean reduced numbers of micturitions per 24 hours from baseline to 12 weeks of treatment in placebo and mirabegron group were 1.45 ± 2.54 and 1.61 ± 2.20 , respectively, and were not significantly different between the two groups ($p = 0.06$). A significant difference between the two groups was observed regarding the reduced amount of scores from baseline to 12 weeks of treatment in OABSS total score ($p = 0.01$), OABSS urgency score ($p = 0.01$), OABSS urgency incontinence score ($p = 0.01$), IPSS storage subscore ($p = 0.01$), and IPSS urgency score ($p = 0.02$). However, the reduced amount of IPSS QoL from baseline to 12 weeks of treatment was not significantly different between the groups ($p = 0.34$). The detailed mean reduced values of each scores are presented in Table 1. TEAEs, blood pressure, pulse rate, PVR, and Qmax of treatment were not significantly different between the two groups at 12 weeks ($p > 0.05$ in all, Table 2).

Interpretation of results

Although the 12 weeks of treatment with mirabegron 50mg did not significantly reduced the numbers of micturitions per 24 hours compared to the placebo, the reduced amount of OAB symptoms in mirabegron group were significantly larger than those in the placebo group. Such result implies that daily dose of mirabegron 50 mg for at least 12 weeks can be an effective treatment method that significantly improves urgency and storage symptoms in male OAB patients. Also, the treatment using mirabegron was well tolerated, without additional important safety findings compared with placebo.

Concluding message

Daily dose of mirabegron 50mg for 12 weeks symptomatically improved male OAB patients without significant adverse events compared to the placebo group.

Table 1. Mean reduced values of the variables from base line to 12 weeks of treatment in placebo and mirabegron group (mean \pm SD).

| Base line vs 12 weeks of treatment | Placebo (n = 154) | Mirabegron 50mg (n = 308) | p-value |
|---|----------------------|------------------------------|---------|
| Reduced mean numbers of micturitions per 24 h | 1.45 \pm 2.54 | 1.61 \pm 2.20 | 0.06 |
| OABSS | | | |
| Reduced total score | 1.90 \pm 2.78 | 2.56 \pm 2.71 | 0.01 |
| Reduced urgency score (question 3) | 0.91 \pm 1.40 | 1.12 \pm 1.33 | 0.01 |
| Reduced urgency incontinence score (question 4) | 0.42 \pm 1.25 | 0.77 \pm 1.28 | 0.01 |
| IPSS | | | |
| Reduced storage subscore (question 2 + 4 + 7) | 1.55 \pm 2.84 | 2.29 \pm 2.84 | 0.01 |
| Reduced urgency score | 0.67 \pm 1.46 | 1.00 \pm 1.35 | 0.02 |
| Reduced QoL score | 0.96 \pm 1.27 | 0.80 \pm 1.31 | 0.34 |

OABSS: Overactive bladder symptom score; IPSS: International prostate symptom score

Table 2. Safety assessment variables at 12 weeks of treatment in placebo and mirabegron group (mean \pm SD).

| | Placebo (n = 154) | Mirabegron 50mg (n = 308) | p-value |
|------------------|----------------------|------------------------------|---------|
| TEAEs (n) | 4 (2.60%) | 13 (4.19%) | 0.39 |
| SBP (mmHg) | 126.86 \pm 12.94 | 127.90 \pm 11.76 | 0.27 |
| DBP (mmHg) | 78.44 \pm 8.79 | 78.97 \pm 8.65 | 0.53 |
| Pulse rate (bpm) | 75.84 \pm 11.03 | 75.26 \pm 9.97 | 0.58 |
| PVR (mL) | 31.24 \pm 44.84 | 35.20 \pm 38.96 | 0.30 |
| Qmax (mL/s) | 15.98 \pm 8.68 | 15.83 \pm 8.35 | 0.95 |

TEAEs: Treatment-emergent adverse events; SBP: Systolic blood pressure, DBP: Diastolic blood pressure; PVR: Postvoid residual volume; Qmax: maximum urinary flow rate

References

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2. Victor W. Nitti (2013) THE JOURNAL OF UROLOGY, Vol. 190, 1320-1327

Disclosures

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