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Krhut J[1], Zachoval R[2], Martan A[3], Hanus T[4], Horcicka L[5], Svabik K[3], Halaska M[6]
1. *Dept.of Urology, University Hospital, Ostrava, Czech Republic,* ***2.*** *Dept. of Urology, Thomayer Hospital, Prague, Czech Republic,* ***3.*** *Dept. of Obstetrics and Gynecology, 1st Faculty of Medicine, Charles University and Faculty Hospital, Prague, Czech Republic,* ***4.*** *Dept. of Urology, 1st Faculty of Medicine, Charles University and Faculty Hospital, Prague, Czech Republic,* ***5.*** *GONA, Urogynecological office, Prague, Czech Republic,* ***6.*** *Department of Obstetrics and Gynecology, 1st Faculty of Medicine, Charles University, Prague, Czech Republic*

EVALUATION OF TREATMENT EFFICACY OF MIRABEGRON FOR OVERACTIVE BLADDER IN PATIENTS PREVIOUSLY FAILING ANTICHOLINERGIC THERAPY

Hypothesis / aims of study
Overactive bladder (OAB) is a debilitating condition affecting quality of life of 10-12% of adult population. Despite data from clinical trials indicating very good efficacy and safety of anticholinergics, a significant proportion of patients will discontinue the treatment. Lack of efficacy and adverse events are the most frequently reported reasons for discontinuation. These patients are generally reffered as non-responders. This study is based on the assumption that non-responders represent at least two different patient populations. It has been documented that treatment with mirabegron, β3-adrenoreceptor agonist, leads to significant improvement of OAB symptoms and displays better tolerability than antimuscarinics. The aim of this study was to evaluate the efficacy of 12 month treatment with mirabegron in OAB patients who have previously failed therapy with anticholinergics. We hypothesized that the mirabegron treatment would be more effective in the patients who discontinued anticholinergics due to adverse events rather than in those who discontinued previous anticholinergics due to lack of efficacy.

Study design, materials and methods
This prospective, multicentre study enrolled total of 173 patients (18 male, 155 female, age 63,4±12,3 years) with OAB symptoms, who were dissatisfied with their previous anticholinergic treatment. Institutional Review Board approval was waived, as the study was considered a non-interventional clinical follow-up and did not alter routine clinical practice. Group A consisted of 107 patients (11 males, 96 females, age 65,8±11,2 years) who discontinued previous anticholinergic treatment due to lack of efficacy, Group B consisted of 66 patients (7 males, 59 females, age 59,8±13,2 years) who discontinued their treatment due to adverse events. All patients were prescribed mirabegron 50 mg/day. Total of one hundred seven patients completed the 1 year treatment period and were included into final analysis (56 patients in Group A and 51 patients in Group B).
Subjective and semi-objective parameters were compared prior to and following 3, 6 and 12 months of uninterrupted treatment. Data obtained from the voiding diaries (number of voids, frequency and severity of urgency episodes per 24 hour period, number of nocturia episodes, Patients' Perception of Intensity of Urgency Scale - PPIUS), Patients' Perception of Bladder Condition (PPBC), Urgency Bother - Visual Analog Scale (UB-VAS) and OAB questionnaire (OAB-q), were used to evaluate the treatment efficacy. Persistence of the patients on mirabegron therapy and reasons for discontinuation was evaluated in both groups. Statistical analysis: data were analyzed using the software STATISTICA 12 (Statsoft, USA). Continuous variables were reported as means ± standard deviation (SD). Paired t-test was used to detect changes in parameters during the treatment period and two sample t-test were used for a comparison of the two groups. Categorical variables were reported as proportions and Pearson's chi-square test was used for a comparison of groups. P-values ≤0.05 were considered statistically significant.

Results
Comparison of treatment outcomes within individual groups showed significant improvement ($p<0.001$) in all parameters and in both groups. The difference between groups did not reach the statistical significance in any of the parameters (Table 1). During one year follow-up period, the drop-out rate in Group A was 51/107 patients (47,7%). Six (11,8%) discontinued the treatment with mirabegron due to adverse events, while 36 (70,6%) discontinued due to lack of efficacy. Twelve patients discontinued due to unknown reasons (lost to follow up).The drop-out rate in Group B was 15/66 patients (22,7%) during treatment period. Seven patients discontinued due to unknown reasons. Three (20,0%) patients discontinued their mirabegron treatment due to adverse event. No significant significant difference has been found between Group A and B ($p = 0,414$). Five (33,3%) patients discontinued their mirabegron treatment due to lack of efficacy, which represent a significant difference between Group A and B ($p = 0,009$).

Interpretation of results
Significant improvement in all measured parameters was recorded in patients who completed one year treatment with mirabegron 50 mg/day in both study groups. When comparing the two groups of patients based on the reason why they previously discontinued anticholinergic treatment (lack of efficacy or side affects), no difference in treatment efficacy with mirabegron was found. However when we compared the reasons for drop-out from the study, significantly higher rate of treatment discontinuation, was found in patients experiencing the lack of efficacy of antimuscarinics. This suggests that patients discontinuing antimuscarinics due to side effects have higher probability to benefit from mirabegron treatment than those who discontinued due to lack of efficacy.

Concluding message
This study provides evidence in support of previously documented data indicating good efficacy of mirabegron in the treatment of OAB. It remains to be determined if higher dose of mirabegron could be benefitial for those patients who discontinued antimuscarinics due to lack of efficacy.

Disclosures
Funding: No **Clinical Trial:** Yes **Public Registry:** No **RCT:** No **Subjects:** HUMAN **Ethics not Req'd:** Institutional Review Board approval was waived, as the study was considered a non-interventional clinical follow-up and did not alter routine clinical practice. **Helsinki:** Yes **Informed Consent:** No