**857**

Illiano E[1], Porena M[1], Balsamo R[2], Natale F[3], Bini V[4], Finazzi Agrò E[5], Costantini E[1]
***1.*** *Urology and Andrology Clinic, Department of Surgical and Biomedical Science, University of Perugia Italy,* ***2.*** *Division of Urology,Magna Graecia University of Catanzaro, Campus of Germaneto, Italy,* ***3.*** *Urogynecologic Department, S.Carlo-IDI, Rome, Italy,* ***4.*** *Department of Medicine Section of Internal Medicine Endocrine & Metabolic Sciences , University of Perugia,Italy,* ***5.*** *Department of Urology, University of Torvergata, Rome, Italy*

# MIRABEGRON: MEDICATION ADHERENCE, PATIENT SATISFACTION AND IMPROVEMENT OF QUALITY OF LIFE IN WOMEN WITH OAB

Hypothesis / aims of study
Overactive bladder (OAB) is defined by ICS as urinary urgency, with or without urinary incontinence, usually with frequency and nocturia, without urinary infection or other urological disease. The incidence of OAB is reported between 12% and 16%, and its prevalence increases with age. Traditionally the antimuscarinic drugs are the recommended therapy. Recently the role of β3 adrenoceptor in the relaxation of the detrusor has been confirmed by in vitro pharmacological studies, and Mirabegron, a β3 adrenoceptor agonist has been approved for the treatment of OAB syndrome. The interest in this new drug is paramount because it seems to improve the success score and at the same time to decrease significantly the side-effects when compared with anticholinergic drugs. Side effects, lack of efficacy, and cost of the drug are at the moment the principal cause of anticholinergic therapy discontinuation in OAB patients. The primary objectives of this prospective study were to evaluate the medication adherence, the patient satisfaction and the improvement of quality of life in women with OAB after treatment with Mirabegron. Secondary objectives were to evaluate the efficacy and safety of treatment.

Study design, materials and methods
This is an multicenter prospective study. It has been approved by the local ethics committee Consecutive female patients affected by OAB were enrolled. OAB was defined as increased daytime frequency: ≥8 micturitions /24 h (F), ≥3 urgency episodes/24 h (U), nocturia: ≥1 micturitions (N), with or without urgency urinary incontinence (UUI) (ICS definition).
Inclusion criteria were: women with OAB naïve, women with refractory OAB to antimuscarinic drugs, age 18 to 70 years. In patients with previous antimuscarinic agents we performed 3 months therapy wash-out. Exclusion criteria were: neurological disease, urinary tract infections, urolithiasis, bladder cancer, symptomatic pelvic organ prolapse (stage ≥ II), stress urinary incontinence, mixed incontinence with predominant stress UI, diabetes, hypersensitivity to the active substance or to any of the excipients, severe uncontrolled hypertension defined as systolic blood pressure ≥180 mm Hg and/or diastolic blood pressure ≥110 mm Hg, severe renal impairment (GFR < 15 mL/min/1.73 m2 ), severe hepatic impairment (Child-Pugh Class C), a known history of QT prolongation or patients who are taking medicinal products known to prolong the QT interval, pregnant women, and breast feeding mothers. Pre-treatment evaluation included medical and urogynecological history, clinical urogynecological examination, microbiological analysis, urine analysis, abdominal ultrasonography, uroflowmetry (UF) with post-void residual (PVR) measurement and voiding diary (VD) for 3 –day period. All the patients completed self-administered Overactive Bladder questionnaire short form (OABq- sf) and signed an informed consent. They received once-daily Mirabegron 50 mg for 6 months. They were followed up at 1, 3 and 6 months post treatment with UF and PVR measurement and 3-days VD, they completed self-administered OABq-sf, Morisky Medication Adherence Scale-4 short form (MMAS-4), satisfaction visual analogic scale (sVAS) and Patient Global Impression-Improvement (PGI-I) questionnaries. The efficacy is defined as ≥50% decrease from baseline in mean number of incontinence episodes /24h, ≤ 8 micturitions/24 h, ≥50% decrease from baseline in mean number of nocturia episodes, ≥50% decrease from baseline in mean number of urgency episodes/24 h.
Statistical analysis was performed by using McNemar and Friedman tests. All calculations were performed using IBM-SPSS® version 22.0 (IBM Corp., Armonk, NY, USA, 2013). A two-sided p-value <0.05 was considered significant

Results
Sixty-three women (mean age of 59.2±12.5 years) were included in the study. Table I shows baseline clinical characteristics of the study population. 23 patients interrupted the treatment in the first 30 days. Graph I showed the discontinuation reasons and the side effects reported by the patients. 40 out of 63 women were evaluated at 3 months with a high drug adherence demonstrated by the median MMAS-4 score of 0 (range 0-2). At 3 months follow-up patient's satisfaction and subjective improvement of symptoms were high, infact median PGI-I and S-VAS were 2 (range 1-4) and 8 (2-10) respectively. At 1 and at 3 months OABq-sf score showed a statistically significant improvement with a baseline median score of 36 (range 19-99), of 28 (range 9-48) at 1 month and of 19 (range 8-35) at 3 months (p=0.001). Mirabegron 50mg/die improved significantly all the OAB symptoms at 1 and 3 months, as showed in Graph.2, reducing F, N, U and UUI. Furthermore a statistically significant decrement of the mean number of pads/die was evident at 1 month (1.45±1.58 vs 0.57 ± 0.98 p<0.0001), and at 3 months (0.30±0.60). UF results showed no statistical changes at 1 month( mean baseline Qmax 18.67±7.71 vs 18.94±7.53 (p=0.218)) at 3 months (mean baseline Qmax 18.67±7.71 vs 18.91±3.02 (p=0.29).The results are not different in women with OAB naïve and women with OAB refractory to antimuscarinic drugs.

Interpretation of results
Mirabegron 50 mg/daily showed a significant improvement of OAB subjective and objective symptoms at 1 month, with further improvement at 3 months. It is demonstrated by the improvement in OABq-sf score and decrement of urgency, nocturia, urinary incontinence episodes and daytime frequency. Quality of life is significantly improved and patient's satisfaction is high as demonstrated PGI-I and S-VAS score (median 2 (range 1-4) and 8 (2-10) respectively). No effect on the voiding phase is demonstrated by the UF parameters with the absence of clinically significant PVR and Q-Max values that do not change during the treatment. Side-effects reported were: in 4.76% tachycardia (average resting pulse rate measured by the patient over 3 days was >100bpm), 3.17% constipation, 1.58% itch, 3.17% legs edema, 1.58% face edema . All the drug discontinuations (7.93%)

are in the first month and later the adherence is high. The major causes of discontinuation are the cost of the drug, the side effects, and other not clear causes leading to no-adherence to the therapy. It seems that the cost of Mirabegron is the major controversial point

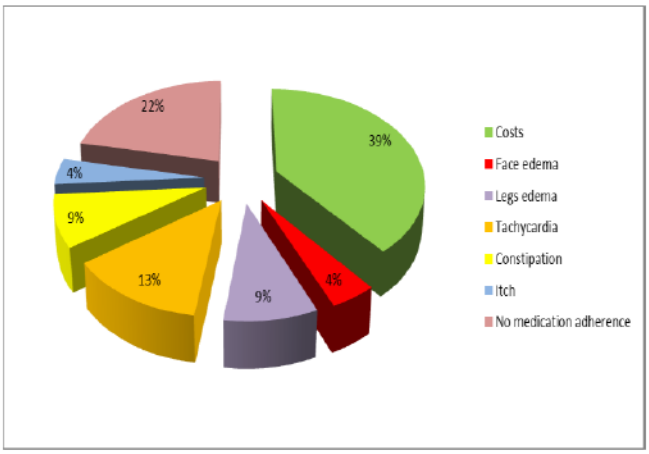
Concluding message

Mirabegron 50mg showed significant subjective and objective efficacy with a high in women with OAB at 1 and 3 months of treatment. For the low side-effects and its impact on QoL, it can be considered the first line therapy in these patients. Long term results are mandatory for patients perspective and counselling for tailored therapy.

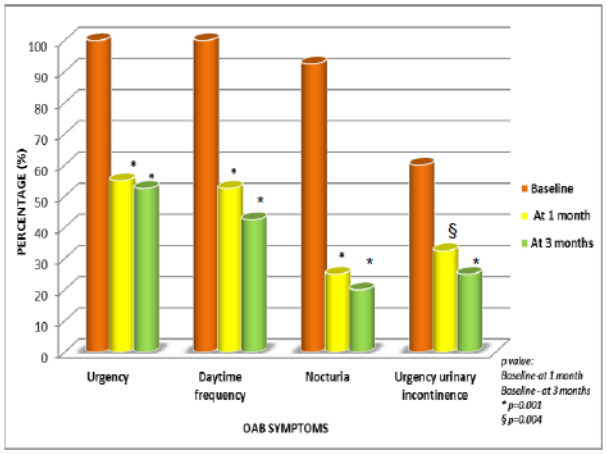
Table I. Baseline clinical characteristics of the study population

| | Total population (n=63) | Study group (n = 40) | Dropout group (n=23) |
|---|---|---|---|
| **Refractory OAB (n,%)** | 23 (36.5) | 14 (22.2) | 9 (39.1) |
| **≥8 micturition/24 h (n%)** | 63 (100) | 40 (100) | 23 (100) |
| **≥1 micturition/ night time (n,%)** | 58 (92.0) | 37(92.5) | 21 (91.3) |
| **Urgency (n,%)** | 63 (100) | 40 (100) | 23 (100) |
| **OAB wet (n,%)** | 44 (69.8) | 24 (60) | 20 (86.9) |
| **OAB dry (n,%)** | 18 ( 28.5) | 16 (40) | 2 (8.6) |
| **Pads/die (mean ± SD)** | 1.37±1.35 | 1.45±1.58 | 1.26±1.48 |

Graph I: The causes of treatment discontinuation and the therapy side effects in 23 patients




Graph II: OAB symptoms at baseline, at 1 and at 3 months




Disclosures

**Funding:** NONE **Clinical Trial:** Yes **Public Registry:** No **RCT:** No **Subjects:** HUMAN **Ethics Committee:** CEAS Regione Umbria **Helsinki:** Yes **Informed Consent:** Yes