International Urology and Nephrology (2020) 52:1035–1042
https://doi.org/10.1007/s11255-020-02412-2

UROLOGY - ORIGINAL PAPER

Italian real-life clinical setting: the persistence and adherence with mirabegron in women with overactive bladder

Ester Illiano[1] · Enrico Finazzi Agrò[2] · Franca Natale[3] · Raffaele Balsamo[4] · Elisabetta Costantini[1]

Received: 17 December 2019 / Accepted: 12 February 2020 / Published online: 21 February 2020

Abstract

Introduction and hypothesis The aims of this study were to evaluate the persistence, the adherence on treatment with mirabegron, the reasons for the interruption in patients with overactive bladder syndrome (OAB) and their satisfaction.

Methods This was an Italian multicentre prospective study. Four tertiary urological centers were involved. We included women with no neurogenic OAB symptoms already in therapy with once-daily mirabegron 50 mg for 1 month. They were followed up at 1, 3 and 6 months post-treatment with uroflowmetry with voiding diary for 3 days and post-void residual measurement. They completed self-administered Overactive Bladder questionnaire short form (OABq), Morisky Medication Adherence Scale-4 short form (MMAS), Patient Global Impression-Improvement questionnaire. Patients were divided in OAB wet and OAB dry groups, and in treatment-naive and treatment-experienced groups.

Results Between January 2018 and July 2018, 80 patients with OAB were included. Fifteen (18.7%) patients continued the treatment for 6 months; 17.5% interrupted the therapy before 1 month: 30% within the third month, while, 33.7% after 1 month. The median time to discontinuation with mirabegron was 62.5 days. The mean adherence was 0.42 ± 0.33, median MMAS was 2 (0–4). The adherence was significantly greater in treatment-naïve (22.4%) than treatment-experienced (6.5%) patients, without statistically significant differences in the different OAB form. The cost is the main cause of interruption of therapy (50% of cases).There was an improvement of OABqSF score and PGI-I score.

Conclusion In Italy, the cost compromises adherence and persistence of therapy with mirabegron despite the good functional outcomes

Keywords Mirabegron · Overactive bladder · Mirabegron adherence · Mirabegron persistence · Urge urinary incontinence · Cause interruption mirabegron

Introduction

Overactive bladder (OAB) was defined by International Continence Society (ICS) as urgency, with or without urgency incontinence, usually with increased daytime frequency and nocturia [1]. OAB is a chronic disease requiring long-term medical treatment and lifestyle changes [2]. According to European Association of Urology, the prevalence of OAB as varying from 8 to 42% in women, with a increase with advancing age [3]. It is a condition that invalidates the patient's quality of life. Urgency limits women in their daily and social life [4]. The condition worsens further if it is a form of OAB with urinary incontinence. The treatment of OAB includes the lifestyle and behavioural modification, bladder training, and pelvic muscle floor therapy [3]. The second line consists in oral drugs (anticholinergics or beta-3 adrenoceptor agonist) [3]. The third line includes using of the injection of onabotulinum-toxin A, sacral neuromodulation, and percutaneous posterior tibial nerve stimulation [3]. It is a pathology with high direct and indirect costs. In Italy, this condition of discomfort is more present because the oral drugs for OAB are not paid by the National Health System. Long-term therapy for a chronic condition that

✉ Ester Illiano
ester.illiano@inwind.it

1 Andrologycal and Urogynecological Clinic, Santa Maria Terni Hospital, University of Perugia, Piazzale di Joanuccio 1, 05100 Terni, Italy

2 Urology Clinic, TorVergata University, Rome, Italy

3 Urogynecology Unic, San Carlo Di Nancy Hospital, Rome, Italy

4 Monaldi Hospital, Naples, Italy

needs to be paid by the patient could influence the persistence and adherence to treatment. The anticolinergics are drugs most commonly prescribed for the treatment of OAB [5]. They decrease OAB symptom severity, but some patients had adverse effects, most commonly dry mouth [6]. Sometimes, in some trials, the balance of efficacy benefits against to adverse effects was unsatisfactory, and discontinue therapy, cause of therapeutic discontinuity [2, 5]. The European Commission granted a marketing authorisation valid throughout the European Union for Mirabegron (a beta-3-adrenergic-receptor agonist) on 20 December 2012. It has been shown to have high efficacy and safety profile by large random placebo-controlled clinical trials [7]. Real-world data, mainly from retrospective study, showed that persistence with mirabegron may be greater than for anti-muscarinics in OAB [8, 9]. In literature, there are no Italian real-life clinical setting studies on the persistence and adherence of mirabegron in women with OAB. The primary objectives of this study were to evaluate the persistence, the adherence on treatment with mirabegron and the switch rates in the total population Secondary objectives were to evaluate the reasons for the no persistence or no adherence; to describe patient characteristics that affected persistence and adherence. Tertiary objectives were to evaluate the patient's satisfaction.

Material and methods

This was an Italian multicentre prospective study. Four Italian tertiary urological centers were involved. The trial has been approved by the local ethics committee (CEAS N 2354/16). We included consecutive women with OAB symptoms. OAB was defined in according ICS definition [1] as increased daytime frequency: ≥ 8 micturitions/24 h, ≥ 3 urgency episodes/24 h, nocturia: ≥ 1 micturitions, with or without urgency urinary incontinence (OAB wet or dry). Inclusion criteria were: women with OAB naïve, women with refractory OAB to antimuscarinic drugs after 3 months therapy wash-out, age ≥ 18 years. 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 urinary incontinence, 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 m^2), 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 history, clinical examination, urine analysis, microbiological analysis, uroflowmetry with post-void residual measurement, abdominal ultrasonography, and voiding diary for 3 days. All the patients completed self-administered Overactive Bladder questionnaire short form (OABq-sf) [10] 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 uroflowmetry with post-void residual measurement and voiding diary for 3 days, they completed self-administered OABq-sf, Morisky Medication Adherence Scale-4 short form (MMAS-4) [11], Patient Global Impression-Improvement (PGI-I) questionnarie [12]. Patients were divided in treatment-naive and treatment-experienced groups, and in OAB wet and OAB dry groups. The primary aim was to evaluate the persistence, the adherence and the switch rate on treatment. *Persistence* was defined as the mean number of days that a patient remained on therapy [13–15]. The therapy was considered discontinued after a period of 30 days without prescription renewal. *Adherence* to a drug was measured by medication possession rate (MPR) at 6 months, and adherent patients [16]. The MPR was the sum of days of supply from the first to the last prescription (inclusive) divided by 180 days of follow-up [16]; while the adherent patients at 6 months was the proportion of patients considered to be adherent (MPR ≥ 0.8) at 6 months [16]. The *switch rate* was calculated as the proportion of patients who changed from the initial (index) medication to any of the other drugs during the 6 months follow-up [17]. Treatment naïve was defined as no prescription for any target drug during the pre-enrollment period [17]; while treatment experienced as prescription for at least one anticolinergic drug during the pre-enrollment period [17].

Statistical analysis

Persistence and adherence rate were not adjusted for potential confounding factors and data were reported descriptively. The persistence was calculated using Kaplan–Meier survival analysis, reported as time to discontinuation (TTD) and differences between groups (Treatment naïve and treatment experienced; OAB wet and OAB dry) were assessed via log-rank test. Hazard ratios (HRs) are reported. Patients were censored if they reached the end of follow-up without discontinuation. Cox proportional-hazards regression models, adjusted for potential confounding factors (age, OAB form, treatment status, hypertension), were used to analyse TTD (expressed as HR and 95% confidence interval [CI]). Adherence was reported as mean MPR and the proportion of adherent patients at the end of the 6-month post-index. Analyses of treatment persistence and adherence were performed, considering the sample in the following patient subgroups: treatment naïve or experienced; < 65 or ≥ 65 years of age, OAB wet or OAB dry. Proportions of adherent patients were

compared between groups using Fisher's exact test or a χ^2 test, depending on the sample size. Wilcoxon tests for paired data, was used to compare ordinal and nonnormally distributed continuous variables. 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

Between Juanary 2018 and July 2018, 200 patients with OAB were identified. A total of 120 (60%) patients were excluded, 80 women were treated with anticolinergic drugs, 20 patients had no inclusion criteria, and 20 women refused to participate in the study, so 80 (40%) patients constituted the study population. All patients were followed for 6 months. Patient's demographic charateristics at baseline are showed in Table 1. Most of the women included in the study have OAB wet (58.7%), and they have not already been treated with antimuscarinics drugs. A higher proportion of patients were < 65 years old (58.7%). The median time to discontinuation with mirabegron was 62.5 days (Table 2). The percentage of patients whose treatment persisted for 6 months without any gaps was 18.7% (15); of these, three patients stopped mirabegron few days before the 6 months of therapy ended, but they were considered persistent for 6 months; 17.5% (14) of women has interrupted the drug before 1 month of treatment (mean of treatment 8 ± 2.28 days); 33.7% (27) of patients continued mirabegron for a month (mean of treatment 30.5 ± 2.88 days), and 30% (24) of women interrupted therapy within the third month (mean of treatment 82 ± 12.9 days). Table 2, Figs. 1 and 2 showed that women who have taken mirabegron for the longest time, without discontinuity, had OAB wet and they were naïve. Figure 3 and Table 2 showed that there is no difference statistically significant according to the age ranges. Mean MPR was 0.42 ± 0.33 (Table 2), 14 women were considered to be adherent to mirabegron. Median MMAS was 2 (0–4), medium adherence. Adherence was significantly greater in treatment-naïve (22.4%) than in treatment-experienced (6.5%) patients; there were no stastically significant differences in the different OAB form and in different age. Only 13.7% (11) of the population switched from the index medication to other OAB drugs, while 33.7% (27) of patients underwent botulin toxin intradetrusor injections. Age, hypertension, treatment status, and OAB form did not affect persistence (Table 3). Fifty % (40) of patients interrupted mirabegron for the cost; 15% (12) for unmet expectation of treatment; 6.2% (5) for adverse events and 3.7% (3) for symptom improvement. The prevalence of patients who discontinued mirabegron for the cost was higher in treatment experienced (75%) and in OAB dry (65%) groups than in treatment naive (25%) and in OAB wet (35%) groups; the prevalence of women who interrupted drug because of unmet expectation of treatment was higher in OAB wet (83.3%) than OAB dry (16.7). As adverse events were recorded: constipation (9%), tachycardia (13%), pruritus (4%), stomach cramps (10%), diarrhea (12%), backache (7%), leg edema (9%), face edema (4%),

Table 1 Baseline characteristics of population

Characteristics	
Age, years	
Mean ± SD	60.4 ± 12.57
Range	36–84
Age, group *n*(%)	
< 65 year	47 (58.7)
≥ 65 year	33 (41.2)
Treatment status, *n* (%)	
Experienced	31 (38.7)
Naive	49 (61.2)
Hypertension, *n* (%)	19 (23.7)
Menopause, *n* (%)	56 (70)
OAB wet, *n* (%)	47 (58.7)
OAB dry, *n* (%)	33 (41.2)

Table 2 Persistence and adherence of mirabegron 50 mg

Time to discontinuation (days)		Log rank (Mantel–Cox)
Global median (range)	62.5 (7–180)	
TTD:treatment-experienced median (range)	30 (11.2–48.8)	0.008
TTD:treatment-naive median (range)	65 (42.0–87.9)	
TTD:OAB wet median (range)	60 (18.6–101.3)	0. 013
TTD:OAB dry median (range)	30 (20.3–39.6)	
TTD: < 65 years old median (range)	30 (12.5–47.9)	0.418
TTD: ≥ 65 years old median (range)	45 (25.6–64.3)	
Adherence		
MPR (mean ± SD)[a]	0.42 ± 0.33	
Total adherent patients, *n* (%)[b]	14	
Sub groups adherent patients, *n* (%)[c]		
Treatment experienced, *n* (range)	2 (6.5)	< 0.001
Treatment naive, *n* (range)	11 (22.4)	
OAB wet, *n* (range)	8 (17)	0.25
OAB dry, *n* (range)	4 (12.1)	
< 65 years, *n* (range)	6 (7.5)	0.30
≥ 65 years, *n* (range)	7 (8.8)	
Median follow-up (days)[c]	52.8	

[a]MPRs ranged from 0 (no adherence) to 1 (perfect adherence)

[b]Patients considered to be adherent when MPR ≥ 0.8

[c]Patients who did not discontinue treatment 6 month after initiation

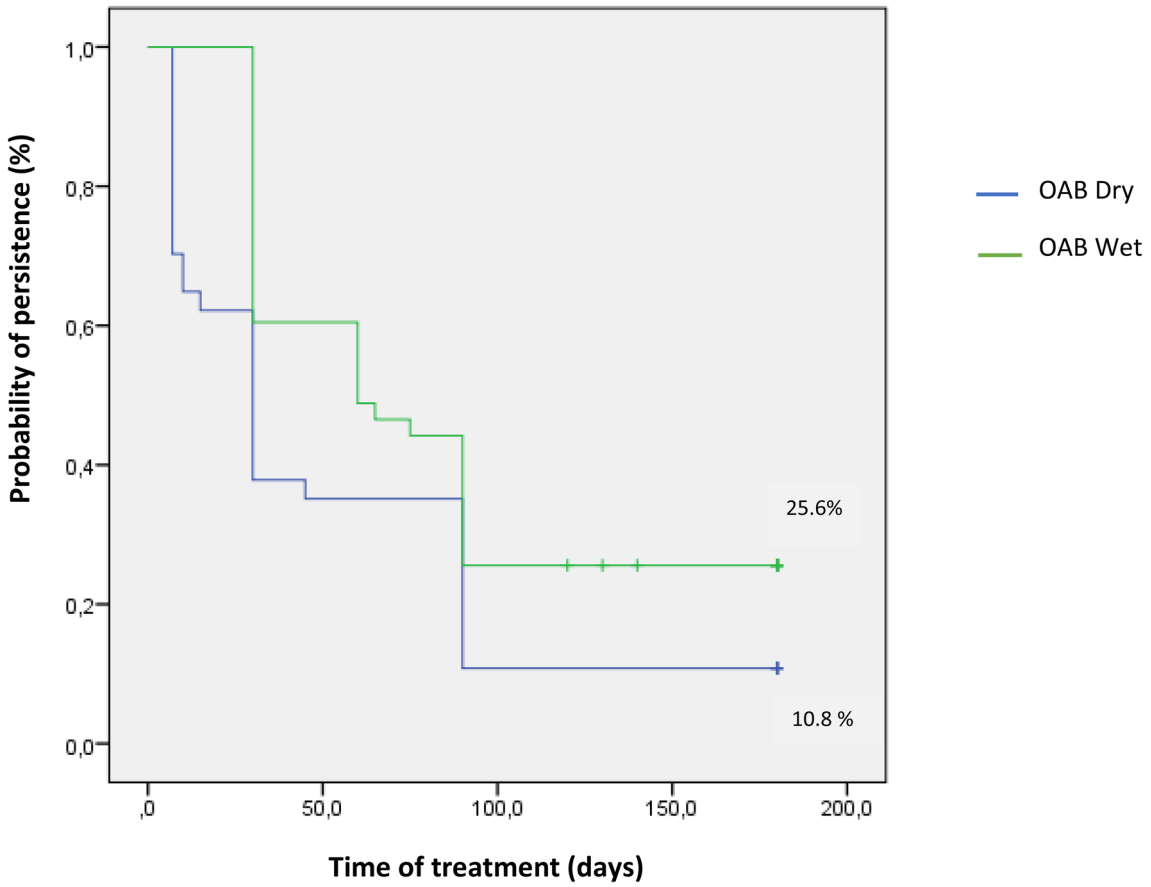

Fig. 1 Kaplan–Meier: persitence for mirabegron in women with OAB dry and OAB wet

dizzy (2%), low energy (2%), others (28%). There was an statistically significant improvement of OABq SF score during follow-up, both in symptom bother scale (median OABq score pre-treatment 30 (24–36) vs OABq score post treatment 12 (10–18), $p < 0.0001$) and in health-related quality of life scale (median OABq score pre-treatment 75 (72–78) vs OABq score post-treatment 26 (23–39), $p < 0.0001$).At 6 months follow-up, patient's satisfaction is high, infact median PGI-I was 2 (range 1–4).

Discussion

This study showed that the therapy with mirabegron has low persistence and low adherence at 6 months among women with OAB, in a country in which patients pay for the treatment as in Italy. The studies with mirabegron or anticolinergic drug had a follow-up ranged from 6 months to 7 years [13, 14, 18]; in this study, we decided for a relative short follow-up of 6 months because the drug was not dispensed from the National Health System, and in the long term, this bias becomes heavier. A 6-month observation period showed a more realistic situation than a longer period.

Yeowell et al. [18] in their systematic literature review showed that overall persistence rates decreased over time, regardless of agent. However the persistence rate with mirabegron was better than the persistence rate with antimuscarinics in previous reports [15, 16]. The persistence rate with beta-3 agonist at 1 year varies widely from 12 to 71% (17, 19–24), and from 63 at 1 year to 46% at 3 years [25]. Our persistence rate at 6 months was 18.7%. This decrease was confirmed by Nitti who has registered a persistence rate from 68.4 at 1 month to 34.7% at 6 months [17].

In our study, the therapy with mirabegron in female drug-naïve patients provided a better persistence rate than previously treated with antimuscarinic drugs. This result is not confirmed in the literature. Nitti [17] recorded that treatment-experienced patients at 6 months had a higher persistence rate (HR 0.68, 95% CI 0.53– 0.88, $p = 0.0025$), and Wagg confirmed the same result at 1 year (19.0% in treatment-naïve women, versus 30.0% in treatment-experienced patients) [11]. Probably, our result can be explained by the naïve patient's greater expectations than a patient who has stopped anticholinergics due to lack of efficacy or tolerability. A women who did not achieve the hoped results after previous therapy, probably interrupts the new

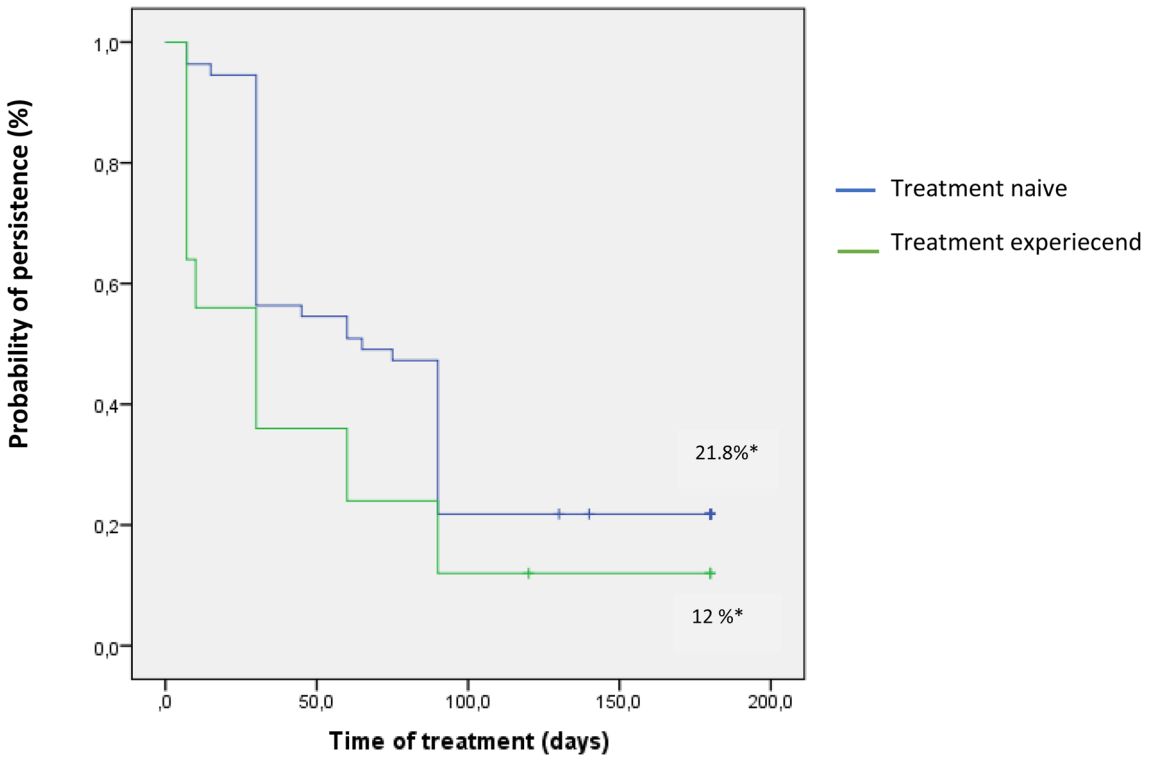

Fig. 2 Kaplan–Meier: persitence for mirabegron in treatment-naive and treatment-experiecend patients. *Proportion of patients persistent at 6 months

treatment early if she does not have an immediate improvement of the symptoms, especially if it is burdened by a high cost of the drug. The persistence was higher in OAB wet. Probably this result can be explained because women with OAB wet have both urge urinary incontinence and OAB symptoms. Urge urinary incontinence and urgency affect quality of life. Mirabegron is known to improve both symptoms. In fact in SCORPIO, statistically significant improvements at final visit were seen for both mirabegron doses versus placebo in mean volume voided/micturition and mean number of urgency incontinence episodes/24 h ($p \leq 0.05$) [18]. Adherence to mirabegron expressed in MPR was 0.42 ± 0.33.At 1 year in Chapple's study, it was 0.59 ± 0.33 [19], while Nitti in his study at 6 months of follow-up does not report this data [9] Adherence was significantly greater in treatment-naïve patients. This data cannot be explained with the greatest efficacy in this group. In fact in the literature, the analysis showed that mirabegron had a numerically positive treatment effect on urge urinary incontinence and micturition frequency both in patients who were treatment-naïve and in those who had received, prior discontinued antimuscarinic therapy [7]. Probably, the patient after careful counselling at the time of the visit follows the doctor's prescription better than patient who has already performed one or more therapies with anticholinergics, and she is perhaps discouraged. This result was confirmed by MMAS-4 score. It reflected a higher adherence in treatment-naïve women.

In the present study, the reasons for discontinuation of mirabegron were cost of drug (50%), unmet expectation of treatment (15%), adverse events (6.2%) or improvement of symptoms (3.7%) in OAB women. Wada [16] reported that the reasons for discontinuation of treatment were unmet expectation of treatment (26%), adverse events (22%) or improvement of symptoms (22%). The most frequent reason for discontinuation was the cost of drug. In literature, there are no studies on the costs of mirabegron in Italy. They have all been conducted in United Kindom [26] or Canada [27]. In Italy, a month of treatment costs € 68.29. 6 months of therapy cost about € 409.74, and not everyone has the financial resources to complete the treatment cycle. Patients are many young or elderly pensioners. Most patients who interrupt therapy are satisfied of the outcomes of the mirabegron and this was confirmed by OAB SF score and PGI-I score; however, they are forced to interrupt the therapeutic cycle, because to continue the treatment, the economic weight is not sustainable. Most women who discontinued mirabegron for cost were treatment-experienced patients and patients with OAB dry. It could be explained by the high costs for the previous therapies that have had to pay the patients. In fact, the other OAB drug had the same cost of mirabegron. If we analysed the reasons for low adherence and persistence

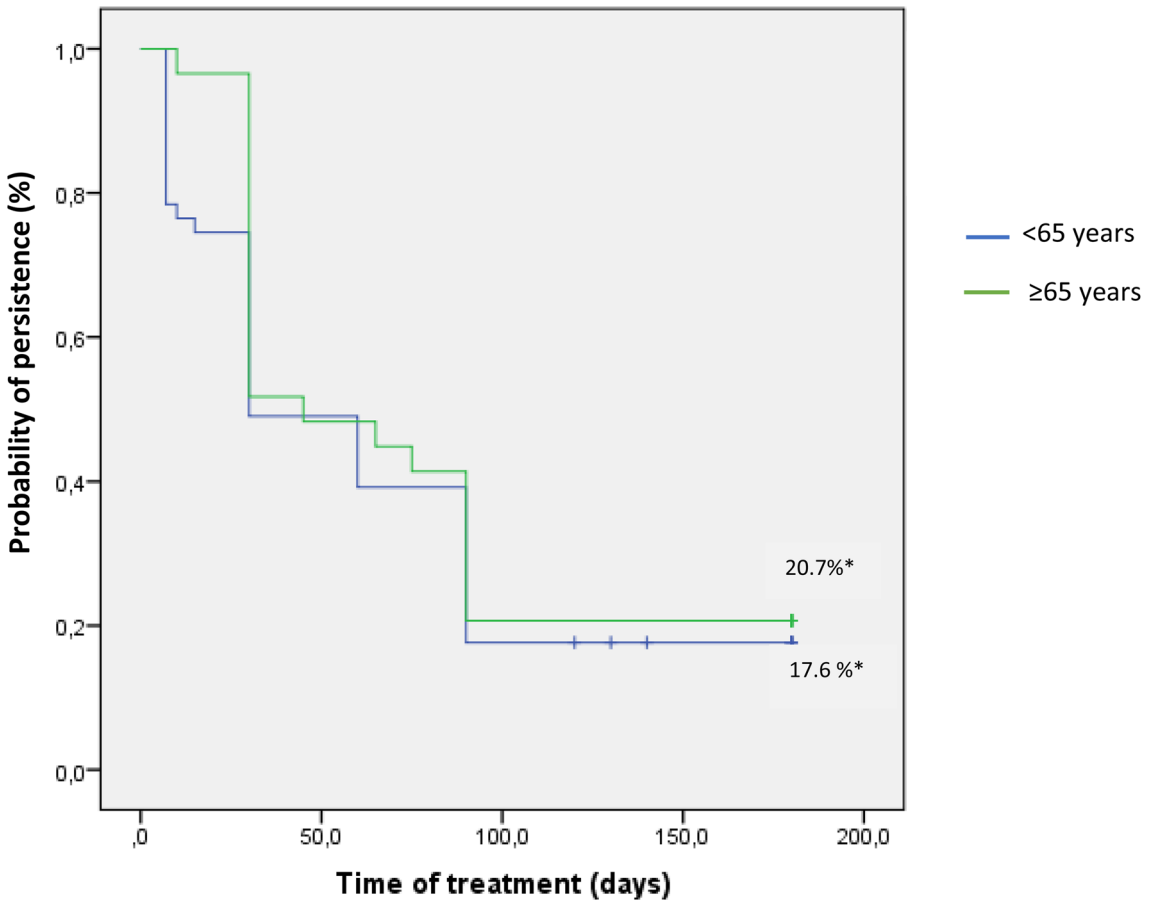

Fig. 3 Kaplan–Meier: Persitence for mirabegron in women < 65 years old and women ≥ 65 years old. *Proportion of patients persistent at 6 months

Table 3 Impact of covariates on time to discontinuation: multivariate Cox regression analysis adjusting for baseline characteristics in all eligible patients

Covariates	HR (95% CI)	*p* value
Age in years		
< 65	1.38 (0.74–2.56)	0.3
≥ 65		
Treatment status		
Naïve	0.63 (0.37–1.08)	0.09
Experienced		
Hypertension		
No	1.07 (0.55–2.06)	0.83
Yes		
OAB form		
Wet	1.66 (0.96–2.88)	0.07
Dry		

with anticholinergic drugs, probably we would discover the same reasons of discontinuity. Moreover, the absence of urge urinary incontinence influences less the quality of life of the woman who more easily suspends the therapy. However, there was no statistically significant difference between age group in persistence rate, older women have greater persistence to therapy than younger one. The same result was found by Wagg in a study on the persistence of antimuscarinics drugs [15]. The reasons can be manifold. Young patients have less time in their hectic daily life and sometimes adherence also decreases. Older women are generally polymedicalised and, therefore, they are used to having adhesions and persistence to therapy. The percentage (15%) of patients with unsatisfied expectations is probably overestimated. In fact, after a careful dialogue with the patient, we sometimes found that the reason for the interruption of the drug was economic rather than really due to dissatisfaction. In these cases, the patients were included in the group economic reasons. However, there could be other cases in which we could not identify the real reason. This hypothesis is confirmed by the high scores of PGI-I.

In our study, the adverse effects were a small percentage (6.2%) compared to previous reports [25] the greatest adverse effect on tachycardia. In a pooled population from SCORPIO, ARIES, and CAPRICORN, a low proportions (3.8%) of patients receiving mirabegron reported tachycardia [7]. In literature, the percentages of each other symptom are slightly smaller than those recorded in our study [7]. It is important to note that in our study, as well as in Nazir's study [28], the majority of patients (58.7%) were defined as treatment naïve. This result highlights our choice to use mirabegron as the first line; in fact, as Serati showed in his study [29] mirabegron is efficacious in improving OAB symptoms in both naïve patients and those with previous primary antimuscarinic therapy; however, its efficacy is superior when prescribed as first-line therapy. Although these results are important, our study has some limitations. The sample is small and the follow-up is shorter than in the previous trials; however, it has many strengths. This study is the only one, to our knowledge, performed on the adherence and persistence of mirabegron in Italian population with OAB in a Real-Life Clinical Setting. It is a prospective multicentre centre. In conclusion, in a country in which women with OAB pay for the treatment with mirabegron 50 mg, it has low adherence and persistence at 6 months, despite the good functional outcomes.

Author contributions EI: manuscript writing and editing; EFA: data analysis and manuscript editing; FN: data management; RB: data collection; EC: project development.

Funding None.

Compliance with ethical standards

Conflict of interest The author(s) declare that they have no conflict of interests.

References

1. Abrams P, Artibani W, Cardozo L, Dmochowski R, van Kerrebroeck P, Sand P (2009) Reviewing the ICS 2002 terminology report: the ongoing debate. Neurourol Urodyn 28:287
2. Haab F, Castro-Diaz D (2005) Persistence with antimuscarinic therapy in patients with overactive bladder. Int J Clin Pract 59:931–937
3. Burkhard FC, Bosch JLHR, Cruz F et al. Urinary incontinence. EAU Guidelines. https://uroweb.org/guideline/urinary-incontinence/
4. Gulur DM, Drake MJ (2010) Management of overactive bladder. Nat Rev Urol 7:572–582
5. Smith AL, Wein AJ (2010) Recent advances in management of bladder overactivity. F1000 Med Rep 2:9
6. Chapple CR (2000) Muscarinic receptor antagonists in the treatment of overactive bladder. Urology 55(Suppl):33–46
7. Chapple CR, Cardozo L, Nitti VW (2014) Mirabegron in overactive bladder: a review of efficacy, safety, and tolerability. Neurourol Urodyn. 33(1):17–30. https://doi.org/10.1002/nau.22505 **[Epub 2013 Oct 11]**
8. Wagg A, Franks B, Ramos B, Berner T (2015) Persistence and adherence with the new beta-3 receptor agonist, mirabegron, versus antimuscarinics in overactive bladder: early experience in Canada. Can Urol Assoc J 9:343–350
9. Nitti VM, Rovner ES, Franks B et al (2016) Persitence with mirabegron versus tolterodine in patients with overactive bladder. Am J Pharm Benefits 8:e25
10. Acquadro C (2006) Kopp Z Translating overactive bladder questionnaires in 14 languages. Urology. 67(3):536–540
11. Fabbrini G, Abbruzzese G (2013) Adherence to anti-Parkinson drug therapy in the "REASON" sample of Italian patients with Parkinson's disease: the linguistic validation of the Italian version of the "Morisky Medical Adherence scale-8 items". Neurol Sci 34:2015–2022
12. Srikrishna S, Robinson D, Cardozo L (2010) Validation of the patient global impression of improvement (PGI-I) for urogenital prolapse. Int Urogynecol J Pelvic Floor Dysfunct 21:523–528
13. Yeowell G, Smith P et al (2018) Real-world persistence and adherence to oral antimuscarinics and mirabegron in patients with overactive bladder (OAB): a systematic literature review. BMJ Open. 8(11):e021889
14. Cramer JA, Roy A, Burrell A et al (2008) Medication compliance and persistence: terminology and definitions. Value Health 11:44–47
15. Wagg A, Compion G, Fahey A, Siddiqui E (2012) Persistence with prescribed antimuscarinic therapy for overactive bladder: a UK experience. BJU Int 110:1767–1774
16. Veenboer PW, Bosch JL (2014) Long-term adherence to antimuscarinic therapy in everyday practice: a systematic review. J Urol 191:1003–1008
17. Martan A, Masata J, Krhut J, Zachoval R, Hanus T, Svabik K (2017) Persistence in the treatment of overactive bladder syndrome (OAB) with mirabegron in a multicenter clinical study. Eur J Obstet Gynecol Reprod Biol 210:247–250
18. Wagg A, Compion G et al (2012) Persistence with prescribed antimuscarinic therapy for overactive bladder: a UK experience. BJU Int 110(11):1767–1774
19. Chapple CR, Jameel N et al (2017) Persistence and adherence with mirabegron versus antimuscarinic agents in patients with overactive bladder: a retrospective observational study in UK. Clin Pract Eur Urol 72(3):389–399
20. Kinjo M, Sekiguchi Y, Yoshimura Y, Nutahara K (2018) Long-term persistence with mirabegron versus solifenacin in women with overactive bladder: Prospective, randomized trial. Low Urin. Tract Symptoms. 10(2):148–152
21. Sussman D, Yehoshua A, Kowalski J et al (2017) Adherence and persistence of mirabegron and anticholinergic therapies in patients with overactive bladder: a real-world claims data analysis. Int J Clin Pract 71:e12824
22. Hill MN, Miller NH, DeGeest S (2010) ASH position paper: adherence and persistence with taking medication to control high blood pressure. J Clin Hypertens (Greenwich) 12:757–764
23. Duckett J, Balachandran A (2016) Tolerability and persistence in a large, prospective case series of women prescribed mirabegron. Int Urogynecol J 27:1163–1167
24. Pindoria N, Malde S, Nowers J, Taylor C, Kelleher C, Sahai A (2017) Persistence with mirabegron therapy for overactive bladder: a real life experience. Neurourol Urodyn 36:404–408
25. Wada N, Watanabe M, Banjo H (2018) Long-term persistence with mirabegron in a real-world clinical setting. Int J Urol 25(5):501–506

26. Hakimi Z (2018) Kelleher C Cost-effectiveness of solifenacin compared with oral antimuscarinic agents for the treatment of patients with overactive bladder in the UK. J Mark Access Health Policy 6(1):1438721
27. Herschorn S, Nazir J (2017) Cost-effectiveness of mirabegron compared to tolterodine ER 4 mg for overactive bladder in Canada. Can Urol Assoc J. 11(3–4):123–130
28. Nazir J, Hakimi A (2018) Z retrospective study of treatment persistence and adherence to mirabegron versus antimuscarinics, for the treatment of overactive bladder in Spain. BMC Urol 18(1):76
29. Serati M, Maggiore LR et al (2017) Is mirabegron equally as effective when used as first- or second-line therapy in women with overactive bladder? Int Urogynecol J 28(7):1033–1039