TITLE:

Mirabegron (Betmiga®) improves quality-of-life, treatment satisfaction, and persistence in patients with overactive bladder: a multi-centre, non-interventional, real-world, 12-month study

AUTHORS:

Robert Freeman, Steve Foley, José Rosa Arias, Eduardo Vicente, Robert Grill, Zuzana Kachlirova, Anny Stari, Moses Huang, Nurul Choudhury

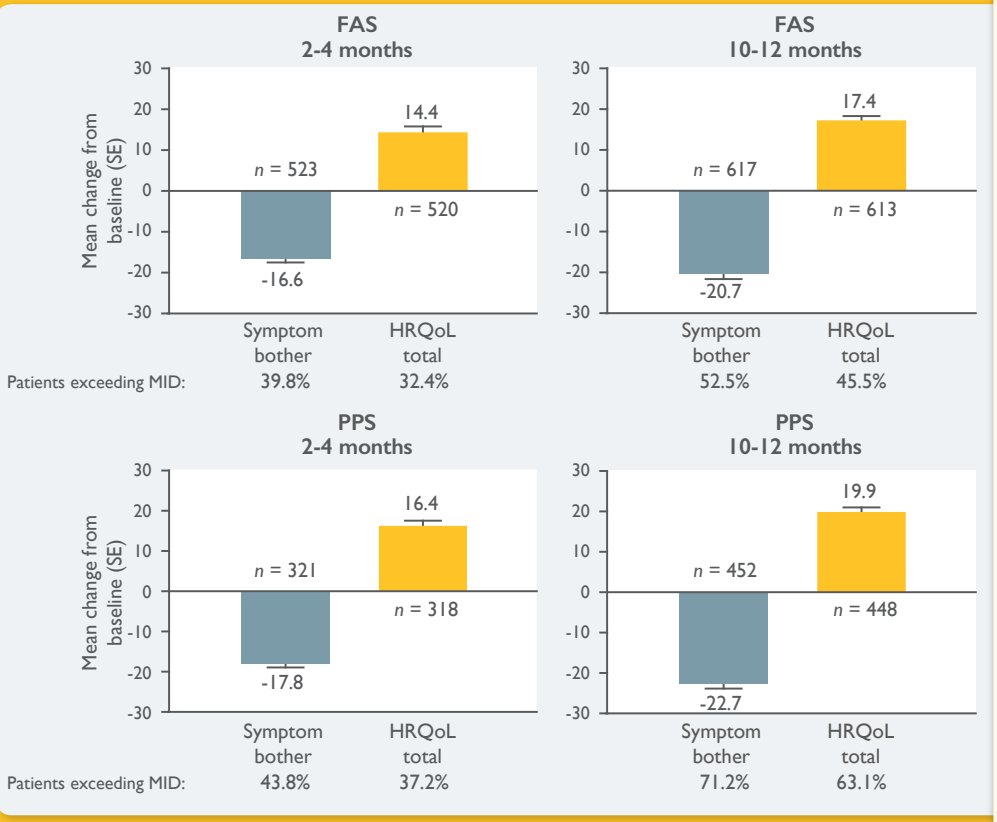
DESIGN:

This was a prospective, observational study in patients with overactive bladder (OAB) who were prescribed Betmiga® as part of routine clinical practice and followed-up for 12 months.

OBJECTIVE:

Primary	Secondary
Assess change from baseline in quality-of-life using the overactive bladder questionnaire (OAB-q) sub-scales	Assessment of treatment persistence, patient satisfaction, healthcare resource utilisation and adverse events (AEs)

RESULTS:



Improvements in OAB-q sub-scales from baseline to 2–4 months and 10–12 months.
Abbreviations. FAS, full analysis set; HRQoL, health-related quality-of-life; MID, minimally important difference (≥10-point improvement); OAB-q, overactive bladder questionnaire; PPS, per protocol set (all enrolled patients on Betmiga® at 10–12 months who completed the OAB-q at baseline and at 10–12 months, i.e. those who remained on Betmiga® for 10–12 months); SE, standard error.

Adapted from Freeman R, et al. Curr Med Res Opin. 2018.

- Patients on Betmiga® had **better symptom bother** and **HRQoL scores** at 10-12 months than at 2-4 months
- More patients **achieved MID** at 10-12 months than at 2-4 months
- The percentage of **patients with an OAB dry episode (the dry rate) increased over time** (34.9% at baseline to 43.7% at 10-12 months) and there was a reduction in pad use
- **High persistence:** 53.8% (more than 1 in 2) of patients were still receiving Betmiga® at 10-12 months
- The overall incidence of AEs was **in line with the established safety profile** of Betmiga®; there were no unexpected safety issues reported

KEY TAKEAWAYS:

Patients on Betmiga® in a real-world setting experienced meaningful **improvements in QoL** and **health status**, with a **persistence rate** of **53.8%** at 12 months

No unexpected safety issues were reported, and AEs were in line with the **established safety profile** of Betmiga®

BETMIGA™ ABBREVIATED PRESCRIBING INFORMATION
Presentation: Prolonged-release tablets containing 25 mg or 50 mg mirabegron. **Indication:** Symptomatic treatment of urgency, increased micturition frequency and/or urgency incontinence as may occur in adult patients with overactive bladder (OAB) syndrome. **Dosage:** Adults 18 years and above (including elderly patients): The recommended starting dose is 25 mg once daily with or without food. Betmiga 25mg is effective within 8 weeks. Based on individual patient efficacy and tolerability the dose may be increased to 50 mg once daily. Renal and hepatic impairment patients: No dose adjustment is necessary in patients with mild to moderate renal impairment. In patients with severe renal impairment, the recommended dose is 25 mg dose once daily. No dose adjustment is necessary in patients with mild hepatic impairment (Child-Pugh Class A). In patients with moderate hepatic impairment (Child-Pugh Class B) the recommended dose is 25 mg once daily. Renal impairment patient with strong CYP3A inhibitors: *Mild to moderate renal impairment* 25 mg once daily. *Severe renal impairment* not recommended. Hepatic impairment patient with strong CYP3A inhibitors: *Mild hepatic impairment (Child-Pugh Class A)* 25 mg once daily. *Moderate hepatic impairment (Child-Pugh Class B)* not recommended. **Method of Administration:** Betmiga is to be taken once daily, with liquids, swallowed whole and is not to be chewed, divided, or crushed. **Contraindication:** Hypersensitivity to the active substance or to any of the excipients listed in section list of excipients. Severe uncontrolled hypertension defined as systolic blood pressure ≥180 mm Hg and/or diastolic blood pressure ≥110 mm Hg. **Special Precautions:** Renal impairment: Betmiga has not been studied in patients with end stage renal disease (GFR < 15 mL/min/1.73 m2 or patients requiring haemodialysis) and, therefore, it is not recommended for use in this patient population. Data are limited in patients with severe renal impairment (GFR 15 to 29 mL/min/1.73m2); based on a pharmacokinetic study (see full prescribing information) a dose reduction to 25 mg is recommended in this population. Betmiga is not recommended for use in patients with severe renal impairment (GFR 15 to 29 mL/min/1.73m2) concomitantly receiving strong CYP3A inhibitors (see full prescribing information). Hepatic impairment: Betmiga has not been studied in patients with severe hepatic impairment (Child-Pugh Class C) and, therefore, it is not recommended for use in this patient population. Betmiga is not recommended for use in patients with moderate hepatic impairment (Child-Pugh B) concomitantly receiving strong CYP3A inhibitors (see full prescribing information). Increases in Blood Pressure: Mirabegron can increase blood pressure. Blood pressure should be measured at baseline and periodically during treatment with Betmiga, especially hypertensive patients. Data are limited in patients with stage 2 hypertension (systolic blood pressure ≥ _160 mm Hg or diastolic blood pressure ≥ _100 mm Hg). In two, randomized, placebo-controlled, healthy volunteer studies, Betmiga was associated with dose-related increases in supine blood pressure. In these studies, at the maximum recommended dose of 50 mg, the mean maximum increase in systolic/diastolic blood pressure was approximately 3.5/1.5 mmHg greater than placebo. In contrast, in OAB patients in clinical trials, the mean increase in systolic and diastolic blood pressure at the maximum recommended dose of 50 mg was approximately 0.5 - 1 mmHg greater than placebo. Worsening of preexisting hypertension was reported infrequently in Betmiga patients. Patients with congenital or acquired QT prolongation: Betmiga, at therapeutic doses, has not demonstrated clinically relevant QT prolongation in clinical studies (see full prescribing information). However, since patients with a known history of QT prolongation or patients who are taking medicinal products known to prolong the QT interval were not included in these studies, the effects of mirabegron in these patients is unknown. Caution should be exercised when administering mirabegron in these patients. Patients with bladder outlet obstruction and patients taking antimuscarinics medications for OAB: Urinary retention in patients with bladder outlet obstruction (BOO) and in patients taking antimuscarinic medications for the treatment of OAB has been reported in postmarketing experience in patients taking mirabegron. A controlled clinical safety study in patients with BOO did not demonstrate increased urinary retention in patients treated with Betmiga; however, Betmiga should be administered with caution to patients with clinically significant BOO. Betmiga should also be administered with caution to patients taking antimuscarinic medications for the treatment of OAB. **Interactions:** Inhibitory effect on the metabolism of CYP2D6 substrates. Betmiga is a moderate and time-dependent inhibitor of CYP2D6 and weak inhibitor of CYP3A. Increased AUC in the presence of the strong inhibitor of CYP3A/P-gp ketoconazole. Caution if co-administered with medicines with a narrow therapeutic index and significantly metabolised by CYP2D6. When initiating in combination with digoxin the lowest dose for digoxin should be prescribed and serum digoxin should be monitored. **Undesirable Effects:** Summary of the safety profile: The safety of Betmiga was evaluated in 8433 patients with OAB, of which 5648 received at least one dose of mirabegron in the phase 2/3 clinical program, and 622 patients received Betmiga for at least 1 year (365 days). In the three 12-week phase 3 double blind, placebo controlled studies, 88% of the patients completed treatment with Betmiga, and 4% of the patients discontinued due to adverse events. Most adverse reactions were mild to moderate in severity. The most common adverse reactions reported for patients treated with Betmiga 50 mg during the three 12- week phase 3 double blind, placebo controlled studies are tachycardia and urinary tract infections. The frequency of tachycardia was 1.2% in patients receiving Betmiga 50 mg. Tachycardia led to discontinuation in 0.1% patients receiving Betmiga 50 mg. The frequency of urinary tract infections was 2.9% in patients receiving Betmiga 50 mg. Urinary tract infections led to discontinuation in none of the patients receiving Betmiga 50 mg. Serious adverse reactions included atrial fibrillation (0.2%). Adverse reactions observed during the 1-year (long term) active controlled (muscarinic antagonist) study were similar in type and severity to those observed in the three 12-week phase 3 double blind, placebo controlled studies. Tabulated list of adverse reactions: The table below reflects the adverse reactions observed with mirabegron in the three 12-week phase 3 double blind, placebo controlled studies. The frequency of adverse reactions is defined as follows: very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1,000 to <1/100); rare (≥1/10,000 to <1/1,000); very rare (<1/10,000). Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness. Infections and infestations: *Common:* Urinary tract infection; *Uncommon:* Vaginal infection Cystitis. Psychiatric disorders: *Not known:* Insomnia (observed during post-marketing experience). Eye disorders: *Rare:* Eyelid oedema. Cardiac disorders: *Common:* Tachycardia; *Uncommon:* Palpitation, Atrial fibrillation. Vascular disorders: Very rare: Hypertensive crisis (observed during post-marketing experience). Gastrointestinal disorders: common: Nausea (observed during post-marketing experience), Constipation (observed during post-marketing experience), Diarrhoea (observed during post-marketing experience); *Uncommon:* Dyspepsia, Gastritis; *Rare:* Lip oedema. Skin and subcutaneous tissue disorders: *Uncommon:* Urticaria, Rash. Rash macular, Rash popular, Pruritus; *Rare:* Leukocytoclastic, vasculitis, Purpura Angioedema (observed during post-marketing experience). Musculoskeletal and connective tissue disorders: *Uncommon:* Joint swelling. Reproductive system and breast disorders: *Uncommon:* Vulvovaginal, pruritus. Investigations: *Uncommon:* Blood pressure increased, GGT increased, AST increased, ALT increased. Renal and urinary disorders: *Rare:* Urinary retention (observed during post-marketing experience). Nervous system disorders: *Common:* Headache (observed during post-marketing experience), Dizziness (observed during post-marketing experience).
Packs: 30 prolonged-release tablets of 25 mg, 50 mg. **API date:** 29th Jan 2018

Reference:
1. Freeman R, Foley S, Arias JR, *et al.* Mirabegron improves quality-of-life, treatment satisfaction, and persistence in patients with overactive bladder: a multi-center, non-interventional, real-world, 12-month study. *Curr Med Res Opin.* 2018 May;34(5):785-793. doi: 10.1080/03007995.2017.1419170. Epub 2018 Jan 10.

Full prescribing information available upon request.
For healthcare professionals only.

Astellas Pharma Malaysia Sdn Bhd
Suite 18.05, Level 18, Centrepoint North Tower, Mid Valley City, Lingkaran Syed Putra, 59200 Kuala Lumpur.
Tel: +603-2202 6999 Fax: +603-2202 6988/977 www.astellas.com

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