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Original article - overactive bladder

Results of a randomized, double-blind, placebo-controlled study of mirabegron in a Taiwanese population with overactive bladder and comparison with other clinical trials☆

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ABSTRACT

Objective: Mirabegron, a β_3-adrenoceptor agonist, has been shown to be effective and safe in the treatment of overactive bladder (OAB). The aim of this study was to assess the efficacy and safety of mirabegron (50 mg) versus placebo in Taiwanese patients with OAB.
Materials and patients: This was a multicenter, randomized, double-blind, parallel-group, placebo- and active-controlled trial conducted at 12 sites in Taiwan. Patients were randomized in a 1:1:1 ratio to receive placebo, mirabegron (50 mg), or tolterodine extended release (4 mg) orally once daily for 12 weeks. The primary efficacy end point was the change in the mean number of micturitions per 24 hours from baseline to the final visit. Secondary end points were volume voided, and the number of urgency, urinary incontinence, urge incontinence, and nocturia episodes per 24 hours; in addition, the King's Health Questionnaire (KHQ) was administered to assess effects on quality of life.
Results: A total of 218 patients were included in the full analysis set (68 in the placebo group; 76 in the mirabegron group; and 74 in the tolterodine group). The adjusted mean difference between the mirabegron and placebo groups for the change in mean number of micturitions per 24 hours was −1.42 ($p = 0.004$). The adjusted mean difference between the mirabegron and placebo groups with regard to the change in volume voided per micturition was 16.7 mL ($p = 0.013$). However, the mirabegron group did not show statistically significant superiority to the placebo group in the other efficacy variables. There was also no statistically significant difference between mirabegron and placebo in any KHQ domain score. The incidence of treatment-emergent adverse events in the mirabegron group was low and similar to that in the placebo group.

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Conclusion: Mirabegron at a dose of 50 mg once daily for 12 weeks is superior to placebo in reducing the frequency of micturitions in Taiwanese patients with symptoms of OAB. No clinically relevant, serious adverse events were identified.

1. Introduction

Overactive bladder (OAB) syndrome is characterized by urinary urgency with or without urgency incontinence,[1] which affects > 400 million people worldwide.[2] Epidemiology studies have also revealed that OAB affects 12–16% of the adult population across Europe, the USA, and Japan.[3–5] Antimuscarinics have been considered the first-line pharmacotherapy for OAB.[6–8] However, a high proportion of patients discontinue antimuscarinic therapy due to suboptimal efficacy or intolerable adverse events (AEs) with < 25% remaining on treatment at 1 year.[9,10] There is therefore an urgent need to develop new drugs for OAB that do not have the adverse effects of antimuscarinic agents.

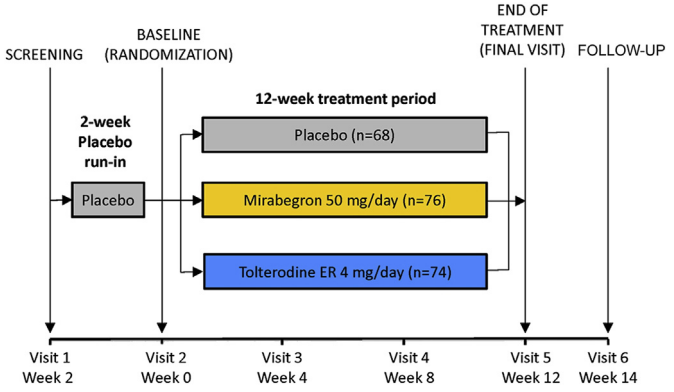

Fig. 1. The study design.

The β_3-adrenergic receptors have been known to promote urine storage in the bladder by inducing detrusor relaxation in animal and human bladders.[11–13] The β_3-adrenoceptor is the predominant β-receptor subtype in the human urinary bladder, representing 97% of total β-adrenoceptor messenger RNA expression in the human bladder.[14] The β_3-adrenoceptor agonists relax the detrusor smooth muscle during the bladder storage phase and increase bladder capacity.[15] Unlike the mechanism of antimuscarinic agents, β_3-adrenoceptor agonists increase bladder capacity without a change in micturition pressure, residual volume, or voiding contraction.[16–18]

Mirabegron, a β_3-adrenoceptor agonist, is a first-in-class drug for the treatment of OAB.[19] Mirabegron demonstrated significant dose-dependent improvements in key OAB symptoms in one phase II study.[20] Pooled safety data indicated that mirabegron may be a valuable treatment option for patients with OAB as the incidence of dry mouth, the chief cause of discontinuation of antimuscarinic agents, was lower than with the use of an active comparator, tolterodine extended release (ER; 4 mg).[21]

Although recent phase III trials have confirmed the efficacy and safety of mirabegron in treatment of OAB in European, Australian, North American, and Japanese populations,[22–25] the therapeutic efficacy and safety had not been demonstrated in Taiwanese people. This phase III study aims to assess the efficacy of

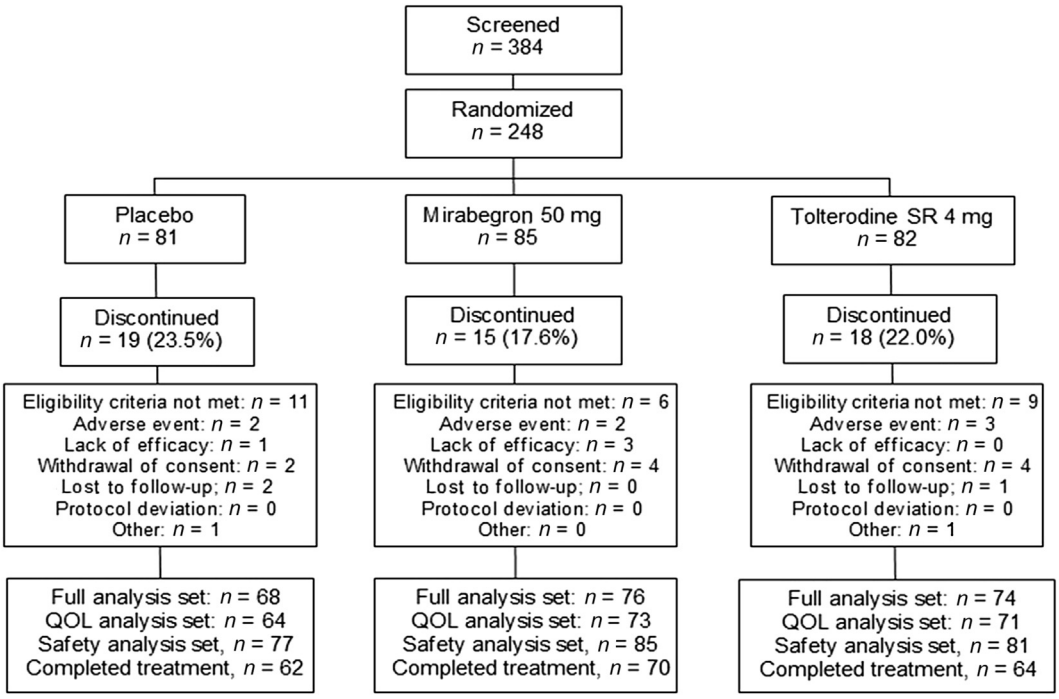

Fig. 2. Disposition of the study patients. QOL = quality of life.