URINARY INCONTINENCE

Patient-reported outcome measures favour use of mirabegron in patients with OAB

Overactive bladder (OAB), a chronic condition characterized by urinary urgency with or without urinary incontinence, can have serious detrimental effects on the quality of life of patients with this condition. Antimuscarinics such as solifenacin, darifenacin and oxybutin have long been the mainstay of noninvasive symptom management in patients with OAB, although these agents are poorly tolerated by many, largely owing to side effects such as dry mouth and blurred vision.

Mirabegron, a β_3 -adrenoceptor agonist that mimics the effects of sympathetic stimulation on the bladder, gained approval from the FDA for treatment of OAB in 2012. This approval followed the findings of the SCORPIO trial, in which mirabegron was found to reduce the number of incontinence episodes and micturition frequency, with significantly fewer incidences of dry mouth. Despite these positive findings, the overall frequency of adverse events was similar between the mirabegron

and tolterodine treatment arms of SCORPIO; thus, the original trial analysis failed to address an important question: which treatment do patients prefer?

To address this question, further analyses of the SCORPIO trial have now been conducted. In this trial, minimum baseline OAB symptoms included an average

daily micturition frequency of ≥ 8 and ≥ 3 episodes of urinary urgency with, or without incontinence. Patients were randomized to receive either mirabegron 50 mg/day, tolterodine extended release (ER) 4 mg/day or placebo for a study duration of 12 weeks. Patient-reported outcomes (PROs) were assessed using a range of validated outcome instruments including the treatment satisfaction visual analogue scale (TS-VAS) OAB questionnaire (OAB-q) and patient perception of bladder condition (PPBC).

“...mirabegron is a better-tolerated treatment of OAB than tolterodine ER...”

Patients receiving treatment with mirabegron reported significant improvements in OAB-q coping and OAB-q concern scores compared with patients who received placebo. Furthermore, significantly more patients receiving mirabegron also reported a ≥ 1 point improvement in PPBC than those receiving placebo, although, the social and sleep components of OAB-q were not affected by treatment with mirabegron.

In a large subgroup of patients with OAB and incontinence ($n = 291$, 293 and 300 in placebo, mirabegron and tolterodine ER groups, respectively), significant improvements in OAB-q coping and concern scores were again observed, in addition to significant improvements in OAB-q concern and TS-VAS scores compared with placebo.

To provide further validation of improvements, self-reported effects on workplace productivity were also assessed, revealing decreases in both absenteeism and impairment at work, although no statistical analyses were conducted.

The trial design used did not allow direct statistical comparisons with PROs

in the mirabegron and tolterodine ER group, although a >1 point improvement in PPBC was the only significantly improved PRO in patients in the tolterodine ER group relative to placebo, suggesting indirectly that management of OAB symptoms with mirabegron is the preferred treatment option for most patients who opt for noninvasive symptom management.

Virtually all phase III clinical trials use objective measurements of responses to treatment, yet few also measure PROs. A patient's perception of the efficacy and tolerability of a treatment, regardless of data on hard clinical end points, arguably provides the most relevant indication of patient adherence and persistence with therapy and, therefore, capacity to improve the quality of life of patients.

With this in mind, findings of this secondary analysis of data from the SCORPIO trial confirm that mirabegron is a better-tolerated treatment of OAB than tolterodine ER, despite the similar reductions in incontinence episodes reported following the primary analysis of data from SCORPIO.

Despite the positive findings of this analysis, certain limitations remain, which will likely require further investigation. This trial was not sufficiently powered to enable a direct statistical comparison between tolterodine ER and mirabegron, nor was the follow-up duration sufficiently long to provide an assessment of long-term efficacy and tolerability of mirabegron: this remains an important and unanswered question, given the long-term and refractory nature of OAB symptoms.

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ERRATUM

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In four places in this article solifenacin ER was incorrectly described as being investigated in this trial and not tolterodine ER. This error has been corrected in the HTML, PDF and print versions of this article.