Solifenacin for neurogenic detrusor overactivity: patient-reported outcomes from the randomised clinical trial SONIC

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INTRODUCTION

- Neurogenic detrusor overactivity (NDO) is defined as an involuntary contraction of the detrusor muscle of the bladder, secondary to a neurologic disorder.
- Symptoms include increased urinary frequency, urgency, urgency incontinence and incontinence without urgency, which can significantly impact quality of life.
- NDO affects a large proportion of patients with central nervous system disorders, such as multiple sclerosis (MS) or spinal cord injury (SCI), as a result of loss of modulation control from the spinal cord's central nervous system structures.
- Antimuscarinics are the standard treatment for patients with neurogenic bladder (NGB), and although low studies have evaluated their efficacy and tolerability in patients with NDO, they are routinely used for the treatment of these patients.
- Solifenacin has been shown to improve urodynamic symptoms in patients with MS and SCI symptoms in a small open-label study.
- The aim of the SONIC study was to evaluate the efficacy and tolerability of solifenacin vs placebo in patients with NDO due to MS or SCI in comparison to placebo treatment and in relation to the effect of oxybutynin 15 mg as an active control.

METHODS

Study design
- SONIC (SOlifenacin in NeurogenIC Detrusor overactivity) was a prospective, randomised, multicentre, double-blind, phase IIIb/IV parallel-group study (ClinicalTrials.gov identifier: NCT01926942).
- After a 2-week placebo run-in period, patients were randomised in a ratio of 1:1:1 to receive solifenacin 15 mg, solifenacin 10 mg or oxybutynin 15 mg (5 mg bid) or matched placebo for 4 weeks (Figure 1).
- Doses were based on licensed doses frequently prescribed in clinical practice.

Patients
- Patients with NDO were enrolled at 45 sites in 10 European countries and Australia from March 2008 to January 2011.
- Adults aged 18–65 years who had MS (Expanded Disability Status Scale (EDSS) < or SCI (partial or complete lesion), with stable NDO for ≥6 months) were eligible for inclusion.
- Patients were excluded if they had NDO owing to Parkinsonian disease or cerebrovascular disease, if they had a maximum bladder capacity ≥400 mL or if they were receiving anticholinergics, muscle relaxants or opioids for treatment of NDO.
- Written informed consent was obtained for all patients.

Efficacy assessments

Primary efficacy endpoint
- Change from baseline to end of treatment in maximum cystometric capacity.

Efficacy PRO
- Efficacy PROs included as secondary efficacy variables were:
  - Patient Perception of Bladder Condition (PPBC) 6-point scale
  - Incontinence Quality of Life (I-QoL) questionnaire (22 questions, each with a 5-point scale response range about avoidance and limiting behavior, psychosocial impact and social embarrassment).21
  - A visual analogue scale (VAS) to rate treatment satisfaction (TS-VAS).
- PROs were assessed at baseline and at the end of treatment.

Safety assessments

Safety assessment
- Change in VAS scores from baseline to end of treatment for dry mouth, constipation, blurred vision, fatigue, memory and attention.

Adverse events
- Adverse events were included the incidence and severity of adverse events (AEs) throughout the study period.

Statistical methodology
- The primary analysis was based on the full analysis set (FAS), defined as patients who took a total of ≥2 doses of the study drug with an efficacy assessment, including a maximum cystometric capacity measurement at baseline and at end of treatment.
- Baseline demographics and safety assessments were based on the safety population (SAF), defined as all randomised subjects who took a maximum cystometric capacity measurement, at baseline and end of treatment.

RESULTS

Baseline characteristics
- A total of 248 patients were screened and 194 subjects were randomised.
- Five patients discontinued at baseline and 189 patients were included in the SAF.
- Six patients (2 on placebo and 4 on solifenacin) discontinued during the treatment period, and 183 subjects completed the study.
- Baseline characteristics were similar between study groups.
- Patients had a mean age of 41.7 years (range 19–66), and 95 (50.3%) were male.

Statistical methodology
- The SONIC study was conceived and funded by Astellas Pharma Europe Ltd. Medical writing and editorial assistance for the preparation of this poster was provided by Lindsay Napier at Darwin Healthcare Communications (UK), and funded by Astellas.
- No external funding or sponsorship was received for this study.
- All authors had full access to all data and can take responsibility for the integrity of the data and the accuracy of the data analysis.
- The SONIC study was conducted in accordance with the principles of good clinical practice and in accordance with the ethical principles in the Declaration of Helsinki.

CONCLUSION

- Treatment with solifenacin 10 mg led to significant improvements in patient perception of bladder condition (PPBC), health-related QoL outcomes, and treatment satisfaction compared with placebo, and was well tolerated in patients with NDO due to MS or SCI.

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REFERENCES

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