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SOLIFENACIN SIGNIFICANTLY REDUCES BOTH URGENCY SEVERITY AND BOTHER: RESULTS FROM THE FLEXIBLE DOSE, PLACEBO CONTROLLED, MULTINATIONAL SUNRISE STUDY

Hypothesis / aims of study

Urgency is considered not only as the central feature of overactive bladder (OAB) but also as the driver for all other symptoms. Recently it has been proposed that urgency should not be treated as an on/off event but one varying in severity. A key objective of the SUNRISE study was to determine the effects of solifenacin, administered according to the approved flexible dosing regimen, on both severity of urgency and the bother associated with it.

Study design, materials and methods

A prospective, double blind, 2-arm, parallel-group, 16-week study was conducted to compare the efficacy of solifenacin and placebo in the reduction of urgency severity and episodes in patients with symptoms of overactive bladder for ≥ 3 months. Patients entered into a single-blind placebo-controlled period of 2 weeks and then randomised to a 16-week, double blind, placebo-controlled (1:3 ratio) active treatment (solifenacin 5 mg) period. After 8 weeks the patients had the option of either continuing on the original dose or requesting a dose increase and this was subject to a second randomisation (patients on solifenacin had a 50% chance of a dose increase from 5 to 10 mg to enable comparison to be presented separately). Urgency severity was assessed on a validated 5-point scale (PPIUS) scored from 'no urgency' (0), 'mild urgency' (1), 'moderate urgency' (2), 'severe urgency' (3) and 'urge incontinence' (4). The primary variable was PPIUS (3+4), i.e. changes from baseline to endpoint in episodes of most severe urgency per 24h. Secondary variables included total urgency episodes/24h (PPIUS 1-4), urgency bother using a VAS, 'traditional' endpoints of micturition frequency/24h, incontinence and urge incontinence episodes/24h and patient reported outcomes (PROs) such as PBC (a validated categorical rating scale for Perception of Bladder Condition) and a Treatment Satisfaction VAS.

Results

503 patients treated with solifenacin as per approved dosing recommendations (5 mg increased to 10 mg if needed) and 206 on placebo were included in the Full Analysis Set (FAS); demographics and baselines were similar. In comparison to placebo patients treated with solifenacin showed significantly greater reductions from baseline to endpoint in episodes of most severe urgency (-2.6 vs. --1.8; p<0.001) and also secondary urgency variables such as total urgency (-2.3 vs. -1.6; p=0.0006) and 'traditional' endpoints such as micturition episodes (-2.1 vs. -1.3; p<0.0001), incontinence (-1.7 vs. -1.4; p=0.0003) and urge incontinence (-1.7 vs. -1.3; p=0.0002). These changes were associated with a significant reduction of 42.4% in VAS urgency bother (p<0.0001 vs. placebo) and 31.7% in the severity of bladder problems using the PBC (p<0.0001 vs. placebo) and significant Treatment Satisfaction (P<0.0001 vs. placebo). The incidence of dry mouth in solifenacin treated patients (15.8%) was significantly greater than placebo (2.7%; p<0.001) as was constipation (6.9% vs. 2.2%; p=0.0123) but incidence of the other key antimuscarinic adverse event (AE) of blurred vision was similar (0.8% vs. 0.9%; NS). Discontinuation rates for all causes were low and similar for solifenacin and placebo (12.1% and 11.6%) as was rates of withdrawal for AEs (3.0% vs. 2.7%).

Interpretation of results

This study has urgency, with severity and bother attributes, as the main focus and enables treatment impact to be considered alongside that on 'traditional' and PRO endpoints.

Concluding message

Patients treated with solifenacin as per approved dosing recommendations showed a highly significant reduction in urgency severity, incidence and bother alongside that in micturition frequency, incontinence and urge incontinence. Associated with this patients perceived a significant reduction in the severity of their OAB problems. The treatment was well tolerated and the balance between efficacy and tolerability may explain the significant treatment satisfaction reported by these patients

FUNDING: Astellas Pharma europe

DISCLOSURES: consultant

CLINICAL TRIAL REGISTRATION: This clinical trial has not yet been registered in a public clinical trials registry.

HUMAN SUBJECTS: This study was approved by the central IECs of 14 countries and followed the Declaration of Helsinki Informed consent was obtained from the patients.