155

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SOLIFENACIN IMPROVES URGENCY SYMPTOMS AS ASSESSED BY VOIDING DIARIES AND PATIENT-REPORTED OUTCOMES (PRO) IN PATIENTS WITH OVERACTIVE BLADDER

Hypothesis / aims of study
The primary aim of the VENUS (**V**ESIcare® **E**fficacy and Safety in Patie**N**ts with **U**rgency **S**tudy) study was to assess the efficacy of solifenacin on the symptom of urinary urgency in patients with overactive bladder (OAB). Urgency has been cited as the most bothersome symptom for patients with OAB [1]. Urgency was assessed quantitatively in the VENUS study using micturition diaries and qualitatively using PRO measures including the Indevus Urgency Severity Scale (IUSS) and the Urgency Perception Scale (UPS).

Study design, materials and methods
VENUS was a randomized, double-blind, placebo-controlled, parallel-group, flexible-dosing multicenter study designed to assess the efficacy and safety of daily oral solifenacin. Patients were enrolled who had at least 1 urinary urgency episode per 24 hours, with or without urge incontinence, documented in a 3-day diary during the screening phase. Eligible patients (n = 739) were randomized to receive either 5 mg solifenacin (n=372) or matching placebo (n=367) for the first four weeks of the study. At Weeks 4 and 8, the dose of solifenacin (or matching placebo) could be maintained, increased to 10 mg/day, or decreased to 5 mg/day. Changes in OAB symptoms including urgency (primary endpoint), frequency, urge incontinence, nocturia, and nocturnal voids, were measured via 3-day micturition diaries. Qualitative measures of urgency were assessed with the IUSS, and the UPS. The IUSS is a validated, single-item patient-reported measure of urgency severity associated with OAB [2]. The UPS is a validated 3-point scale used to describe the patient's perception of urgency when they feel the desire to urinate [3]. A 3-day micturition diary was completed before the baseline visit and the week 4, 8, and 12 visits. The IUSS and UPS were completed by patients at the baseline and week 12 visits.

Results
Solifenacin treatment provided consistent and significant reductions in urgency episodes. The mean number of urgency episodes at baseline was 6.15 and 6.03 per 24 hours for the solifenacin and placebo groups, respectively. At endpoint, mean urgency episodes decreased by 3.91 (P<.001) for the patients treated with solifenacin and by 2.73 (P <.0001) for patients receiving placebo. The difference between the solifenacin treatment and placebo groups was statistically significant (P <.0001). Using the IUSS, most patients assessed their degree of urgency as "moderate" at baseline. At endpoint, more patients receiving solifenacin (193/332, 58.1%) compared to the placebo group (135/323, 41.7%) who had assessed their degree of urgency as "moderate" or "severe" at baseline assessed their degree of urgency at endpoint as either "mild" or "moderate". At endpoint, more patients in the solifenacin group (140/332, 42.1%) had reported an improvement in their perception of urgency on the UPS compared to the placebo group (107/323, 33.1%). Statistically significant improvements were observed in the solifenacin group compared with the placebo group for mean change in IUSS and UPS scores from baseline to endpoint. In the patients who reported 2 or 3 (moderate or severe urgency discomfort) in the IUSS at baseline, 73.9% (212/287) reported 0 or 1 (none or mild discomfort) at endpoint in the solifenacin group compared to 49.0% (127/259) in the placebo group. Among all the patients who reported a score of 1 or 2 on the UPS at baseline, 40.3% (118/293) reported 3 (able to finish task before voiding) at endpoint in the solifenacin group compared to 30.0% (81/270) in the placebo group.

Interpretation of results
These results demonstrated that solifenacin is effective at reducing urgency in patients with OAB. The use of 2 validated PRO measures of urgency allows the symptom of urgency to be assessed qualitatively in addition to the quantitative findings from micturition diaries. IUSS scores have been show to correlate well with measures of symptom bother and health-related quality of life [1]. The UPS has been shown to correlate well with patients' perception of bladder condition, changes in urinary diary variables, and pad usage [2].

Concluding message
Several instruments have been developed to measure urgency in OAB patients. Solifenacin provided consistent and statistically significant improvements in urgency as measured by micturition diary data and two additional urgency-specific PRO measures, the IUSS and UPS, when compared to placebo. This is the first solifenacin trial to utilize urgency as a primary endpoint in addition to multiple urgency measures including PROs. This study confirms that solifenacin significantly improves urgency in OAB patients compared to placebo.

IUSS
Patients rate the degree of urgency according to the following scale:

0 None, no urgency
1 Mild, awareness of urgency, but easily tolerated
2 Moderate, enough urgency discomfort that it interferes with usual activity/tasks
3 Severe, extreme urgency discomfort that abruptly stops all activity/tasks

UPS

Patients choose 1 of the following responses:
1 I am usually not able to hold urine.
2 I am usually able to hold urine until I reach the toilet if I go immediately.
3 I am usually able to finish what I am doing before going to the bathroom.

References

1. Value Health. 2004 Jul-Aug;7(4):455-63.
2. J Urol. 2005 Aug;174(2):604-7.
3. BJU Int. 2005 Mar;95(4):591-6.

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