123

Toglia M[1], Andoh M[2], Hussain I[2]
1. Urogynecology Associates of Philadelphia, Media, PA, 2. Astellas Pharma, Inc., Deerfield, IL

SOLIFENACIN IMPROVED WARNING TIME SIGNIFICANTLY COMPARED TO PLACEBO IN PATIENTS WITH OVERACTIVE BLADDER

Hypothesis / aims of study
The ICS definition of overactive bladder (OAB) highlights urgency as the predominant symptom, although it is commonly acknowledged that this symptom is the most difficult to define and quantify. Objective measurements of the time interval between the first sensation of urgency and the time of bladder emptying (Warning Time; WT) has been one attempt by researchers to quantify urgency. Increasing warning time may be an important goal of therapy, especially if this increase enables a patient to avoid an episode of incontinence. The VENUS (VESIcare® Efficacy and Safety in PatieNts with Urgency Study) trial was designed to assess changes in urgency with solifenacin treatment using multiple endpoints. Data presented here focus on changes in WT in patients treated with solifenacin according to a flexible dosing regimen and compared to placebo.

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 micturition diary during the screening phase. The primary efficacy variable in VENUS was the mean change from baseline to endpoint in the number of urgency episodes per 24 hours. WT was measured using a stopwatch for the voids on the day preceding the baseline and the 12 week 3-day diary assessment. Eligible patients (n = 739) were randomized to receive either 5 mg solifenacin (n=372) or matching placebo (n=367) for the initial 4 weeks of the trial. At Weeks 4 and 8, the dose of solifenacin (or matching placebo) could be maintained, increased to 10 mg/day, or decreased back to 5 mg/day.

Results
The mean change from baseline to endpoint in the number of urgency episodes per 24 hours was 3.91 for the solifenacin group compared with 2.73 for the placebo group (*P*<.001). The change from baseline to endpoint in median length of WT was a statistically significant increase of 31.5 seconds for the solifenacin group and 12.0 seconds for the placebo group (*P*=0.032). The mean change in WT, from baseline to endpoint, increased over 2 minutes more in the solifenacin-treated versus placebo study arms. Specifically, WT increased by 186.4 seconds for patients treated with solifenacin and by 54.7 seconds for patients treated with placebo.

Interpretation of results
These results demonstrated that WT was significantly increased in patients treated with approved doses of solifenacin compared to placebo. Previous studies evaluating antimuscarinic therapy have not demonstrated significant increases in warning time when these agents were tested in a large clinical trial setting [1-3]. A randomized study of tolterodine extended release did not demonstrate a significant difference in WT compared to placebo. Similarly, a large trial of darifenacin at the highest approved dose (15mg) failed to show significant improvement in WT over placebo in ambulatory patients.

Concluding message
Solifenacin is the first antimuscarinic, administered at an approved dose in an ambulatory setting, to show a significant treatment effect versus placebo in prolonging WT.

1. Int J Clin Pract. 2006 60(1):119-126.
2. J Urol. 2005 173(4):1214-1218.
3. Abstract presented at the International Continence Society Annual Meeting, Paris, France, March 18-19 2004 (# 172).

FUNDING: **NONE**
DISCLOSURES: **NONE**
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 The study protocol and amendments were reviewed and approved by either the Institutional Review Board of each center or the Copernicus Group Institutional Review Board. and followed the Declaration of Helsinki Informed consent was obtained from the patients.**