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EFFICACY AND SAFETY OF FESOTERODINE TREATMENT FOR OVERACTIVE BLADDER (OAB) SYMPTOMS IN ELDERLY WOMEN WITH AND WITHOUT HYPERTENSION

Hypothesis / aims of study
Metabolic diseases, including hypertension (HT), diabetes mellitus, hyperlipidemia, have been identified as risk factors for the development of lower urinary tract symptoms. The majority of patients with OAB are elderly, have comorbidities, and take concomitant medications. We assessed the efficacy and safety of fesoterodine versus placebo (PBO) in elderly females with OAB symptoms, including urgency urinary incontinence (UUI), and with or without concomitant HT.

Study design, materials and methods
In this post-hoc analysis, the efficacy and safety of fesoterodine (4 mg or 8 mg) versus PBO were assessed using pooled data from ten 12-week, double-blind, placebo-controlled, parallel-group studies. The study population consisted of female subjects aged ≥65 years with OAB symptoms for a minimum of 6 months and reporting >0 UUI episodes/24 hours at baseline. Efficacy outcomes included the change from baseline to week 12 in UUI episodes/24 hours, micturitions/24 hours, nocturnal micturitions/24 hours, and urgency episodes (Urinary Sensation Scale rating ≥3)/24 hours; diary-dry rate responders (UUI/24 h = 0 at endpoint); micturition responders (<8 micturitions/24 h at endpoint); and the change from baseline to week 12 in scores for the OAB questionnaire (OAB-q) and Patient Perception of Bladder Condition (PPBC). Continuous efficacy endpoints were analyzed using an ANCOVA model, with baseline value as a covariate and treatment and study as factors. For the PPBC, diary-dry rate responders, and micturition responders, the Cochran-Mantel-Haenszel (CMH) test with modified ridit scoring stratified by study was used to compare the two treatment groups. Comparisons for all efficacy analyses used the 5% level of type 1 error. Adverse events (AEs) were analyzed descriptively. All studies had ethical committee approval and enrolled patients who provided informed consent.

Results
Of the 2527 eligible elderly female patients with OAB symptoms, including UUI, 1523 patients (60.3%) had a medical history of HT and 1004 patients (39.7%) had no history of HT. Mean body weight, BMI, and OAB symptom values at baseline were significantly higher in patients with HT than in those without HT (all *P* <0.05; **Table 1**).The improvements from baseline to week 12 in all OAB symptoms with fesoterodine were significantly greater than PBO in both elderly females with HT and those without HT (all *P* <0.05; **Table 2**). The proportion of elderly females who were dry (no UUI episodes) and the proportion who had <8 micturitions at week 12 were statistically significantly greater with fesoterodine versus PBO in both patient populations. OAB symptom bother, health-related quality of life (HRQL) outcomes, and PPBC scores also were statistically significantly improved with fesoterodine versus PBO in elderly females with or without HT. Overall, the incidence of treatment-related AEs in the fesoterodine group was not higher in elderly women with HT (39.3%) than in those without HT (44.6%). In elderly females treated with fesoterodine, dry mouth and constipation were the most common treatment-related AEs in those with HT (26.2% and 5.2%, respectively) and those without HT (30.5% and 8.0%, respectively).

Interpretation of results
HT is a possible risk factor for aggravating OAB symptoms. Fesoterodine demonstrated significantly greater efficacy versus PBO in reducing UUI episodes, micturitions, nocturnal micturitions, and urgency episodes per 24 hours from baseline to week 12 in both elderly females with HT and those without HT. Patient-reported OAB symptom bother and HRQL outcomes, as assessed with the OAB-q, also demonstrated significantly greater improvements with fesoterodine versus PBO in elderly females with HT or without HT. Fesoterodine was generally well tolerated in these two patient populations.

Concluding message
These results suggest that concomitant HT does not affect the efficacy and safety of fesoterodine in elderly women with OAB symptoms, including UUI.

Table 1: Baseline Characteristics

	WITH HYPERTENSION (n=1523)	**WITHOUT HYPERTENSION (n=1004)**
Age (years) [a,b]	73.6 (5.6)	72.9 (5.5)*
Weight (kg) [a,b]	78.2 (16.4)	72.0 (16.0)†
Body mass index (kg/m^2) [a,b]	30.5 (6.3)	27.8 (5.8)†
Height (cm) [a,b]	160.1 (7.4)	160.8 (7.2)*
OAB symptoms [a,b]		
UUI episodes/24 h	3.63 (2.88)	3.29 (2.54)*
Micturitions/24 h	11.95 (3.18)	11.66 (2.94)*
Nocturnal micturitions/24 h	2.90 (1.47)	2.60 (1.34)†
Urgency episodes/24 h	10.07 (3.79)	9.73 (3.53)*

[a]Student's t-test. [b]Mean (SD) values for patients with UUI/24 h >0 at baseline.

*P <0.05 with HT vs without HT. †P <0.001 with HT vs without HT.

Table 2: Efficacy Outcomes at Week 12

Outcome	WITH HYPERTENSION		WITHOUT HYPERTENSION	
	PBO (n=569)	**FESO (n=954)**	**PBO (n=381)**	**FESO (n=623)**
UUI episodes/24 h[a]				
Change BL to Wk 12	-0.78 (0.09)	-1.61 (0.07)†	0.03 (0.13)	-0.80 (0.10)†
Micturitions/24 h[a]				
Change BL to Wk 12	-1.32 (0.11)	-2.29 (0.08)†	-1.24 (0.13)	-2.22 (0.10)†
Nocturnal micturitions/24 h				
Change BL to Wk 12	-0.42(0.05)	-0.55 (0.04)*	-0.32 (0.06)	-0.59 (0.05)†
Urgency episodes/24 h[a]				
Change BL to Wk 12	-2.27(0.16)	-3.86 (0.13)†	-1.86 (0.19)	-3.34 (0.15)†
Diary-dry responders (%)[b]				
Wk 12	33.6	45.5†	32.9	41.8†
Micturition responders, %[c]				
Wk 12	17.9	30.6†	18.8	30.1†
PPBC, %[d]				
BL to Wk 12*				
Deterioration	10.9	6.3	16.8	6.7
No change	36.0	25.4	34.1	25.0
Minor improvement	29.8	28.6	25.0	29.2
Major improvement	23.3	39.7	24.1	39.1
OAB-q scores[e]				
Symptom Bother				
Change BL to Wk 12 HRQL Total	-17.70 (1.03)	-27.54 (0.81)†	-14.43 (1.24)	-27.25 (1.03)†
Change BL to Wk 12	14.76 (0.92)	21.50 (0.72)†	11.10 (1.07)	21.51 (0.88)†

[a]BL and wk-12 data represent mean (SD) for patients with BL value >0 and with non-missing change from BL to wk 12, with ANCOVA to analyze treatment difference; [b]Proportion of patients with no UUI episode at wk 12, with CMH test to analyze treatment difference; [c]Proportion of patients with <8 micturitions/24 h at wk 12 analyzed with CMH test; [d]Proportion of patients with improvement from BL to wk 12 analyzed with CMH test, with *P* values for categorical changes in PPBC (with ≥2-point=major improvement, 1-point=minor improvement); [e]BL and wk-12 data depicted as mean (SD) for patients with non-missing change from BL to wk 12, with ANCOVA to analyze treatment difference (score range: 0 to 100; negative change in Symptom Bother score=improvement; positive change in HRQL Total score= improvement).
*P <0.05 for change from BL to wk 12 FESO vs PBO; †P <0.001 for FESO vs PBO.

Disclosures
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