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EFFICACY AND TOLERABILITY OF FESOTERODINE IN OLDER PEOPLE WITH OVERACTIVE BLADDER: RESULTS OF THE OPEN-LABEL PHASE OF THE SOFIA TRIAL

Hypothesis / aims of study: The Study of Fesoterodine in an Aging Population (SOFIA) trial, a 12-week randomized, double-blind (DB), placebo-controlled, parallel-group study followed by a 12-week open-label (OL) phase, assessed the efficacy, safety, and tolerability of flexible-dose fesoterodine (FESO) in elderly subjects with overactive bladder (OAB). During DB treatment FESO was associated with clinically and statistically significant improvements in most diary variables and patient-reported outcomes (PROs). For the primary endpoint, urgency episodes/24 h, improvements with FESO were greater than PBO for younger (<75 y) and older (≥75 y) subjects and with morning or evening dosing. Here, we assess FESO efficacy and tolerability during the 12-week OL phase.

Study design, materials and methods: At baseline, men and women aged ≥65 y with OAB symptoms for ≥3 months, a mean of ≥8 micturitions and ≥3 urgency episodes/24h, at least some moderate problems on the Patient Perception of Bladder Condition (PPBC), and a Mini Mental State Examination score ≥20 were randomized to DB treatment with FESO or placebo (PBO) for 12 weeks. Randomization was stratified by age (>75 y, ≤75 y) with a 1:1 ratio of FESO:PBO per stratum. Within each treatment group, subjects were randomized 1:1 to morning or evening dosing. At the beginning of the OL phase, subjects who received placebo during the DB phase started treatment with FESO 4 mg; the dose could be increased to 8 mg after 4 weeks of OL treatment and decreased again to 4 mg at any time thereafter. Subjects who received FESO during the DB phase continued on the same dose that they received at the end of the DB phase; their dose could not be increased, but could be decreased at any time. Efficacy was assessed descriptively with 3-day bladder diaries, the Overactive Bladder Questionnaire (OAB-q), PPBC, Urgency Perception Scale (UPS), Treatment Benefit Scale (TBS), and Overactive Bladder Satisfaction Questionnaire (OAB-S).

Results: Of the 314 and 341 subjects who received DB FESO or PBO, respectively, and completed the DB phase, 282 (90%) and 299 (88%) completed the OL phase, respectively. During OL FESO treatment, With OL FESO treatment, clinically significant improvements in diary variables (**Figure 1**) and PROs (**Figure 2**) were achieved in the group who had received DB PBO, whereas the group that had received DB FESO maintained the improvements achieved during the DB phase. Improvements in diary variables, the OAB-q, PPBC, and UPS from week 12 to 24 were greater in subjects who had previously received DB PBO. By week 24, the overall level of improvement in diary variables and the percentage of responders on the TBS and OAB-S were comparable among all subjects regardless of initial treatment group. The most common adverse events (AEs) during OL treatment for subjects who received DB FESO and DB PBO were dry mouth and constipation (**Table 1**). There were 3 serious AE's in the OL phase that were considered treatment-related by the investigators (urinary retention, TIA, and rash).

Interpretation of results: As expected, improvements during 12 weeks of OL FESO treatment allowed subjects who received PBO during the DB phase to achieve similar improvements to those initially receiving FESO. Subjects who received FESO during the DB phase maintained their improvement over the 12 week OL phase with few additional adverse effects.

Concluding message: OL treatment with FESO was associated with improvements in diary variables and PROs for subjects previously on DB PBO and maintained in subjects previously on DB FESO. FESO was generally well tolerated in this elderly population.

Figure 1

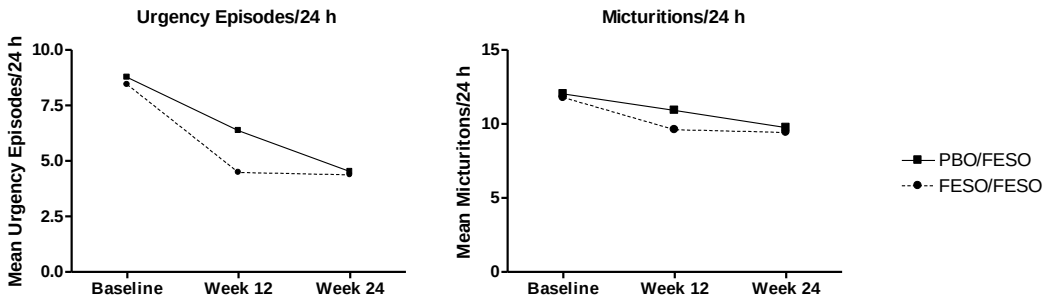
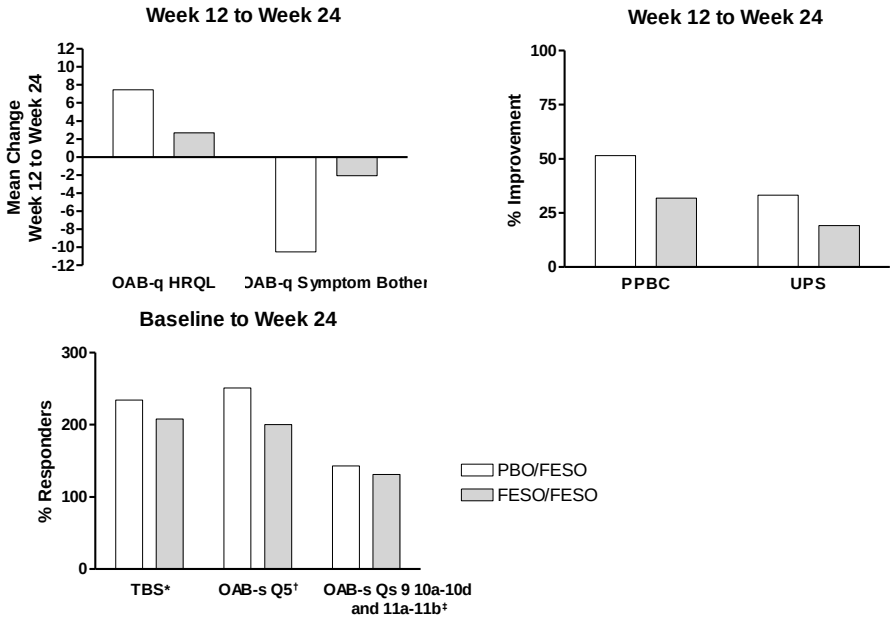


Figure 2



*My condition 'improved' or 'greatly improved' during treatment.

†OAB medication "met" or "somewhat" or "greatly exceeded my expectation."

‡Response of "very" or "somewhat satisfied" on all 7 items of OAB control.

Table 1: Treatment-emergent AEs Occurring in ≥3% of Patients in Any Group, Serious AE's, and Discontinuations Due to AEs

	Double-blind Phase		Open-Label Phase	
Adverse Event, n (%)	**PBO n=393**	**FESO n=392**	**PBO/FESO n=341**	**FESO/FESO n=313**
Dry mouth	21 (5.3)	133 (33.9)	95 (27.9)	21 (6.7)
Constipation	10 (2.5)	35 (8.9)	21 (6.2)	5 (1.6)
Dizziness	4 (1.0)	14 (3.6)	6 (1.8)	2 (0.6)
Nasopharygitis	9 (2.3)	12 (3.1)	2 (0.6)	6 (1.9)
Urinary tract infection	7 (1.8)	10 (2.6)	4 (1.2)	14 (4.5)
Serious AEs	9 (2.3)	14 (3.6)	7 (2.1)	11 (3.5)
Discontinuations due to AEs	20 (5.1)	53 (13.5)	32 (9.4)	6 (1.9)

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Is this a clinical trial?	**Yes**
Is this study registered in a public clinical trials registry?	**Yes**
Specify Name of Public Registry, Registration Number	**ClinicalTrials.gov ID NCT00798434**
Is this a Randomised Controlled Trial (RCT)?	**Yes**
What were the subjects in the study?	**HUMAN**
Was this study approved by an ethics committee?	**Yes**
Specify Name of Ethics Committee	**Newcastle and North Tyneside 1 Research Ethics Committee, United Kingdom**
Was the Declaration of Helsinki followed?	**Yes**
Was informed consent obtained from the patients?	**Yes**