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DOES FESOTERODINE PROVIDE EFFICACY, TOLERABILITY, AND TREATMENT SATISFACTION? A STUDY OF BRITISH PATIENTS WITH THE OVERACTIVE BLADDER SYNDROME

Hypothesis / aims of study

This study was conducted to evaluate the efficacy, safety, and tolerability of flexible-dose fesoterodine, as well as patient-reported treatment satisfaction, in individuals managed for overactive bladder (OAB) symptoms in the UK National Health Service.

Study design, materials and methods

This was an open-label trial conducted at 39 sites across the UK. Men and women aged ≥18 years with self-reported OAB symptoms for ≥3 months before screening, a mean of ≥8 micturitions/24 h and ≥3 urgency episodes/24 h on 3-day bladder diaries at baseline, and who reported at least “moderate” bladder-related problems on the Patient Perception of Bladder Condition at baseline were eligible to participate. All study participants received fesoterodine 4 mg once daily for the first 4 weeks, at which time they could increase their dose to 8 mg or remain at the 4-mg dose for the remaining 8 weeks of treatment based upon discussion of treatment efficacy and tolerability with the investigator. Following the 12-week treatment period, there was a 4-week post-treatment follow-up period. Three-day bladder diaries were completed immediately before baseline and week 12 visits. The Treatment Satisfaction Question (TSQ) was completed at week 12. Endpoints included changes in micturitions/24 hours (primary endpoint), urgency episodes/24 hours, and number of incontinence pads used/24 hours from baseline to week 12, as well as the percentage of subjects reporting treatment satisfaction (defined as responses of “very satisfied” or “somewhat satisfied”) on the TSQ at week 12. Adverse events (AEs) were monitored throughout the study. Continuous efficacy endpoints were summarized using descriptive statistics (ie, arithmetic mean, standard deviation, median, minimum, maximum, 95% confidence interval for the mean). Categorical endpoints were summarized using frequency counts and percentages. All efficacy analyses are conducted using the Full Analysis Set, which included subjects receiving ≥1 dose of study medication and providing baseline and post-baseline data for ≥1 efficacy endpoint during the study. Missing values were imputed using the Last Observation Carried Forward (LOCF) method. Adverse events were summarized for the Safety Analysis Set which subjects receiving ≥1 dose of study medication.

Results

Of the 331 enrolled subjects, 283 (85%) completed the 12-week treatment period, and 251 (76%) completed the entire (16-week) study period. Reasons for study discontinuation during the 12-week treatment period included adverse events (n=29; 9%), lack of efficacy (n=6; 2%), withdrawn consent (n=3; 1%), lost to follow up (n=2; 1%), and “other” (n=8; 2%); an additional 32 discontinuations occurred during the post-treatment follow-up period between weeks 12 and 16. Most study participants (79%) were women; 40% reported incontinence at baseline (Table 1). Approximately 53% of subjects elected dose escalation at week 4. Clinically-relevant improvements were observed for micturitions/24 hours and urgency episodes/24 hours between baseline and week 12 (Table 2). Of the 150 subjects reporting incontinence pad use at baseline, 42 (28%) reported no pad usage at week 12, and 117 (78%) had some reduction in pad usage by week 12 (Table 2). Seventy-four percent of subjects (n=243) reported satisfaction with fesoterodine at week 12. Fesoterodine treatment was well tolerated, with no observed safety concerns, unexpected AEs, or cases of urinary retention. A total of 254 subjects (77%) experienced ≥1 treatment-emergent AE; 159 (48%) of these individuals experienced ≥1 treatment-related AE. Dry mouth and constipation were the most frequently-reported treatment-emergent AEs (30% and 9%, respectively); these AEs were typically of mild severity and infrequently resulted in discontinuation of study treatment (n=11 [3%] and n=2 [<1%]).

Interpretation of results

Use of a flexible-dose fesoterodine regimen resulted in clinically-relevant improvements in micturition frequency and urgency episodes, which was supported by reductions in incontinence pad use. Flexible-dose fesoterodine was also associated with a high rate of patient-reported treatment satisfaction and was well tolerated.

Concluding message

Flexible-dosing allows clinicians to optimize the balance between efficacy and tolerability in individual patients [1], and is a better reflection of clinical antimuscarinic use compared with fixed dosing. Consistent with outcomes of previous flexible-dose fesoterodine studies [2,3], the results of this open-label, UK-based study show that once-daily, flexible-dose fesoterodine (adjustable from 4 to 8 mg) is effective in reducing key OAB symptoms, is associated with a high rate of treatment satisfaction, and is well tolerated in subjects with OAB symptoms.

Table 1. Baseline Demographic and Disease Characteristics*

Characteristic	N=331
Gender, n %	
Male	68 (20.5)
Female	263 (79.5)
Mean (SD) age, y	60 (23-86)
Race, n (%)	
White	325 (98.2)
Other	6 (1.8)

Duration since first diagnosis of OAB, y	7 (0.1–53.8)
Incontinent, n (%)	132 (39.9)
Previous antimuscarinic use, n (%)	
Darifenacin	2 (0.6)
Fesoterodine	2 (0.6)
Oxybutynin	59 (17.8)
Propiverine	2 (0.6)
Solifenacin	50 (15.1)
Tolterodine	88 (26.6)
Trospium	6 (1.8)

*Safety Analysis Set.
SD, standard deviation; OAB, overactive bladder.

Table 2. Bladder Diary Outcomes*

	Baseline Mean (SD) (n=330)	Week 12 Mean (SD) (n=317)	Change From Baseline to Week 12 Mean (95% CI)
Micturitions/24 h	12.8 (3.5)	9.6 (3.0)	–3.3 (–3.6, –2.9)
Urgency episodes/24 h	9.1 (4.3)	4.0 (3.8)	–5.1 (–5.6, –4.6)
Incontinence pad use/24 h†	3.1 (2.2)	1.7 (2.1)	–1.4 (–1.7, –1.2)

SD, standard deviation; CI, confidence interval.
*Full Analysis Set.
†Includes only subjects reporting incontinence pad use at baseline (n=150).

References
1. Chapple CR, et al. BJU Int. 2009 Epub ahead of print.
2. Dmochowski R, et al. Urology. 2010;75:62-8.
3. Wyndaele JJ, et al. Int J Clin Pract. 2009;63:560-7.

Specify source of funding or grant	**Pfizer Inc**
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 NCT00806494**
Is this a Randomised Controlled Trial (RCT)?	**No**
What were the subjects in the study?	**HUMAN**
Was this study approved by an ethics committee?	**Yes**
Specify Name of Ethics Committee	**Multi-centre Research Ethics Committee for Wales**
Was the Declaration of Helsinki followed?	**Yes**
Was informed consent obtained from the patients?	**Yes**