PFIZER INC.

These results are supplied for informational purposes only.
Prescribing decisions should be made based on the approved package insert.
For publications based on this study, see associated bibliography.

PROPRIETARY DRUG NAME®/GENERIC DRUG NAME: Toviaz® / Fesoterodine

THERAPEUTIC AREA AND FDA APPROVED INDICATIONS: See United States Package Insert (USPI)

NATIONAL CLINICAL TRIAL NO.: NCT00658684

PROTOCOL NO.: A0221006

PROTOCOL TITLE: An Open-Label, Multicenter, Long Term Study to Evaluate The Safety, Tolerability and Efficacy of Fesoterodine in Patients With Overactive Bladder

Study Center(s): 12 centers in Japan

Study Initiation Date and Completion Dates: 01 February 2008 to 06 August 2009

Phase of Development: Phase 3

Study Objective(s):

The primary objective of the study was to assess the long term safety and tolerability of fesoterodine in patients with overactive bladder (OAB).

The secondary objective of the study was to assess the long term efficacy of fesoterodine in patients with OAB.

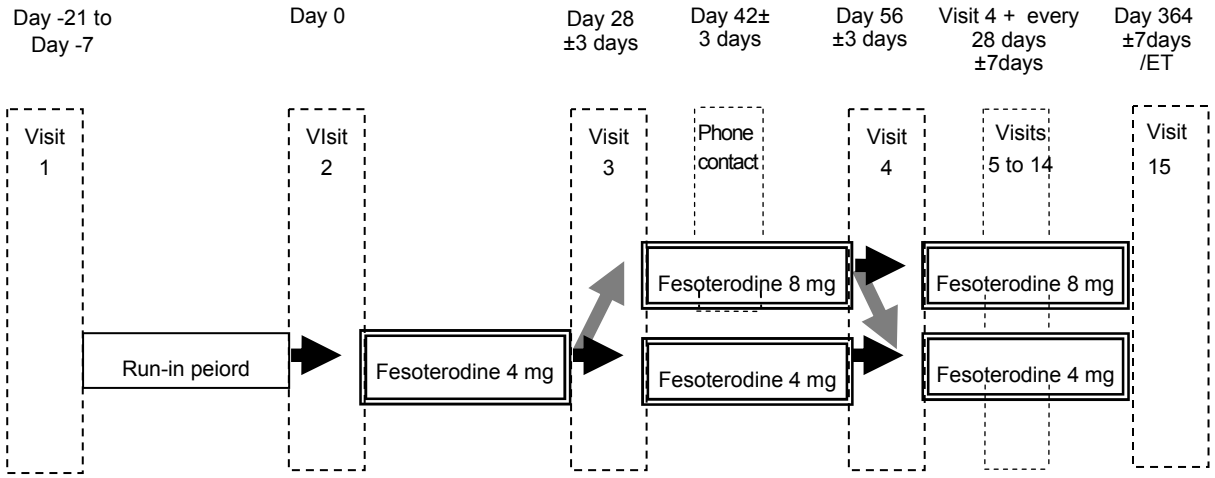
METHODS

Study Design: This was an open-label, multicenter, long term study in Japanese patients with OAB. Subjects were to be treated with fesoterodine for up to 52 weeks requiring a total of 15 clinic visits during the study. The study design is presented in Figure S1.

Subjects were screened at Visit 1 (Screening/enrollment visit). Eligible subjects then entered a run-in phase during which they completed a 3-day micturition diary for 3 consecutive days in 7 days prior to Visit 2 (Baseline visit). At Visit 2, the diary data and screening laboratory data were checked against the entry criteria, and the eligible subjects received fesoterodine 4 mg/day for 4 weeks. At Visit 3, the investigator confirmed the efficacy of fesoterodine 4 mg by the diary data and interview. It was possible to increase the dose to 8 mg, if the investigator judged that the efficacy of 4 mg was insufficient and that there were no safety/tolerability issues for the subject. This increase only occurred when requested by the subject. The dose was allowed to be reduced from 8 mg to 4 mg at Visit 4, provided that the investigator judged that the continued treatment with 4 mg would be useful to the patient and

that the continued treatment with 8 mg might result in tolerability issues and that the patient requested continued treatment with fesoterodine 4 mg. Thereafter, all subjects remained on the dose selected at Visit 4 until the end of the trial unless a safety/tolerability problem occurred. If safety/tolerability problem occurred and the subject could not continue treatment with 8 mg, the investigator could consider the discontinuing the patient's participation in the study.

Figure S1 Study Design



Visit 1: Screening/enrollment visit
Visit 2: Baseline visit
Visit 3: Week 4
Visits 4 to 14: Every 4 weeks after Visit 3
Visit 15: End-of-trial visit (Week 52 or early termination [ET])

Number of Subjects (Planned and Analyzed): A total of 150 subjects were planned and 153 subjects were assigned to treatment. As study drug administration could not be verified for 1 subject, 152 subjects were analyzed for safety, and 150 subjects were analyzed for efficacy.

Diagnosis and Main Criteria for Inclusion: Male or female outpatients 20 years or older who exhibit signs or symptoms of OAB with urinary urgency and increased urinary frequency (a known medical history ≥ 6 months prior to Visit 1). OAB patients with or without urgency urinary incontinence who exhibit, during the 3-day micturition diary period prior to Visit 2 (Baseline visit), a total of at least 3 urinary urgency episodes and at least 8 micturitions per 24 hours, document the voided volume of each micturition during any 1 day and the first micturition of the following day, and indicate at least moderate problems (moderate, severe or many severe problems) based on Patient Perception of Bladder Condition (PPBC) at Visit 2. Patients who have a known neurological disease influencing bladder function, a complication of lower urinary tract pathology potentially responsible for urgency or incontinence, clinically relevant lower urinary tract obstruction or pelvic organ prolapse, or predominant symptoms of stress urinary incontinence based on the assessment of the investigator were excluded.

Study Treatment: This was an open-label study. Subjects took one fesoterodine 4-mg or 8-mg tablet with water every morning with or without food. All enrolled subjects were treated with fesoterodine 4 mg for the first 4 weeks and were permitted a one-time dose increase to 8 mg at Visit 3 (at Week 4). The dose was allowed to be reduced from 8 mg to 4 mg at Visit 4 (at Week 8), and thereafter, all subjects remained on the dose selected at Visit 4 until the end of the trial. The decision to maintain, increase or decrease the dose was based on a discussion between the subject and the investigator regarding drug efficacy and tolerability.

Efficacy Evaluations: A micturition diary was completed by subjects to evaluate changes from baseline in mean number of urgency urinary incontinence (UUI) episodes per 24 hours, mean number of micturitions per 24 hours, mean number of incontinence episodes per 24 hours, mean number of urgency episodes per 24 hours, mean number of nighttime micturitions per 24 hours and mean voided volume per micturition at Weeks 4, 8, 28 and 52. Subjects were also required to complete King's Health Questionnaire (KHQ), Overactive Bladder Questionnaire (OAB-q) and Patient Perception of Bladder Condition (PPBC) at Weeks 28 and 52.

Safety Evaluations: Adverse events, clinical laboratory test (hematological test, chemistry test, urine test), vital signs (blood pressure, pulse rate), weight, 12-lead electrocardiogram (ECG) and residual urine volume (sonographic).

Statistical Methods:
Efficacy: The efficacy analysis set included all subjects who took at least one dose of study drug and contribute data to baseline and at least one valid post-baseline efficacy assessment. For micturition diary endpoints, actual value and change from baseline at each visit were summarized with descriptive statistics (number of subjects, mean, standard deviation, minimum, median, maximum and the 95% confidence interval for the mean). For KHQ, OAB-p and PPBC, actual values and changes from baseline at each visit were summarized using descriptive statistics. Shift tables were also prepared for PPBC response from baseline to Week 28 and 52.

Subgroup analyses by treatment dose history (fesoterodine 4 mg for the entire treatment period; increased to fesoterodine 8 mg at Week 4 and reduced to 4 mg at Week 8; increased to fesoterodine 8 mg at Week 4 and remained at 8 mg) were performed for the above efficacy analyses.

Safety: The safety analysis set included all subjects who took at least one dose of study drug. Standard tables were produced for adverse events, vital signs, ECG data and clinical laboratory data in accordance with Pfizer Data Standards (PDS). For residual urinary volume (mL), actual sonographic values and change from the baseline values at each visit were summarized using descriptive statistics. Subgroup analyses by treatment dose history for the above analyses were performed.

RESULTS

Subject Disposition and Demography: The disposition of subjects is summarized in Table S1. Of 152 treated subjects, 99 (65.1%) remained on a dose of fesoterodine 4 mg throughout the study period (subjects who remained on a dose of 4 mg), and 53 (34.9%) increased the dose to 8 mg at Week 4. Of 53 subjects whose dose was increased to 8 mg, the dose of 25 subjects (16.4% of 152 subjects) was reduced to 4 mg at Week 8 (subjects whose dose was increased to 8 mg and then reduced to 4 mg) and 28 (18.4% of 152 subjects) remained on a dose of 8 mg after Week 4 (increased to 8 mg and maintained).

Of 152 subjects, 19 subjects (12.5%) discontinued treatment. The most commonly reported reasons for discontinuations were adverse events (10 subjects, 6.6%) and consent withdrawal (6 subjects, 3.9%).

Table S1 Subject Disposition From the Start of the Trial to Week 52 [Number (%) of Subjects]

	Total	Treatment dose history		
		4 mg	4 mg> 8 mg> 4 mg	4 mg > 8 mg
Number of treated subjects	152[a)]	99	25	28
Efficacy analysis set	150[b)]	97	25	28
Safety analysis set	152	99	25	28
Discontinuations	19 (12.5)	15 (15.2)	3 (12.0)	1 (3.6)
Adverse events				
Not related to treatment	3 (2.0)	2 (2.0)	1 (4.0)	0
Related to treatment	7 (4.6)	6 (6.1)	1 (4.0)	0
Consent withdrawal	6 (3.9)	4 (4.0)	1 (4.0)	1 (3.6)
Lack of efficacy	1 (0.7)	1 (1.0)	0	0
Others[c)]	2 (1.3)	2 (2.0)	0	0

a) Excluding 1 subject whose study drug administration could not be verified
b) Excluding 2 subjects without any valid post-baseline micturition dairy assessment
c) Inclusion criteria not met (1 subject) and pregnancy (1 subject)
4 mg: Remained on a dose of fesoterodine 4 mg for the entire treatment period (subjects who remained on a dose of 4 mg)
4 mg > 8 mg > 4 mg: Increased to fesoterodine 8 mg at Week 4 and reduced to 4 mg at Week 8 (subjects whose dose was increased to 8 mg and then reduced to 4 mg)
4 mg > 8 mg: Increased to fesoterodine 8 mg at Week 4 and remained on a dose of 8 mg after Week 4 (subjects whose dose was increased to 8 mg and maintained)

The mean age of the total of 152 subjects was 52.7 years, and approximately 20% of the subjects were 65 years or older. Nineteen subjects (12.5%) were male, and 133 subjects (87.5%) were female. The mean weight was 56.3 kg, the mean BMI was 22.8 kg/m^2, and the mean height was 157.3 cm. The mean OAB duration (range) was 6.2 years (0.6 to 35.2 years), and 47 subjects (30.9%) received drug treatment for OAB within 4 weeks before the start of the study.

Efficacy Results: The results of micturition diary endpoints are summarized in Table S2. In all subjects, for all of the micturition diary endpoints (mean number of UUI episodes per 24 hours, mean number of micturitions per 24 hours, mean number of incontinence episodes per

24 hours, mean number of urgency episodes per 24 hours, mean number of nighttime micturitions per 24 hours and mean voided volume per micturition), most of the improvement occurred by Week 8 and the level of improvement was maintained up to Week 52.

For all of the diary endpoints by treatment dose history, the subjects who increased the dose to 8 mg at Week 4 (including those whose dose was reduced to 4 mg at Week 8) had more severe symptoms of OAB at baseline than those who remained on a dose of 4 mg (subjects who remained on a dose of 4 mg). The subjects who remained on a dose of 4 mg showed marked improvement in all diary endpoints by Week 8, and the level of improvement was maintained up to Week 52. The subjects who increased the dose to 8 mg at Week 4 due to insufficient efficacy showed marked improvement after a dose increase. Of these subjects, those subjects whose dose was reduced to 4 mg mainly due to tolerability problems at Week 8 (increased to 8 mg and reduced to 4 mg) maintained the level of improvement even after dose reduction. In subjects who continued a dose of 8 mg after Week 8 (increased to 8 mg and maintained), a trend toward improvement over time was shown following dose increase and the level of improvement was greater than that seen with subjects who remained on a dose of 4 mg or whose dose was reduced to 4 mg.

Table S2 Changes From Baseline in Micturition Diary Endpoints: Total and by Treatment Dose History

Efficacy endpoints[a)]	Total (N=150)		Treatment dose history					
			4 mg (N=97)		4mg>8mg>4mg (N=25)		4 mg > 8 mg (N=28)	
Mean UUI episodes [b)]	n	Mean±SD	n	Mean±SD	n	Mean±SD	n	Mean±SD
Baseline	101	1.6±1.48	60	1.4±1.23	17	1.7±1.24	24	2.1±2.04
At Week 4	101	-0.86±1.104	60	-0.99±1.117	17	-0.73±1.281	24	-0.63±0.918
At Week 8	100	-1.15±1.293	59	-1.16±1.173	17	-1.31±1.450	24	-1.00±1.491
At Week 28	95	-1.28±1.282	56	-1.24±1.185	16	-1.25±1.518	23	-1.41±1.385
At Week 52	92	-1.34±1.553	54	-1.23±1.228	15	-1.18±1.661	23	-1.71±2.097
At Week 52 (LOCF)	101	-1.35±1.521	60	-1.19±1.176	17	-1.22±1.568	24	-1.82±2.120
Mean number of micturition								
Baseline	150	11.3±2.85	97	11.0±2.69	25	11.2±2.71	28	12.3±3.31
At Week 4	150	-1.42±1.855	97	-1.73±1.899	25	-1.28±1.403	28	-0.45±1.757
At Week 8	148	-2.11±1.946	95	-2.03±1.897	25	-1.81±2.035	28	-2.63±2.005
At Week 28	137	-2.33±2.338	87	-2.18±2.351	23	-2.06±2.260	27	-3.02±2.315
At Week 52	133	-2.63±2.220	84	-2.48±2.020	22	-2.21±2.196	27	-3.44±2.683
At Week 52 (LOCF)	150	-2.49±2.172	97	-2.35±1.970	25	-2.04±2.135	28	-3.36±2.673
Mean incontinence episodes[c)]								
Baseline	103	1.8±1.74	62	1.6±1.34	17	1.8±1.33	24	2.5±2.63
At Week 4	103	-0.84±1.140	62	-0.99±1.166	17	-0.80±1.225	24	-0.49±0.963
At Week 8	102	-1.23±1.354	61	-1.16±1.272	17	-1.43±1.504	24	-1.28±1.486
At Week 28	97	-1.39±1.476	58	-1.26±1.322	16	-1.31±1.542	23	-1.77±1.779
At Week 52	94	-1.37±1.589	56	-1.26±1.331	15	-1.16±1.847	23	-1.75±1.962
At Week 52 (LOCF)	103	-1.38±1.557	62	-1.24±1.282	17	-1.20±1.740	24	-1.86±1.990
Mean number of urgency episodes								
Baseline	150	4.5±3.40	97	3.9±3.31	25	6.2±3.72	28	5.1±2.87
At Week 4	150	-1.69±2.009	97	-1.77±1.856	25	-1.75±2.572	28	-1.37±2.001
At Week 8	148	-2.44±2.194	95	-2.32±1.881	25	-2.59±2.940	28	-2.70±2.463
At Week 28	137	-2.54±2.597	87	-2.41±1.855	23	-3.12±3.304	27	-2.46±3.780
At Week 52	133	-2.76±2.901	84	-2.55±2.579	22	-2.80±3.193	27	-3.37±3.565
At Week 52 (LOCF)	150	-2.61±2.885	97	-2.30±2.531	25	-2.93±3.319	28	-3.40±3.504
Mean number of nighttime micturitions[d)]								
Baseline	116	1.4±1.04	69	1.2±1.04	23	1.6±0.93	24	1.6±1.05
At Week 4	116	-0.31±0.727	69	-0.34±0.752	23	-0.45±0.556	24	-0.08±0.776
At Week 8	115	-0.43±0.797	68	-0.33±0.812	23	-0.55±0.845	24	-0.60±0.688
At Week 28	106	-0.47±0.752	62	-0.36±0.788	21	-0.56±0.694	23	-0.71±0.661
At Week 52	103	-0.57±0.807	60	-0.46±0.904	20	-0.68±0.546	23	-0.75±0.698
At Week 52 (LOCF)	116	-0.50±0.826	69	-0.38±0.908	23	-0.62±0.614	24	-0.71±0.718

N, Efficacy analysis set; n, Number of subjects evaluated; SD, standard deviation; hrs, hours

a) Number of times per 24 hours is shown.

b) Of the efficacy analysis set, the subjects whose mean number of UUI episodes per 24 hours at baseline was greater than 0 (OAB Wet subjects) were analyzed.

c) Of the efficacy analysis set, the subjects whose mean number of incontinence episodes per 24 hours at baseline was greater than 0 were analyzed.

d) Of the efficacy analysis set, the subjects whose mean number of nighttime micturitions per 24 hours at baseline was greater than 0 were analyzed.

4 mg: Remained on a dose of fesoterodine 4 mg for the entire treatment period (subjects who remained on a dose of 4 mg)

4 mg > 8 mg > 4 mg: Increased to fesoterodine 8 mg at Week 4 and reduced to 4 mg at Week 8 (subjects whose dose was increased to 8 mg and then reduced to 4 mg)

4 mg > 8 mg: Increased to fesoterodine 8 mg at Week 4 and remained on a dose of 8 mg after Week 4 (subjects whose dose was increased to 8 mg and maintained)

Table S2 Changes From Baseline in Micturition Diary Endpoints: Total and by Treatment Dose History (continued)

Efficacy endpoints	Total (N=150)		Treatment dose history					
			4 mg (N=97)		4 mg>8 mg>4 mg (N=25)		4 mg > 8 mg (N=28)	
Mean voided volume per micturition (mL)	n	Mean±SD	n	Mean±SD	n	Mean±SD	n	Mean±SD
Baseline	150	158.1±48.09	97	162.8±48.78	25	156.1±42.75	28	143.6±48.73
At Week 4	150	16.67±41.908	97	20.58±44.357	25	12.18±43.399	28	7.16±29.231
At Week 8	148	22.34±51.339	95	21.86±58.194	25	23.00±35.061	28	23.37±38.273
At Week 28	137	32.59±46.389	87	31.98±50.365	23	40.20±41.613	27	28.10±36.431
At Week 52	133	35.92±44.007	84	40.21±47.646	22	33.02±40.772	27	24.95±32.414
At Week 52 (LOCF)	150	33.42±45.175	97	37.08±49.276	25	28.22±40.693	28	25.38±31.890

N, Efficacy analysis set; n, Number of subjects evaluated; SD, standard deviation; hrs, hours
4 mg: Remained on a dose of fesoterodine 4 mg for the entire treatment period (subjects who remained on a dose of 4 mg)
4 mg > 8 mg > 4 mg: Increased to fesoterodine 8 mg at Week 4 and reduced to 4 mg at Week 8 (subjects whose dose was increased to 8 mg and then reduced to 4 mg)
4 mg > 8 mg: Increased to fesoterodine 8 mg at Week 4 and remained on a dose of 8 mg after Week 4 (subjects whose dose was increased to 8 mg and maintained)

The changes in KHQ, OAB-q and PPBC scores showed improvement in quality of life (QOL) from baseline at Week 52. The KHQ and OAB-q scores improved particularly in those who increased the dose to 8 mg and maintained the dose, whose QOL was more severely impaired at baseline than those who remained on a dose of 4 mg or whose dose was reduced to 4 mg.

Safety Results: Adverse events reported during the study period are summarized in Table S3. Of 152 subjects, 138 (90.8%) experienced 434 all causality adverse events, and 102 (67.1%) experienced 170 treatment-related adverse events. By treatment dose history, the incidence of all causality adverse events was 91.9% in 4 mg-treated subjects (91/99) and 88.7% in subjects who increased the dose to 8 mg at Week 4 (47/53; including those whose dose was reduced to 4 mg at Week 8). The incidence of all causality adverse events with or without dose increase was similar. The incidence of treatment-related adverse events was 61.6% in 4 mg-treated subjects (61/99) and 77.4% in subjects who increased the dose to 8 mg at Week 4 (41/53; including those whose dose was reduced to 4 mg at Week 8). The incidence of treatment-related adverse events was slightly higher for those who increased the dose to 8 mg at Week 4.

Table S3 Overall Summary of Treatment-Emergent Adverse Events: Total and by Treatment Dose History [Number (%) of Subjects]

	Total	Treatment dose history		
		4 mg	4 mg > 8 mg > 4 mg	4 mg > 8 mg
Subjects evaluable for safety	152	99	25	28
Number of subjects with adverse events				
All causality	138 (90.8)	91 (91.9)	25 (100)	22 (78.6)
Treatment-related	102 (67.1)	61 (61.6)	25 (100)	16 (57.1)
Number of adverse events				
All causality	434	269	92	73
Treatment-related	170	94	48	28
Subjects with serious adverse events	1 (0.7)	1 (1.0)	0	0
Subjects with severe adverse events	0	0	0	0
Number of subjects who discontinued treatment due to adverse events				
All causality	10 (6.6)	8 (8.1)	2 (8.0)	0
Treatment-related	7 (4.6)	6 (6.1)	1 (4.0)	0
Number of subjects with dose reduction or temporary discontinuation due to adverse events				
All causality	30 (19.7)	6 (6.1)	23 (92.0)	1 (3.6)
Treatment-related	23 (15.1)	0	23 (92.0)	0

4 mg: Remained on a dose of fesoterodine 4 mg for the entire treatment period (subjects who remained on a dose of 4 mg)
4 mg > 8 mg > 4 mg: Increased to fesoterodine 8 mg at Week 4 and reduced to 4 mg at Week 8 (subjects whose dose was increased to 8 mg and then reduced to 4 mg)
4 mg > 8 mg: Increased to fesoterodine 8 mg at Week 4 and remained on a dose of 8 mg after Week 4 (subjects whose dose was increased to 8 mg and maintained)

All causality adverse events reported in ≥2% of subjects are summarized in Table S4. The majority of adverse events observed were mild, and no severe adverse events were reported.

Table S4. Adverse Events Reported by ≥ 2% of Subjects: Total and by Treatment Dose History [Number (%) of Subjects]

MedDRA System Organ Class Preferred Term (ver. 11.1)	Total (N=152)	Treatment dose history		
		4 mg (N=99)	4 mg > 8 mg > 4 mg (N=25)	4 mg > 8 mg (N=28)
Number of subjects with adverse events	138 (90.8)	91 (91.9)	25 (100)	22 (78.6)
Number of adverse events	434	269	92	73
Ear and labyrinth disorders				
Vertigo	3 (2.0)	2 (2.0)	0	1 (3.6)
Eye disorders				
Vision blurred	3 (2.0)	2 (2.0)	1 (4.0)	0
Gastrointestinal disorders				
Abdominal pain upper	5 (3.3)	3 (3.0)	1 (4.0)	1 (3.6)
Constipation	20 (13.2)	11 (11.1)	7 (28.0)	2 (7.1)
Diarrhoea	11 (7.2)	5 (5.1)	3 (12.0)	3 (10.7)
Dry mouth	77 (50.7)	43 (43.4)	21 (84.0)	13 (46.4)
Gastritis	9 (5.9)	8 (8.1)	1 (4.0)	0
Nausea	4 (2.6)	1 (1.0)	2 (8.0)	1 (3.6)
Periodontitis	3 (2.0)	0	1 (4.0)	2 (7.1)
Stomatitis	4 (2.6)	3 (3.0)	0	1 (3.6)
Infections and infestations				
Cystitis	12 (7.9)	8 (8.1)	1 (4.0)	3 (10.7)
Gastroenteritis	3 (2.0)	3 (3.0)	0	0
Nasopharyngitis	50 (32.9)	35 (35.4)	7 (28.0)	8 (28.6)
Upper respiratory tract infection	12 (7.9)	8 (8.1)	2 (8.0)	2 (7.1)
Injury, poisoning and procedural complications				
Contusion	3 (2.0)	1 (1.0)	2 (8.0)	0
Joint sprain	3 (2.0)	3 (3.0)	0	0
Investigations				
ALT increased	4 (2.6)	3 (3.0)	1 (4.0)	0
AST increased	4 (2.6)	3 (3.0)	1 (4.0)	0
Musculoskeletal and connective tissue disorders				
Arthralgia	6 (3.9)	5 (5.1)	1 (4.0)	0
Back pain	16 (10.5)	12 (12.1)	1 (4.0)	3 (10.7)
Nervous system disorders				
Dizziness	6 (3.9)	3 (3.0)	2 (8.0)	1 (3.6)
Headache	5 (3.3)	5 (5.1)	0	0
Somnolence	5 (3.3)	1 (1.0)	2 (8.0)	2 (7.1)
Psychiatric disorders				
Insomnia	3 (2.0)	2 (2.0)	0	1 (3.6)
Renal and urinary disorders				
Dysuria	6 (3.9)	2 (2.0)	3 (12.0)	1 (3.6)
Residual urine	3 (2.0)	1 (1.0)	2 (8.0)	0
Urine flow decreased	4 (2.6)	1 (1.0)	2 (8.0)	1 (3.6)
Respiratory, thoracic and mediastinal disorders				
Rhinitis allergic	7 (4.6)	4 (4.0)	1 (4.0)	2 (7.1)
Skin and subcutaneous tissue disorders				
Eczema	4 (2.6)	3 (3.0)	0	1 (3.6)

4 mg: Remained on a dose of fesoterodine 4 mg for the entire treatment period (subjects who remained on a dose of 4 mg)
4 mg > 8 mg > 4 mg: Increased to fesoterodine 8 mg at Week 4 and reduced to 4 mg at Week 8 (subjects whose dose was increased to 8 mg and then reduced to 4 mg)
4 mg > 8 mg: Increased to fesoterodine 8 mg at Week 4 and remained on a dose of 8 mg after Week 4 (subjects whose dose was increased to 8 mg and maintained)
N: Safety analysis set, ALT: alanine aminotransferase, AST: aspartate aminotransferase

The adverse events leading to discontinuation are summarized in Table S5. A total of 10 subjects (6.6%) discontinued treatment due to adverse events.

Table S5 Summary of Adverse Events Leading to Discontinuations [Number (%) of Subjects]

MedDRA System Organ Class Preferred Term (ver. 11.1)	Total (N=152)
Ear and labyrinth disorders	
Tinnitus	1 (0.7)
Gastrointestinal disorders	
Chapped lips	1(0.7)
Dry mouth	2(1.3)
Gastritis	1(0.7)
Nausea	1(0.7)
Investigations	
ALT increased	3(2.0)
AST increased	1(0.7)
Gamma-glutamyltransferase increased	1(0.7)
Urobilin urine present	1(0.7)
Musculoskeletal and connective tissue disorders	
Intervertebral disc disorder	1(0.7)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	
Colon cancer	1(0.7)
Renal and urinary disorders	
Dysuria	1(0.7)

N: Safety analysis set, ALT: alanine aminotransferase, AST: aspartate aminotransferase

One serious adverse event (Intervertebral disc disorder) was reported in 1 patient, but no causality to the study drug was identified. No deaths were reported in this study.

Overall, there were no clinically significant findings observed in clinical laboratory tests, blood pressure, pulse rate or 12 lead ECG, and no clinically significant changes were observed in residual urinary volume.

CONCLUSIONS:

Based on the results of the open-label, multicenter, long term study of fesoterodine 4 mg or 8 mg once daily in patients with OAB for 52 weeks, the following overall conclusions were obtained;

- The majority of adverse events reported was mild in severity and were those related to antimuscarinic action such as dry mouth.
- The treatment with fesoterodine for 52 weeks in patients with OAB was safe and well tolerated.
- Fesoterodine demonstrated sustained efficacy throughout 52 weeks of treatment in patients with OAB.

- OAB symptoms were improved by increasing the dose to 8 mg in subjects who had insufficient efficacy at a dose of 4 mg.

- The subjects who experienced tolerability problems after a dose increase to 8 mg were able to continue treatment by reducing the dose back to 4 mg, thereby maintaining the level of improvement in OAB symptoms.