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

PROTOCOL NO.: A0221008

PROTOCOL TITLE: 12-Week, Randomized, Double-Blind, Double-Dummy, Placebo-Controlled, Parallel-Group, Multicenter Trial to Evaluate the Efficacy and Safety of Fesoterodine in Comparison to Tolterodine ER in Patients with Overactive Bladder

Study Centers: A total of 169 centers took part in the study and enrolled subjects; 39 centers in United States, 14 centers in Germany, 9 centers in Canada, 8 centers in Denmark, 7 centers in Brazil, 6 centers each in Republic of Korea, Norway, Russian federation, and South Africa, 5 centers each in Czech Republic, Poland, Romania, Taiwan, and Ukraine, 4 centers each in Costa Rica, Greece, Hungary, India, Spain, and Sweden, 3 centers each in Italy and Belgium, 2 centers each in Chile, Colombia, Hong Kong, Peru, Singapore, and Switzerland, and 1 center in Malaysia.

Study Initiation and Final Completion Dates: 17 April 2007 to 17 July 2008

Phase of Development: Phase 3b

Study Objectives:

Primary Objective:

- To compare the efficacy of fesoterodine to placebo and tolterodine extended-release (ER) in subjects with overactive bladder (OAB) after 12 weeks of treatment

Secondary Objectives:

- To compare the effect of fesoterodine to placebo on patient-reported outcomes (PROs) in subjects with OAB after 12 weeks of treatment
- To compare the efficacy of fesoterodine 4 mg daily (QD) to placebo in subjects with OAB after 1 week of treatment
- To summarize safety data for 12 weeks of treatment with either fesoterodine, tolterodine ER, or placebo in subjects with OAB

METHODS

Study Design: This was a 12-week, randomized, double-blind, double-dummy, placebo-controlled, parallel-group, multi-center study to compare the efficacy of fesoterodine to placebo and tolterodine ER in subjects with OAB.

Subjects were expected to begin study treatment at the Screening/Enrolment Visit (Visit 1) with a 2-week, single-blind, double-dummy placebo run-in period. If eligible, subjects were then randomized into a 12-week double-blind, double-dummy treatment period and received either fesoterodine at 4 mg QD for 1 week followed by a forced dose-escalation to fesoterodine 8 mg QD for 11 weeks, or tolterodine ER at 4 mg QD for 12 weeks, or placebo QD for 12 weeks.

Over the 14-weeks planned for individual subject participation in this study, each subject was required to present for 5 in-clinic visits: a Screening/Enrollment visit (Week -2), a Randomization/Baseline Visit (Week 0), a Week 1 Visit, a Week 4 Visit, and an End-of-Study Visit (Week 12 or Early Termination [ET] Visit).

Efficacy was measured by a 3-day bladder diary completed for 3 consecutive days prior to each in-clinic visit. In addition, the following validated patient-reported outcome (PRO) measures, Patient Perception of Bladder Condition question (PPBC), Urgency Perception Scale ([UPS] formerly known as the Patient Perception of Urgency Scale [PPUS]), and Overactive Bladder Questionnaire (OAB-q) were administered according to the visit schedule (Table 1).

Table 1. Timetable of Study Procedures/Evaluations

Activities & Forms to Be Completed	Visit 1 Screening/ Enrolment, Week -2 (±5 Days)	Visit 2 Randomization/ Baseline, Week 0	Visit 3 End of Week 1 (-1 to +3 Days)	Visit 4 End of Week 4 (±7 Days)	Visit 5 End of Study Week 12 or Early Termination (±7 Days)
Written informed consent	X				
Demographics and medical history	X				
Sitting blood pressure and pulse rate	X	X	X	X	X
Physical exam and 12-lead ECG	X				
Inclusion/exclusion criteria	X	X			
Blood draw (hematology and chemistry)	X				X
Urine dipstick test	X				
Urine pregnancy test for women of child-bearing potential	X				
Patient's Perception of Bladder Condition (PPBC)		X	X	X	X
Urgency Perception Scale ([UPS] formerly known as PPUS)		X	X	X	X
Overactive Bladder Questionnaire (OAB-q)		X			X
Dispense micturition bladder diary (3-day)	X	X	X	X	
Evaluation of micturition bladder diary (3-day)		X	X	X	X
Adverse events[a]		X	X	X	X
Concomitant medication	X	X	X	X	X
Concomitant non-drug treatment/procedures	X	X	X	X	X
Assess overall compliance		X	X	X	X
Access impala[b]	X	X		X	X
Dispense study medication	X	X		X	
Study medication return/count		X		X	X
Subject summary page					X

AE = adverse event; ECG = electrocardiogram; PPUS = Patient Perception of Urgency Scale; QD = once daily; SAE = serious adverse event.

a. SAEs were reported once informed consent had been obtained. Serious and non-SAEs were collected (recorded on the case report form) once the subject had taken at least 1 dose of study medication.

b Impala was a centralized randomization system used to obtain single subject identification numbers, randomization numbers, and randomization assignments. It also functioned to predict and trigger drug re-supply for a center.

Number of Subjects (Planned and Analyzed): Assuming that approximately 90% of the randomized subjects would contribute to the full analysis set (FAS), it was planned to randomize 1675 subjects in a 2:2:1 ratio to obtain a sample size of 1515 evaluable subjects (606 in fesoterodine, 606 in tolterodine ER, and 303 in placebo). Of the 2685 subjects

screened, 2446 were enrolled and received single-blind placebo during the run-in period; 1697 of these subjects further progressed to randomization and were treated during the double-blind treatment period (fesoterodine: 679; tolterodine ER: 684; placebo: 334). "Treated subjects" refers to those who received at least 1 dose of double-blind study drug, ie, the safety population.

The study enrolled a total of 1697 subjects which included 441 in United States, 147 in Germany, 95 in Norway, 81 in Republic of Korea, 79 in Costa Rica, 73 in Denmark, 64 each in Russian federation and Ukraine, 61 in Sweden, 59 each in Canada and Hungary, 48 in Brazil, 44 in Belgium, 42 in Czech Republic, 40 in Poland, 39 each in Romania and South Africa, 37 in Spain, 30 in Taiwan, 27 in Chile, 26 in India, 21 in Colombia, 20 in Greece, 16 in Peru, 15 in Hong Kong, 9 each in Italy, Singapore and Switzerland, 3 in Malaysia.

Diagnosis and Main Criteria for Inclusion: Eligible for enrolment in this study were individuals, male or female, at least 18 years of age with OAB symptoms including urinary frequency ≥8 per day and urgency urinary incontinence (UUI) ≥1 per day. Subjects with conditions that would contraindicate for fesoterodine use, eg, hypersensitivity to the active substance (fesoterodine) or to peanut or soya or any of the excipients, urinary retention, and gastric retention, subjects who had significant hepatic and renal disease or other significant unstable diseases and OAB symptoms caused by neurological conditions, known pathologies of urinary tract, et cetera were excluded from the study.

Study Treatment: During a 2-week run-in period, subjects were treated with placebo in a single-blind, double-dummy fashion. Eligible subjects were then randomized to receive either fesoterodine at 4 mg QD for 1 week then fesoterodine 8 mg QD for 11 weeks, or tolterodine ER at 4 mg QD for 12 weeks, or placebo QD for 12 weeks in a double-blind, double-dummy fashion.

Fesoterodine was supplied as 4 mg or 8 mg ER tablets dispensed from a blister pack. Tolterodine was provided as 4 mg ER capsules dispensed from a bottle. Placebo was provided as either a dummy tablet dispensed from a blister pack or a dummy capsule dispensed from a bottle.

To support the double-dummy model, each subject received both a blister pack of tablets (fesoterodine or placebo) and a bottle of capsules (tolterodine ER or placebo) at the Randomization/Baseline visit and the Week 4 visit. Subjects were instructed to swallow without chewing 1 tablet and 1 capsule with water every morning. Blister package medications were to be taken in number order to comply with the forced titration schedule in the fesoterodine treatment arm.

Efficacy Endpoints:

Primary Endpoint:

- Change in mean number of UUI episodes per 24 hours at Week 12 relative to the baseline (UUI episodes are defined as those with Urinary Sensation Scale [USS] rating of 5 in the diary)

Secondary Endpoints:

Bladder Diary:

- Change in mean number of UUI episodes per 24 hours at Weeks 1 and 4 relative to baseline
- Percent change of UUI episodes per 24 hours at Weeks 1, 4, and 12 relative to baseline
- Change in mean voided volume per micturition at Weeks 1, 4, and 12 relative to baseline
- Change in mean number of micturitions per 24 hours at Weeks 1, 4, and 12 relative to baseline
- Percent change of micturitions per 24 hours at Weeks 1, 4, and 12 relative to baseline
- Change in mean number of nocturnal micturitions per 24 hours at Weeks 1, 4, and 12 relative to baseline (nocturnal micturitions were those recorded in the bedtime section of the diary)
- Percent change of nocturnal micturitions per 24 hours at Weeks 1, 4, and 12 relative to baseline
- Change in mean number of urgency episodes per 24 hours at Weeks 1, 4, and 12 relative to baseline (urgency episodes were defined as those with USS rating of ≥3 in the diary)
- Percent change of urgency episodes per 24 hours at Weeks 1, 4, and 12 relative to baseline
- Change in mean number of severe urgency episodes per 24 hours at Weeks 1, 4, and 12 relative to baseline (severe urgency episodes were defined as those with USS rating ≥4)
- Percent change of severe urgency episodes per 24 hours at Weeks 1, 4, and 12 relative to baseline
- Change in mean USS rating per micturition at Weeks 1, 4, and 12 relative to baseline (USS defined as the sum of Urinary Sensation rating scores per diary day)
- Change in frequency-urgency sum per 24 hours (defined as the sum of USS rating scores per diary day) at Weeks 1, 4, and 12 relative to baseline

- Proportion of diary dry subjects (UUI =0) at Weeks 1, 4, and 12 among subjects who had UUI >0 at Baseline

Patient Perception of Bladder Condition:

- Change in PPBC at Weeks 1, 4, and 12 relative to baseline

Urgency Perception Scale (formerly known as Patient Perception of Urgency Scale):

- Change in UPS at Weeks 1, 4, and 12 relative to baseline

Overactive Bladder Questionnaire:

- Change in OAB-q symptom bother score at Week 12 relative to baseline
- Change in score of each HRQL (Health-Related Quality of Life) domain of OAB-q at Week 12 relative to baseline

Safety Evaluations: Incidences of adverse events (AEs) were monitored for each subject once the subject had received 1 dose of study medication; incidence of serious AEs (SAEs) were monitored for each subject once the subject had signed the informed consent through to the end-of-study or ET visit. Vital signs (blood pressure and pulse rate) were measured at each visit. Blood samples for hematology and serum chemistry were performed at screening and at the Week 12 visit or ET visit. Physical examination and electrocardiogram (ECG) were each performed at screening only.

Statistical Methods:

Safety Analysis Set: The safety set included all subjects who took at least one dose of study drug.

Full Analysis Set (FAS): FAS included all subjects who took at least 1 dose of assigned study drug and contributed data to at least 1 baseline or postbaseline efficacy assessment.

Supporting Full Analysis Set (SFAS): The FAS including those subjects who were excluded.

Efficacy data were analyzed based on the FAS (all subjects who took at least 1 dose of assigned study drug and contributed data to at least 1 baseline or postbaseline efficacy assessment. Key efficacy endpoints (change in number UUI episodes, number of micturitions, and number of urgency episodes per 24 hours at Week 12 relative to Baseline) were also analyzed based on the supporting FAS (SFAS; the FAS including subjects with unreliable efficacy data). Safety and baseline characteristics were analyzed based on the safety analysis set (all subjects who were randomized and received at least 1 dose of double-blind study medication).

The last valid postbaseline observation was carried forward (LOCF) to handle missing efficacy data at Week 4 and Week 12. Baseline data were not carried forward.

Regression diagnostics were performed to verify model assumptions and adequacy of the fitted model. Residual plots were generated to diagnose potential problems of non-normality or outliers. If the normality assumption was violated, appropriate variable transformations or non-parametric analyses were to be performed; robust regression methods were to be considered as well. An analysis of covariance (ANCOVA) model was planned for analysis of the primary endpoint. However, when running the planned regression diagnostics on the observed data for the primary endpoint, it was found that one of the model assumptions (normal distribution of residuals) was violated. As a result, the planned ANCOVA model did not adequately predict the results for observations with large changes from Baseline or high baseline values. Instead of the planned ANCOVA model, a nonparametric methodology, Van-Elteren test (a stratified Wilcoxon-Mann-Whitney test) with baseline quartiles as strata, was used to calculate the p-values for inferences about central tendency (treatment effect) of the change from Baseline. The use of a non-parametric methodology (if necessary) was pre-specified in the statistical analysis plan.

For continuous endpoints (except UUI), pair wise treatment group comparisons were carried out using an ANCOVA model that included baseline value as a covariate with treatment and country as factors. All comparisons were performed with 2-sided testing at a 5% significance level. The results that were generated included p-value from pair wise treatment comparisons, the least squares mean (LSMean) and standard error (SE) for change from Baseline for each treatment, the LSMean difference and SE between treatments, and the 95% confidence interval (CI) of the LSMean difference. ANCOVA models were repeated with 2 additional interaction terms, treatment by baseline and treatment by country.

The Cochran-Mantel-Haenszel (CMH) test with modified ridit scoring was used for ordinal variables and the CMH general association test was used for nominal variables. The CMH analyses were stratified by country. Summary statistics including cell counts and percentages were generated.

RESULTS

Subject Disposition and Demography: In total, 2685 subjects were screened and 1697 subjects were treated.

Approximately 90% of subjects in each treatment group completed the study, with no marked difference among the 3 treatment arms (91.0%, 91.8%, and 88.1% in placebo, tolterodine ER and fesoterodine groups, respectively). Subjects in the active treatment groups discontinued most frequently due to treatment-related AEs (fesoterodine: 34 subjects [5.0%]; tolterodine ER: 19 subjects [2.8%]). Subjects in the placebo treatment group discontinued most frequently due to other reasons not related to the study drug (7 subjects [2.1%]). There were 3 subjects in the placebo group (0.9%) who discontinued due to treatment-related AEs.

Efficacy analyses were performed on the FAS (all subjects who took at least 1 dose of assigned study drug and contributed data to at least 1 baseline or postbaseline efficacy assessment excluding subjects with unreliable efficacy data identified through for-cause audits) and SFAS (the FAS including those subjects who were excluded). Safety analyses were performed on the safety analysis set.

Subject disposition and subjects analyzed is summarized in Table 2.

Table 2. Subject Disposition and Subjects Analyzed

Variable	Number of Subjects		
	Placebo	Tolterodine ER	Fesoterodine
Single-blind placebo run-in period			
Started	2446	0	0
Completed	1712[a]	0	0
Not completed	734	0	0
Double-blind treatment period			
Randomized	337	690	685
Never returned after randomization	3	6	6
Treated	334 (100%)	684 (100%)	679 (100%)
Completed	304 (91%)	628 (91.8%)	598 (88.1%)
Discontinued	30 (9%)	56 (8.2%)	81 (11.9%)
Adverse event	6 (1.8%)	28 (4.1%)	44 (6.5%)
Lack of efficacy	5 (1.5%)	5 (0.7%)	13 (1.9%)
Lost to follow-up	4 (1.2%)	8 (1.2%)	5 (0.7%)
Death	2 (0.6%)	0	0
Withdraw by subject	6 (1.8%)	8 (1.2%)	7 (1.0%)
Unknown	7 (2.1%)	7 (1%)	12 (1.8%)
Randomized into and treated during the double-blind treatment period (safety set)	334 (100%)	684 (100%)	679 (100%)
Analyzed for efficacy			
Supporting FAS	334 (100%)	684 (100%)	679 (100%)
Analyzed for safety			
Adverse events	334 (100%)	684 (100%)	679 (100%)
Laboratory data	305 (91.3)	635 (92.8)	617 (90.9)

ER = extended-release formulation; FAS = full analysis set (all subjects who took at least 1 dose of assigned study drug and contributed data to at least 1 baseline or postbaseline efficacy assessment).
a. Progressed to randomization in double-blind treatment period.

Demographic and baseline characteristics for all treated subjects are presented in Table 3.

Table 3. Demographic and Baseline Characteristics - Safety Analysis Set

Number of Subjects (%)	Placebo			Tolterodine ER			Fesoterodine		
	Male	Female	Total	Male	Female	Total	Male	Female	Total
	65 (19.5)	269 (80.5)	334 (100.0)	120 (17.5)	564 (82.5)	684 (100.0)	121 (17.8)	558 (82.2)	679 (100.0)
Age (years)									
18-44	11 (16.9)	44 (16.4)	55 (16.5)	14 (11.7)	89 (15.8)	103 (15.1)	13 (10.7)	83 (14.9)	96 (14.1)
45-64	30 (46.2)	137 (50.9)	167 (50)	53 (44.2)	296 (52.5)	349 (51.0)	52 (43.0)	315 (56.5)	367 (54.1)
≥65	24 (36.9)	88 (32.7)	112 (33.5)	53 (44.2)	179 (31.7)	232 (33.9)	56 (46.3)	160 (28.7)	216 (31.8)
Mean	59.6	58.1	58.4	61	58	58.5	60.8	57.2	57.8
SD	14.4	13.5	13.7	12.9	13.2	13.2	13.1	12.7	12.8
Race									
White	49 (75.4)	212 (78.8)	261 (78.1)	88 (73.3)	446 (79.1)	534 (78.1)	83 (68.6)	456 (81.7)	539 (79.4)
Black	2 (3.1)	9 (3.3)	11 (3.3)	1 (0.8)	21 (3.7)	22 (3.2)	3 (2.5)	20 (3.6)	23 (3.4)
Asian	10 (15.4)	22 (8.2)	32 (9.6)	21 (17.5)	50 (8.9)	71 (10.4)	30 (24.8)	37 (6.6)	67 (9.9)
Other	4 (6.2)	26 (9.7)	30 (9)	10 (8.3)	47 (8.3)	57 (8.3)	5 (4.1)	45 (8.1)	50 (7.4)
Weight (kg)									
Mean	82.9	74.4	76.1	80.2	75.1	76	82	76.2	77.2
SD	17.9	17.4	17.8	17.5	17.4	17.5	19.6	17.8	18.3
N	65 (100)	269 (100)	334 (100)	120 (100)	562 (99.6)	682 (99.7)	121 (100)	556 (99.6)	677 (99.7)
BMI (kg/m^2)									
Mean	27.3	28.7	28.4	27	28.8	28.5	27.2	29	28.7
SD	5.1	6.3	6.1	4.8	6.1	6	5.4	6.4	6.2
N	65 (100)	269 (100)	334 (100)	120 (100)	561 (99.5)	681 (99.6)	121 (100)	555 (99.5)	676 (99.6)
Height (cm)									
Mean	173.9	161.1	163.6	172.1	161.3	163.2	173.1	161.9	163.9
SD	8	7.4	9.1	8.6	7.2	8.5	8	6.9	8.3
N	65 (100)	269 (100)	334 (100)	120 (100)	562 (99.6)	682 (99.7)	121 (100)	556 (99.6)	677 (99.7)
Smoking Status									
Never smoked	43 (66.2)	189 (70.3)	232 (69.5)	66 (55.0)	374 (66.3)	440 (64.3)	68 (56.2)	373 (66.8)	441 (64.9)
Smoker	9 (13.8)	34 (12.6)	43 (12.9)	16 (13.3)	78 (13.8)	94 (13.7)	19 (15.7)	74 (13.3)	93 (13.7)
Ex-smoker	13 (20)	46 (17.1)	59 (17.7)	38 (31.7)	110 (19.5)	148 (21.6)	32 (26.4)	111 (19.9)	143 (21.1)
Not recorded	0	0	0	0	2 (0.4)	2 (0.3)	2 (1.7)	0	2 (0.3)
Menstrual Status									
Premenopausal		39 (14.5)			86 (15.2)			73 (13.1)	
Perimenopausal		34 (12.6)			57 (10.1)			61 (10.9)	
Postmenopausal		195 (72.5)			421 (74.6)			424 (76)	

BMI = body mass index; ER = extended-release; N = number of subjects; SD = standard deviation.

Efficacy Results:

All diary endpoints based on numeric changes and percent change from Baseline and all PRO endpoints described in Table 4.

Table 4. Summary of Efficacy Endpoints at Week 12 – Full Analysis Set

Variable	Placebo	Tolterodine ER	Fesoterodine	p-Value		
				Tolterodine ER vs Placebo at Week 12	Fesoterodine vs Placebo at Week 12	Fesoterodine vs Tolterodine ER at Week 12
Bladder diary endpoints (Mean change from Baseline to Week 12)						
UUI (episodes per 24 hours)[a]	-1.46	-1.61	-1.72	0.0107	<0.0001	0.0172
Diary dry rate (%)[b]	45	57.2	64	0.0004	<0.0001	0.0153
Voided volume per micturition (mL)[c]	16.8	23.5	32.9	0.1029	<0.0001	0.0048
Micturitions (episodes per 24 hours)[c]	-1.5	-2.1	-2.2	0.0005	<0.0001	0.3798
Nocturnal micturitions (episodes per 24 hours)[c]	-0.5	-0.6	-0.6	0.5059	0.3269	0.6990
Urgency (episodes per 24 hours)[c]	-2	-3.1	-3.5	<0.0001	<0.0001	0.0542
Severe urgency (episodes per 24 hours)[c]	-1.9	-2.8	-3.0	0.0001	<0.0001	0.1391
USS rating per micturition[c]	-0.4	-0.6	-0.7	<0.0001	<0.0001	0.0289
Frequency-urgency Sum[c]	-8.2	-12.1	-13.2	<0.0001	<0.0001	0.1047
Percent change of UUI (episodes per 24 hours)	-82.1	-100	-100	<0.0001	<0.0001	0.0220
Percent change of micturitions (episodes per 24 hours)	-12.1	-16.2	-18.9	<0.0001	0.0003	NR
Percent change in nocturnal micturitions (episodes per 24 hours)	-25	-27.9	-28.6	NR	NR	NR
Percent change in urgency episodes (episodes per 24 hours)	-17.6	-30.8	-37.9	<0.0001	0.0001	NR
Percent change in severe urgency (episodes per 24 hours)	-48	-63.4	-71.4	<0.0001	0.0001	NR
Patient-reported outcome endpoints (Mean change from Baseline to Week 12)						
PPBC - percent of subjects with ≥2 points improvement[d]	21.4	33.2	40.3	NR	<0.0001	NR
UPS - percent of subjects with improvement[d]	35.8	40.1	46.2	NR	0.0008	NR
OABq Symptom Bother Score[c]	-16.3	-22.5	-27.1	NR	<0.0001	NR

Table 4. Summary of Efficacy Endpoints at Week 12 – Full Analysis Set

Variable	Placebo	Tolterodine ER	Fesoterodine	p-Value		
				Tolterodine ER vs Placebo at Week 12	Fesoterodine vs Placebo at Week 12	Fesoterodine vs Tolterodine ER at Week 12
OABq HRQL total score[c]	12	16.3	19.3	NR	<0.0001	NR
Concern domain[c]	13.4	19.3	22.6	NR	<0.0001	NR
Coping domain[c]	14	18.5	22.6	NR	<0.0001	NR
Sleep domain[c]	12.2	15.1	17.3	NR	0.0008	NR
Social interaction domain[c]	6.8	9.4	11.6	NR	<0.0001	NR

ER = extended-release; HRQL = Health-Related Quality of Life; LSMean = least squares mean; NR = not reported; OABq = Overactive Bladder Questionnaire; PPBC = Patient Perception of Bladder Condition question; UPS = Urgency Perception Scale (formerly known as Patient Perception of Urgency Scale); USS = Urinary Sensation Scale; UUI = Urgency urinary incontinence; vs = versus.

a. The primary endpoint; the data in the 3 treatment columns are Winsorized mean changes from Baseline to Week 12.
b. A post-hoc analysis; the data in the 3 treatment columns are the diary dry rate (percentages) at Week 12.
c. The secondary endpoints; the data in the 3 treatment columns are LSMean changes from Baseline to Week 12.
d. The data in the 3 treatment columns are the value (percentage) at Week 12.

The mean number of UUI episodes per 24 hours was decreased in all 3 treatment arms at the Weeks 1 and 4. The reductions were statistically significantly greater in the active treatment groups compared with placebo at Weeks 1 and 4 (p<0.0001, Table 5).

Table 5. Change in Mean Number of UUI Episodes per 24 Hours at Weeks 1 and 4 Relative to Baseline – Full Analysis Set (Subjects Reporting This Symptom at Baseline)

Mean Number of UUI Episodes per 24 Hours	Placebo N=334	Tolterodine ER N=684	Fesoterodine N=679
Week 1	**n=302**	**n=614**	**n=612**
Baseline mean (SD)	2.6 (2.4)	2.5 (2.2)	2.4 (2)
Mean change from Baseline to Week 1 (SEM)[a]	-0.54 (0.09)	-0.92 (0.06)	-0.95 (0.06)
Treatment difference[a]	Mean difference	p-value[b]	
Fesoterodine vs placebo	-0.41	<0.0001	
Tolterodine ER vs placebo	-0.38	<0.0001	
Fesoterodine vs tolterodine ER	-0.03	0.8460	
Week 4	**n=307**	**n=626**	**n=618**
Baseline mean (SD)	2.6 (2.3)	2.5 (2.2)	2.4 (2)
Mean change from Baseline to Week 4 (SEM)[a]	-1.06 (0.10)	-1.40 (0.06)	-1.52 (0.06)
Treatment difference[a]	Mean difference	p-value[b]	
Fesoterodine vs placebo	-0.45	<0.0001	
Tolterodine ER vs placebo	-0.34	<0.0001	
Fesoterodine vs tolterodine ER	-0.11	0.1937	

ER = extended-release formulation; LOCF = last observation carried forward; N = number of subjects in the respective treatment group; n = number of subjects with baseline UUI >0 per 24 hours and non-missing change from Baseline to the respective postbaseline value (Week 1 or Week 4 [LOCF]); SD = standard deviation; SEM = standard error of the mean; UUI = urgency urinary incontinence; vs = versus.

a. Winsorized means (5% of the tails were censored, ie, replaced with the value at the 5th and 95th percentile, respectively).

b. p-Value based on Van Elteren's Test adjusted by baseline UUI quartile.

The percent reductions from Baseline were statistically significantly greater in the active treatment groups compared with placebo at Weeks 1, 4 and 12 (p <0.0001, Table 6).

Table 6. Percent Change of UUI Episodes per 24 Hours at Weeks 1, 4, and 12 Relative to Baseline – Full Analysis Set (Subjects Reporting This Symptom at Baseline)

Percent Change of UUI Episodes per 24 Hours	Placebo N=334	Tolterodine ER N=684	Fesoterodine N=679
Percent change from Baseline to Week 1	**n=302**	**n=614**	**n=612**
Baseline mean (SD)	2.6 (2.4)	2.5 (2.2)	2.4 (2)
Week 1 mean (SD)	2.0 (2.4)	1.5 (2.2)	1.5 (2)
Percent change median (min, max)	-28.6 (-100, 300)	-55.1 (-100, 537.5)	-53.6 (-100, 525)
p-Value for treatment difference[a]			
Fesoterodine vs placebo	<0.0001	-	-
Tolterodine ER vs placebo	<0.0001	-	-
Fesoterodine vs tolterodine ER	Not done[b]	-	-
Percent change from Baseline to Week 4	**n=307**	**n=626**	**n=618**
Baseline mean (SD)	2.6 (2.3)	2.5 (2.2)	2.4 (2)
Week 4 mean (SD)	1.5 (2.1)	1.0 (1.9)	0.9 (1.6)
Percent change median (min, max)	-60.0 (-100, 300)	-85.7 (-100, 650)	-93.2 (-100, 450)
p-Value for treatment difference[a]			
Fesoterodine vs placebo	<0.0001	-	-
Tolterodine ER vs placebo	<0.0001	-	-
Fesoterodine vs tolterodine ER	Not done[b]	-	-
Percent change from Baseline to Week 12	**n=307**	**n=626**	**n=619**
Baseline mean (SD)	2.6 (2.3)	2.5 (2.2)	2.4 (2)
Week 12 mean (SD)	1.1 (2)	0.7 (1.5)	0.7 (1.4)
Percent change median (min, max)	-82.1 (-100, 300)	-100.0 (-100, 450)	-100.0 (-100, 400)
p-Value for treatment difference[a]			
Fesoterodine vs placebo	<0.0001	-	-
Tolterodine ER vs placebo	<0.0001	-	-
Fesoterodine vs tolterodine ER	0.0220	-	-

ER = extended-release formulation, LOCF = last observation carried forward, min = minimum, max = maximum, N = number of subjects in the respective treatment group, n = number of subjects with baseline UUI >0 per 24 hours and non-missing change from Baseline to the respective postbaseline value (Week 1, Week 4 [LOCF], or Week 12 [LOCF]), UUI = urgency urinary incontinence, SD = standard deviation, vs = versus.

a. Based on a ranked analysis of covariance model with country and treatment as factors, and ranked Baseline value as a covariate.

b. In accordance with a closed testing procedure, statistical testing for percent change was not performed since the corresponding numerical change result was not statistically significant.

To further understand the observations in the percent change of UUI from Baseline, post-hoc analyses of diary dry rates at Weeks 1, 4, and 12 were performed. The diary dry rates were statistically significantly higher in the active treatment groups than in the placebo group at all-time points ($p<0.05$). At Week 12, the dry rate was 64.0% in the fesoterodine group versus 57.2% in the tolterodine ER group; the difference was statistically significant in favor of fesoterodine ($p=0.0153$; Table 7).

Table 7 Diary Dry Rates at Weeks 1, 4, and 12 - Full Analysis Set

Variable	Placebo N=334	Tolterodine ER N=684	Fesoterodine N=679
Week 1	**n (%)**	**n (%)**	**n (%)**
Subjects with non-missing baseline and Week 1 values[a]	302 (100)	614 (100)	612 (100)
Diary dry rate[b]	54 (17.9)	153 (24.9)	159 (26)
Treatment difference in continent rate	Percentage (%)	p-value[c]	
Fesoterodine vs placebo	8.1	0.0072	
Tolterodine ER vs placebo	7.0	0.0116	
Fesoterodine vs tolterodine ER	1.1	0.7828	
Week 4	**n (%)**	**n (%)**	**n (%)**
Subjects with non-missing baseline and Week 4 values[a]	307 (100)	626 (100)	618 (100)
Diary dry rate	97 (31.6)	290 (46.3)	306 (49.5)
Treatment difference in continent rate	Percentage (%)	p-value[c]	
Fesoterodine vs placebo	17.9	<0.0001	
Tolterodine ER vs placebo	14.7	<0.0001	
Fesoterodine vs tolterodine ER	3.2	0.3104	
Week 12	**n (%)**	**n (%)**	**n (%)**
Subjects with non-missing baseline and Week 12 values[a]	307 (100)	626 (100)	619 (100)
Diary dry rate	138 (45)	358 (57.2)	396 (64)
Treatment difference in continent rate	Percentage (%)	p-value[c]	
Fesoterodine vs placebo	19	<0.0001	
Tolterodine ER vs placebo	12.2	0.0004	
Fesoterodine vs tolterodine ER	6.8	0.0153	

ER = extended-release formulation; N = number of subjects in the respective treatment group; n = number of subjects in the respective category; vs = versus

a. Only subjects with baseline urgency urinary incontinence >0 per 24 hours are included.

b. Diary dry rate = no urgency urinary incontinence episode reported in the 3 day diary at the respective time-point.

c. Based on Cochran-Mantel-Haenszel test stratified by baseline urgency urinary incontinence quartile.

The mean voided volume per micturition was comparable across treatment groups at Baseline (148.5 to 155.3 mL), and increased in all 3 treatment arms at Weeks 1, 4, and 12 (Table 8). The increases were statistically significantly greater in the fesoterodine group than in the placebo group at all postbaseline time-points ($p<0.05$), relative to baseline. The increases were significantly greater in tolterodine ER group than in the placebo group at Weeks 1 and 4 ($p<0.05$) but not at Week 12 ($p=0.1029$). At Week 12, the LSMean increase was statistically significant in favor of fesoterodine ($p=0.0048$). The increase was 32.9 mL in the fesoterodine group versus 23.5 mL in the tolterodine ER group.

Table 8. Change in Mean Voided Volume per Micturition at Weeks 1, 4, and 12 Relative to Baseline – Full Analysis Set

Mean Voided Volume per Micturition	Placebo N=334	Tolterodine ER N=684	Fesoterodine N=679
Week 1	**n=306**	**n=622**	**n=623**
Baseline mean (SD)	148.5 (57.6)	154.4 (64.3)	155.3 (61.8)
Week 1 mean (SD)	158.3 (62.2)	171.8 (74.6)	172 (74.9)
Change from Baseline to Week 1			
LSMean (SE)	11 (3.2)	19.2 (2.5)	18.7 (2.5)
95% CI for mean	5, 14.5	13.6, 21.3	12.6, 20.9
p-Value[a]	<0.0001	<0.0001	<0.0001
Treatment difference[b]	LSMean difference (SE)	95% CI	p-value
Fesoterodine vs placebo	7.8 (3.4)	1.2, 14.4	0.0214
Tolterodine ER vs placebo	8.2 (3.4)	1.6, 14.9	0.0149
Fesoterodine vs tolterodine ER	-0.5 (2.7)	-5.8, 4.9	0.8659
Week 4	**n=313**	**n=633**	**n=625**
Baseline mean (SD)	147.9 (58.3)	154.1 (64.5)	155.4 (61.8)
Week 4 mean (SD)	160.8 (72.5)	178.4 (81.2)	184.1 (81.3)
Change from Baseline to Week 4			
LSMean (SE)	14.0 (3.8)	25.7 (3)	30.5 (3)
95% CI for mean	6.9, 18.9	19.4, 29.0	24, 33.3
p-Value[a]	<0.0001	<0.0001	<0.0001
Treatment difference[b]	LSMean difference (SE)	95% CI	p-value
Fesoterodine vs placebo	16.5 (4)	8.6, 24.4	<0.0001
Tolterodine ER vs placebo	11.7 (4)	3.8, 19.6	0.0036
Fesoterodine vs tolterodine ER	4.7 (3.3)	-1.7, 11.2	0.1484
Week 12	**n=313**	**n=633**	**n=626**
Baseline mean (SD)	147.9 (58.3)	154.1 (64.5)	155.3 (61.8)
Week 12 mean (SD)	164.2 (74.6)	176.1 (74.9)	186.2 (81.2)
Change from Baseline to Week 12			
LSMean (SE)	16.8 (3.9)	23.5 (3.0)	32.9 (3.1)
95% CI for mean	9.9, 22.7	17.1, 26.9	26.1, 35.8
p-value[a]	<0.0001	<0.0001	<0.0001
Treatment difference[b]	LSMean difference (SE)	95% CI	p-value
Fesoterodine vs placebo	16.1 (4.1)	8.1, 24.2	<0.0001
Tolterodine ER vs placebo	6.7 (4.1)	-1.4, 14.7	0.1029
Fesoterodine vs tolterodine ER	9.4 (3.3)	2.9, 16.0	0.0048

CI = confidence interval; ER = extended-release formulation; LOCF = last observation carried forward; LSMean = least square of the mean; N = number of subjects in the respective treatment group; n = number of subjects with non-missing numerical change from Baseline to the respective postbaseline value (Week 1, Week 4 [LOCF], or Week 12 [LOCF]); SD = standard deviation; SE = standard error; vs = versus.

a. Based on a paired t-test comparing baseline with postbaseline values.
b. Based on an analysis of covariance model with country and treatment as factors, and centered baseline value as a covariate.

The mean number of micturitions per 24 hours was comparable across treatment groups at Baseline (11.7 to 11.9 per 24 hours), and decreased in all 3 treatment arms at Weeks 1, 4, and 12 (Table 9). The reductions were statistically significantly greater in the active treatment groups compared with placebo at all postbaseline time-points (p<0.05). At Week 12, the LSMean reduction from Baseline was 2.2 per 24 hours in the festerodine group versus 2.1 in the tolterodine ER group; the difference was not statistically significant (p=0.3798).

Table 9. Change in Mean Number of Micturitions per 24 Hours at Weeks 1, 4, and 12 Relative to Baseline – Full Analysis Set

Mean Number of Micturitions per 24 Hours	Placebo N=334	Tolterodine ER N= 84	Fesoterodine N=679
Week 1	**n=307**	**n=622**	**n=623**
Baseline mean (SD)	11.9 (3.5)	11.7 (3.4)	11.7 (3.1)
Week 1 mean (SD)	11.5 (3.8)	10.9 (3.6)	10.8 (3.3)
Change from Baseline to Week 1			
LSMean (SE)	-0.5 (0.1)	-1.0 (0.1)	-1.0 (0.1)
95% CI for mean	-0.6, -0.1	-1.1, -0.7	-1.1, -0.7
p-Value[a]	0.0018	<0.0001	<0.0001
Treatment difference[b]	LSMean difference (SE)	95% CI	p-value
Fesoterodine vs placebo	-0.6 (0.2)	-0.9, -0.3	0.0002
Tolterodine ER vs placebo	-0.5 (0.2)	-0.8, -0.2	0.0006
Fesoterodine vs tolterodine ER	-0.0 (0.1)	-0.3, 0.2	0.7395
Week 4	**n=313**	**n=634**	**n=627**
Baseline mean (SD)	11.9 (3.5)	11.7 (3.4)	11.7 (3.1)
Week 4 mean (SD)	10.8 (3.7)	10.1 (3.5)	9.9 (3.2)
Change from Baseline to Week 4			
LSMean (SE)	-1.2 (0.2)	-1.8 (0.1)	-1.9 (0.1)
95% CI for mean	-1.5, -0.9	-1.9, -1.5	-2.0, -1.6
p-Value[a]	<0.0001	<0.0001	<0.0001
Treatment difference[b]	LSMean difference (SE)	95% CI	p-value
Fesoterodine vs placebo	-0.7 (0.2)	-1.0, -0.3	<0.0001
Tolterodine ER vs placebo	-0.6 (0.2)	-0.9, -0.2	0.0007
Fesoterodine vs tolterodine ER	-0.1 (0.1)	-0.4, 0.2	0.4185
Week 12	**n=313**	**n=634**	**n=628**
Baseline mean (SD)	11.9 (3.5)	11.7 (3.4)	11.7 (3.1)
Week 12 mean (SD)	10.5 (3.7)	9.7 (3.3)	9.6 (3.3)
Change from Baseline to Week 12			
LSMean (SE)	-1.5 (0.2)	-2.1 (0.1)	-2.2 (0.1)
95% CI for mean	-1.8, -1.2	-2.2, -1.8	-2.3, -1.9
p-Value[a]	<0.0001	<0.0001	<0.0001
Treatment difference[b]	LSMean difference (SE)	95% CI	p-value
Fesoterodine vs placebo	-0.7 (0.2)	-1.1, -0.4	<0.0001
Tolterodine ER vs placebo	-0.6 (0.2)	-0.9, -0.3	0.0005
Fesoterodine vs tolterodine ER	-0.1 (0.1)	-0.4, 0.2	0.3798

CI = confidence interval; ER = extended-release formulation; LOCF = last observation carried forward; LSMean = least square of the mean; N = number of subjects in the respective treatment group; n = number of subjects with non-missing numerical change from Baseline to the respective postbaseline value (Week 1, Week 4 [LOCF], or Week 12 [LOCF]); SD = standard deviation; SE = standard error; vs = versus.

a. Based on a paired t-test comparing baseline with postbaseline values.

b. Based on an analysis of covariance model with country and treatment as factors, and centered baseline value as a covariate.

The percent reductions of micturitions from Baseline were statistically significantly greater in the active treatment groups compared with placebo at Weeks 1, 4 and 12 ($p<0.001$). At Week 12, the median percentage reduction from Baseline was 18.9% in festerodine group versus 16.2% in tolterodine ER group. No statistical test between fesoterodine and tolterodine ER was performed since the differences of the corresponding numerical changes were not statistically significant. A summary of percent change of micturitions per 24 hours is provided in Table 10.

Table 10. Percent Change of Micturitions per 24 Hours at Weeks 1, 4, and 12 Relative to Baseline – Full Analysis Set

Percent Change of Micturitions per 24 Hours	Placebo N=334	Tolterodine ER N=684	Fesoterodine N=679
Percent Change From Baseline to Week 1	**n=307**	**n=622**	**n=623**
Baseline mean (SD)	11.9 (3.5)	11.7 (3.4)	11.7 (3.1)
Week 1 mean (SD)	11.5 (3.8)	10.9 (3.6)	10.8 (3.3)
Percent change median (min, max)	-2.7 (-48.5, 68.3)	-7.7 (-68.2, 70)	-7.9 (-66, 184)
p-Value for treatment difference[a]			
Fesoterodine vs placebo	0.0001	-	-
Tolterodine ER vs placebo	0.0002	-	-
Fesoterodine vs tolterodine ER	Not done[b]	-	-
Percent Change From Baseline to Week 4	**n=313**	**n=634**	**n=627**
Baseline mean (SD)	11.9 (3.5)	11.7 (3.4)	11.7 (3.1)
Week 4 mean (SD)	10.8 (3.7)	10.1 (3.5)	9.9 (3.2)
Percent change median (min, max)	-10.3 (-67.4, 75.0)	-15.0 (-66.2, 82.9)	-14.8 (-67.6, 135.7)
p-Value for treatment difference[a]			
Fesoterodine vs placebo	<0.0001	-	-
Tolterodine ER vs placebo	<0.0001	-	-
Fesoterodine vs tolterodine ER	Not done[b]	-	-
Percent Change From Baseline to Week 12	**n=313**	**n=634**	**n=628**
Baseline mean (SD)	11.9 (3.5)	11.7 (3.4)	11.7 (3.1)
Week 12 mean (SD)	10.5 (3.7)	9.7 (3.3)	9.6 (3.3)
Percent change median (min, max)	-12.1 (-69.6, 73)	-16.2 (-69.6, 55.6)	-18.9 (-66.7, 185.7)
p-Value for treatment difference[a]			
Fesoterodine vs placebo	<0.0001	-	-
Tolterodine ER vs placebo	0.0003	-	-
Fesoterodine vs tolterodine ER	Not done[b]	-	-

ER = extended-release formulation; LOCF = last observation carried forward; min = minimum; max = maximum; N = number of subjects in the respective treatment group; n = number of subjects with non-missing percent change from Baseline to the respective postbaseline value (Week 1, Week 4 [LOCF], or Week 12 [LOCF]); SD = standard deviation; vs = versus.

a. Based on a ranked analysis of covariance model with country and treatment as factors, and ranked baseline value as a covariate.

b. In accordance with a closed testing procedure, statistical testing for percent change was not performed since the corresponding numerical change result was not statistically significant.

The mean number of nocturnal micturitions per 24 hours was comparable across treatment groups at Baseline (2.2 to 2.3 episodes per 24 hours), and decreased in all 3 treatment arms at Weeks 1, 4, and 12 (Table 11). There was no statistically significant difference for the reductions from Baseline among the treatment groups at any postbaseline time-point. At Week 12, the LSMean reduction from Baseline was 0.6 episodes per 24 hours in both the festerodine and tolterodine ER groups compared to 0.5 in the placebo group.

Table 11. Change in Mean Number of Nocturnal Micturitions per 24 Hours at Weeks 1, 4, and 12 Relative to Baseline – Full Analysis Set (Subjects Reporting this Symptom at Baseline)

Mean Number of Nocturnal Micturitions per 24 Hours	Placebo N=334	Tolterodine ER N=684	Fesoterodine N=679
Week 1	**n=288**	**n=584**	**n=596**
Baseline mean (SD)	2.3 (1.3)	2.2 (1.3)	2.2 (1.3)
Week 1 mean (SD)	2.2 (1.5)	1.9 (1.4)	2.0 (1.4)
Change from Baseline to Week 1			
LSMean (SE)	-0.1 (0.1)	-0.3 (0)	-0.2 (0)
95% CI for mean	-0.3, -0	-0.3, -0.2	-0.2, -0.1
p-value[a]	0.0203	<0.0001	<0.0001
Treatment difference[b]	LSMean difference (SE)	95% CI	p-value
Fesoterodine vs placebo	-0.1 (0.1)	-0.2, 0.1	0.2730
Tolterodine ER vs placebo	-0.1 (0.1)	-0.2, 0	0.0652
Fesoterodine vs tolterodine ER	0.0 (0.1)	-0.1, 0.2	0.3503
Week 4	**n=293**	**n=596**	**n=600**
Baseline mean (SD)	2.3 (1.3)	2.2 (1.3)	2.2 (1.3)
Week 4 mean (SD)	1.9 (1.4)	1.7 (1.4)	1.7 (1.3)
Change from Baseline to Week 4			
LSMean (SE)	-0.4 (0.1)	-0.5 (0)	-0.5 (0.1)
95% CI for mean	-0.5, -0.3	-0.5, -0.4	-0.5, -0.3
p-value[a]	<0.0001	<0.0001	<0.0001
Treatment difference[b]	LSMean difference (SE)	95% CI	p-value
Fesoterodine vs placebo	-0.1 (0.1)	-0.2, 0.1	0.2667
Tolterodine ER vs placebo	-0.1 (0.1)	-0.2, 0	0.1643
Fesoterodine vs tolterodine ER	0.0 (0.1)	-0.1, 0.1	0.7264
Week 12	**n=293**	**n=596**	**n=601**
Baseline mean (SD)	2.3 (1.3)	2.2 (1.3)	2.2 (1.3)
Week 12 mean (SD)	1.8 (1.4)	1.7 (1.3)	1.6 (1.4)
Change from Baseline to Week 12			
LSMean (SE)	-0.5 (0.1)	-0.6 (0.1)	-0.6 (0.1)
95% CI for mean	-0.7, -0.4	-0.6, -0.4	-0.6, -0.5
p-value[a]	<0.0001	<0.0001	<0.0001
Treatment difference[b]	LSMean difference (SE)	95% CI	p-value
Fesoterodine vs placebo	-0.1 (0.1)	-0.2, 0.1	0.3269
Tolterodine ER vs placebo	-0.0 (0.1)	-0.2, 0.1	0.5059
Fesoterodine vs tolterodine ER	-0.0 (0.1)	-0.1, 0.1	0.6990

CI = confidence interval; ER = extended-release formulation; LOCF = last observation carried forward; LSMean = least square of the mean; N = number of subjects in the respective treatment group; n = number of subjects with baseline nocturnal micturitions >0 per 24 hours and non-missing change from Baseline to the respective postbaseline value (Week 1, Week 4 [LOCF], or Week 12 [LOCF]); SD = standard deviation; SE = standard error; vs = versus.

a. Based on a paired t-test comparing baseline with postbaseline values.
b. Based on an analysis of covariance model with country and treatment as factors, and centered baseline value as a covariate.

At Week 12, the median percent reduction from Baseline was 28.6%, 27.9%, and 25.0% in the fesoterodine, tolterodine ER and placebo groups, respectively. No statistical test among the 3 treatment groups was performed since the differences of the corresponding numerical changes were not statistically significant. A summary of percent change in nocturnal micturitions per 24 hours is provided in Table 12.

Table 12. Percent Change of Nocturnal Micturitions per 24 Hours at Weeks 1, 4, and 12 Relative to Baseline – Full Analysis Set (Subjects Reporting This Symptom at Baseline)

Percent Change of Nocturnal Micturitions per 24 Hours	Placebo N=334	Tolterodine ER N=684	Fesoterodine N=679
Percent change From Baseline to Week 1	**n=288**	**n=584**	**n=596**
Baseline mean (SD)	2.3 (1.3)	2.2 (1.3)	2.2 (1.3)
Week 1 mean (SD)	2.2 (1.5)	1.9 (1.4)	2 (1.4)
Percent change median (min, max)	-10 (-100, 500)	-12.5 (-100, 350)	0 (-100, 800)
p-Value for treatment difference	Not done[a]	Not done[a]	Not done[a]
Percent Change From Baseline to Week 4	**n=293**	**n=596**	**n=600**
Baseline mean (SD)	2.3 (1.3)	2.2 (1.3)	2.2 (1.3)
Week 4 mean (SD)	1.9 (1.4)	1.7 (1.4)	1.7 (1.3)
Percent change median (min, max)	-22.2 (-100, 600)	-25.0 (-100, 400)	-20.0 (-100, 900)
p-Value for treatment difference	Not done[a]	Not done[a]	Not done[a]
Percent Change From Baseline to Week 12	**n=293**	**n=596**	**n=601**
Baseline mean (SD)	2.3 (1.3)	2.2 (1.3)	2.2 (1.3)
Week 12 mean (SD)	1.8 (1.4)	1.7 (1.3)	1.6 (1.4)
Percent change median (min, max)	-25 (-100, 600)	-27.9 (-100, 500)	-28.6 (-100, 400)
p-Value for treatment difference	Not done[a]	Not done[a]	Not done[a]

ER = extended-release formulation; LOCF = last observation carried forward; min = minimum; max = maximum; N = number of subjects in the respective treatment group; n = number of subjects with baseline nocturnal micturitions >0 per 24 hours and non-missing change from Baseline to the respective postbaseline value (Week 1, Week 4 [LOCF], or Week 12 [LOCF]); SD = standard deviation.

a. In accordance with a closed testing procedure, statistical testing for percent change was not performed since the corresponding numerical change result was not statistically significant.

The mean number of urgency episodes per 24 hours was comparable for the treatment groups at Baseline (9.3 to 9.4 episodes per 24 hours), and decreased for subjects in all treatment groups at Weeks 1, 4 and 12 (Table 13). The reductions were statistically significantly greater in the active treatment groups compared with placebo at all postbaseline time-points ($p<0.001$). At Week 12, the LSMean reduction was 3.5 episodes per 24 hours in the festerodine group versus 3.1 in the tolterodine ER group; the difference was not statistically significant ($p=0.0542$).

Table 13. Change in Mean Number of Urgency Episodes per 24 Hours at Weeks 1, 4, and 12 Relative to Baseline – Full Analysis Set (Subjects Reporting This Symptom at Baseline)

Mean Number of Urgency Episodes per 24 Hours	Placebo N=334	Tolterodine ER N=684	Fesoterodine N=679
Week 1	**n=306**	**n=619**	**n=621**
Baseline mean (SD)	9.4 (4.2)	9.3 (3.7)	9.3 (3.9)
Week 1 mean (SD)	9 (4.4)	8.1 (4.2)	8.2 (4.4)
Change from Baseline to Week 1			
LSMean (SE)	-0.4 (0.2)	-1.3 (0.2)	-1.1 (0.2)
95% CI for mean	-0.7, -0	-1.4, -0.9	-1.3, -0.8
p-Value[a]	0.0285	<0.0001	<0.0001
Treatment difference[b]	LSMean difference (SE)	95% CI	p-value
Fesoterodine vs placebo	-0.7 (0.2)	-1.1, -0.3	0.0008
Tolterodine ER vs placebo	-0.9 (0.2)	-1.3, -0.4	<0.0001
Fesoterodine vs tolterodine ER	0.2 (0.2)	-0.2, 0.5	0.3820
Week 4	**n=311**	**n=631**	**n=627**
Baseline mean (SD)	9.4 (4.2)	9.3 (3.7)	9.3 (3.9)
Week 4 mean (SD)	8.2 (4.4)	6.9 (4.2)	6.8 (4.4)
Change from Baseline to Week 4			
LSMean (SE)	-1.2 (0.2)	-2.4 (0.2)	-2.6 (0.2)
95% CI for mean	-1.6, -0.7	-2.7, -2.1	-2.8, -2.2
p-Value[a]	<0.0001	<0.0001	<0.0001
Treatment difference[b]	LSMean difference (SE)	95% CI	p-value
Fesoterodine vs placebo	-1.4 (0.2)	-1.9, -0.9	<0.0001
Tolterodine ER vs placebo	-1.2 (0.2)	-1.7, -07	<0.0001
Fesoterodine vs tolterodine ER	-0.2 (0.2)	-0.6, 0.2	0.3498
Week 12	**n=311**	**n=631**	**n=628**
Baseline mean (SD)	9.4 (4.2)	9.3 (3.7)	9.3 (3.9)
Week 12 mean (SD)	7.4 (4.8)	6.2 (4.3)	5.8 (4.5)
Change from Baseline to Week 12			
LSMean (SE)	-2 (0.3)	-3.1 (0.2)	-3.5 (0.2)
95% CI for mean	-2.5, -1.5	-3.4, -2.7	-3.8, -3.2
p-Value[a]	<0.0001	<0.0001	<0.0001
Treatment difference[b]	LSMean difference (SE)	95% CI	p-value
Fesoterodine vs placebo	-1.5 (0.3)	-2.1, -1	<0.0001
Tolterodine ER vs placebo	-1.1 (0.3)	-1.6, -0.6	<0.0001
Fesoterodine vs tolterodine ER	-0.4 (0.2)	-0.8, 0	0.0542

CI = confidence interval; ER = extended-release formulation; LOCF = last observation carried forward; LSMean = least square of the mean; N = number of subjects in the respective treatment group; n = number of subjects with baseline urgency episodes >0 per 24 hours and non-missing change from Baseline to the respective postbaseline value (Week 1, Week 4 [LOCF], or Week 12 [LOCF]); SD = standard deviation; SE = standard error; vs = versus.

a. Based on a paired t-test comparing baseline with postbaseline values.
b. Based on an analysis of covariance model with country and treatment as factors, and centered baseline value as a covariate.

The percent reductions from Baseline were statistically significantly greater in the active treatment groups compared with placebo at Weeks 1, 4 and 12 (p<0.001). At Week 12, the median percent reduction from Baseline was 37.9% in the fesoterodine group versus 30.8% in the tolterodine ER group. No statistical test between fesoterodine and tolterodine ER was performed since the differences of the corresponding numerical changes were not statistically

significant. A summary of percent change in urgency episodes per 24 hours is provided in Table 14.

Table 14. Percent Change of Urgency Episodes per 24 Hours at Weeks 1, 4, and 12 Relative to Baseline – Full Analysis Set (Subjects Reporting This Symptom at Baseline)

Percent Change of Urgency Episodes per 24 Hours	Placebo N=334	Tolterodine ER N=684	Fesoterodine N=679
Percent Change From Baseline to Week 1	**n=306**	**n=619**	**n=621**
Baseline mean (SD)	9.4 (4.2)	9.3 (3.7)	9.3 (3.9)
Week 1 mean (SD)	9.0 (4.4)	8.1 (4.2)	8.2 (4.4)
Percent change median (min, max)	-5.6 (-100, 271.4)	-12.5 (-100, 400)	-9.7 (-100, 485.7)
p-Value for treatment difference[a]			
Fesoterodine vs placebo	0.0004	-	-
Tolterodine ER vs placebo	0.0001	-	-
Fesoterodine vs tolterodine ER	Not done[b]	-	-
Percent Change From Baseline to Week 4	**n=311**	**n=631**	**n=627**
Baseline mean (SD)	9.4 (4.2)	9.3 (3.7)	9.3 (3.9)
Week 4 mean (SD)	8.2 (4.4)	6.9 (4.2)	6.8 (4.4)
Percent change median (min, max)	-11.4 (-100, 560)	-23.1 (-100, 233.3)	-26.9 (-100, 385.7)
p-Value for treatment difference[a]			
Fesoterodine vs placebo	<0.0001	-	-
Tolterodine ER vs placebo	<0.0001	-	-
Fesoterodine vs tolterodine ER	Not done[b]	-	-
Percent Change From Baseline to Week 12	**n=311**	**n=631**	**n=628**
Baseline mean (SD)	9.4 (4.2)	9.3 (3.7)	9.3 (3.9)
Week 12 mean (SD)	7.4 (4.8)	6.2 (4.3)	5.8 (4.5)
Percent change median (min, max)	-17.6 (-100, 560)	-30.8 (-100, 372.7)	-37.9 (-100, 385.7)
p-Value for treatment difference[a]			
Fesoterodine vs placebo	<0.0001	-	-
Tolterodine ER vs placebo	0.0001	-	-
Fesoterodine vs tolterodine ER	Not done[b]	-	-

ER = extended-release formulation; LOCF = last observation carried forward; min = minimum; max = maximum; N = number of subjects in the respective treatment group; n = number of subjects with baseline urgency episodes >0 per 24 hours and non-missing change from Baseline to the respective postbaseline value (Week 1, Week 4 [LOCF], or Week 12 [LOCF]); SD = standard deviation; vs = versus.

a. Based on a ranked analysis of covariance model with country and treatment as factors, and ranked baseline value as a covariate.

b. In accordance with a closed testing procedure, statistical testing for percent change was not performed since the corresponding numerical change result was not statistically significant.

The mean number of severe urgency episodes per 24 hours was comparable across treatment groups at Baseline (5.8 to 5.9 episodes per 24 hours), and decreased in all 3 treatment arms at Weeks 1, 4, and 12 (Table 15). The reductions were statistically significantly greater in the active treatment groups compared with the placebo group at all postbaseline time-points ($p<0.001$). At Week 12, the LSMean reduction was 3.0 episodes per 24 hours in the fesoterodine group versus 2.8 in the tolterodine ER group; the difference was not statistically significant ($p=0.1391$).

Table 15. Change in Mean Number of Severe Urgency Episodes per 24 Hours at Weeks 1, 4, and 12 Relative to Baseline – Full Analysis Set (Subjects Reporting This Symptom at Baseline)

Mean Number of Severe Urgency Episodes per 24 Hours	Placebo N=334	Tolterodine ER N=684	Fesoterodine N=679
Week 1	**n=306**	**n=618**	**n=618**
Baseline mean (SD)	5.8 (3.6)	5.9 (3.6)	5.8 (3.7)
Week 1 mean (SD)	5.5 (4.1)	4.6 (3.9)	4.6 (3.8)
Change from Baseline to Week 1			
LSMean (SE)	-0.4 (0.2)	-1.3 (0.2)	-1.2 (0.2)
95% CI for mean	-0.7, 0.1	-1.6, -1.1	-1.5, -0.9
p-Value[a]	0.0938	<0.0001	<0.0001
Treatment difference[b]	LSMean difference (SE)	95% CI	p-value
Fesoterodine vs placebo	-0.9 (0.2)	-1.3, -0.5	<0.0001
Tolterodine ER vs placebo	-1.0 (0.2)	-1.4, -0.6	<0.0001
Fesoterodine vs tolterodine ER	0.1 (0.2)	-0.2, 0.4	0.5581
Week 4	**n=311**	**n=630**	**n=624**
Baseline mean (SD)	5.7 (3.6)	5.9 (3.6)	5.9 (3.7)
Week 4 mean (SD)	4.5 (3.8)	3.6 (3.7)	3.3 (3.6)
Change from Baseline to Week 4			
LSMean (SE)	-1.2 (0.2)	-2.2 (0.2)	-2.4 (0.2)
95% CI for mean	-1.7, -0.8	-2.6, -2.0	-2.8, -2.2
p-Value[a]	<0.0001	<0.0001	<0.0001
Treatment difference[b]	LSMean difference (SE)	95% CI	p-value
Fesoterodine vs placebo	-1.2 (0.2)	-1.7, -0.8	<0.0001
Tolterodine ER vs placebo	-1.0 (0.2)	-1.4, -0.5	<0.0001
Fesoterodine vs tolterodine ER	-0.3 (0.2)	-0.6, 0.1	0.1510
Week 12	**n=311**	**n=630**	**n=625**
Baseline mean (SD)	5.7 (3.6)	5.9 (3.6)	5.9 (3.7)
Week 12 mean (SD)	3.8 (3.7)	3.0 (3.6)	2.7 (3.6)
Change from Baseline to Week 12			
LSMean (SE)	-1.9 (0.2)	-2.8 (0.2)	-3.0 (0.2)
95% CI for mean	-2.5,-1.5	-3.2, -2.6	-3.5, -2.9
p-Value[a]	<0.0001	<0.0001	<0.0001
Treatment difference[b]	LSMean difference (SE)	95% CI	p-value
Fesoterodine vs placebo	-1.1 (0.2)	-1.6, -0.7	<0.0001
Tolterodine ER vs placebo	-0.9 (0.2)	-1.3, -0.4	0.0001
Fesoterodine vs tolterodine ER	-0.3 (0.2)	-0.6, 0.1	0.1391

CI = confidence interval; ER = extended-release formulation; LOCF = last observation carried forward; LSMean = least square of the mean; N = number of subjects in the respective treatment group; n = number of subjects with baseline severe urgency episodes >0 per 24 and non-missing change from Baseline to the respective postbaseline value (Week 1, Week 4 [LOCF], or Week 12 [LOCF]); SD = standard deviation; SE = standard error; vs = versus.

a. Based on a paired t-test comparing baseline with postbaseline values.
b. Based on an analysis of covariance model with country and treatment as factors, and centered baseline value as a covariate.

The percent reductions from Baseline were statistically significantly greater in the active treatment groups compared with placebo at Weeks 1, 4 and 12 (p<0.001). At Week 12, the median percentage reduction from Baseline was 71.4% in the festerodine group versus 63.4% in the tolterodine ER group. No statistical test between fesoterodine and tolterodine ER was performed since the differences of the corresponding numerical changes were not statistically

significant. A summary of percent change in severe urgency episodes per 24 hours is provided in Table 16.

Table 16. Percent Change of Severe Urgency Episodes per 24 Hours at Weeks 1, 4, and 12 Relative to Baseline – Full Analysis Set (Subjects Reporting This Symptom at Baseline)

Percent Change of Severe Urgency Episodes per 24 Hours	Placebo N=334	Tolterodine ER N=684	Fesoterodine N=679
Percent Change From Baseline to Week 1	**n=306**	**n=618**	**n=618**
Baseline mean (SD)	5.8 (3.6)	5.9 (3.6)	5.8 (3.7)
Week 1 mean (SD)	5.5 (4.1)	4.6 (3.9)	4.6 (3.8)
Percent change median (min, max)	-9.4 (-100, 500)	-25.0 (-100, 775)	-25.0 (-100, 680)
p-Value for treatment difference[a]			
Fesoterodine vs placebo	<0.0001	-	-
Tolterodine ER vs placebo	<0.0001	-	-
Fesoterodine vs tolterodine ER	Not done[b]	-	-
Percent Change From Baseline to Week 4	**n=311**	**n=630**	**n=624**
Baseline mean (SD)	5.7 (3.6)	5.9 (3.6)	5.9 (3.7)
Week 4 mean (SD)	4.5 (3.8)	3.6 (3.7)	3.3 (3.6)
Percent change median (min, max)	-25.0 (-100, 866.7)	-45.8 (-100, 460)	-54.5 (-100, 550)
p-Value for treatment difference[a]			
Fesoterodine vs placebo	<0.0001	-	-
Tolterodine ER vs placebo	<0.0001	-	-
Fesoterodine vs tolterodine ER	Not done[b]	-	-
Percent Change From Baseline to Week 12	**n=311**	**n=630**	**n=625**
Baseline mean (SD)	5.7 (3.6)	5.9 (3.6)	5.9 (3.7)
Week 12 mean (SD)	3.8 (3.7)	3.0 (3.6)	2.7 (3.6)
Percent change median (min, max)	-48.0 (-100, 733.3)	-63.4 (-100, 412.5)	-71.4 (-100, 585.7)
p-Value for treatment difference[a]			
Fesoterodine vs placebo	<0.0001	-	-
Tolterodine ER vs placebo	0.0001	-	-
Fesoterodine vs tolterodine ER	Not done[b]	-	-

ER = extended-release formulation; LOCF = last observation carried forward; min = minimum; max = maximum; N = number of subjects in the respective treatment group; n = number of subjects with baseline severe urgency episodes >0 per 24 hours and non-missing change from Baseline to the respective postbaseline value (Week 1, Week 4 [LOCF], or Week 12 [LOCF]); SD = standard deviation; vs = versus.

a. Based on a ranked analysis of covariance model with country and treatment as factors, and ranked baseline value as a covariate.

b. In accordance with a closed testing procedure, statistical testing for percent change was not performed since the corresponding numerical change result was not statistically significant.

Mean USS rating per micturition was comparable across treatment groups at Baseline (rating 3.4), and decreased in all 3 treatment arms at Weeks 1, 4, and 12 (Table 17). The reductions were statistically significantly greater in the active treatment groups compared with the placebo group at all postbaseline time-points (p<0.0001). At Week 12, the LSMean reduction was 0.7 in the fesoterodine group versus 0.6 in the tolterodine ER group; the difference was statistically significant in favor of fesoterodine (p=0.0289).

Table 17. Change in Mean USS Rating per Micturition per 24 Hours at Weeks 1, 4, and 12 Relative to Baseline – Full Analysis Set

Mean USS Rating per Micturition per 24 Hours	Placebo N=334	Tolterodine ER N=684	Fesoterodine N=679
Week 1	**n=306**	**n=619**	**n=621**
Baseline mean (SD)	3.4 (0.6)	3.4 (0.6)	3.4 (0.6)
Week 1 mean (SD)	3.4 (0.7)	3.2 (0.7)	3.2 (0.7)
Change from Baseline to Week 1			
LSMean (SE)	-0.1 (0)	-0.2 (0)	-0.2 (0)
95% CI for mean	-0.1 (0)	-0.3, -0.2	-0.3, -0.2
p-Value[a]	0.0158	<0.0001	<0.0001
Treatment difference	LSMean difference (SE)	95% CI	p-value
Fesoterodine vs placebo	-0.2 (0)	-0.2, -0.1	<0.0001
Tolterodine ER vs placebo	-0.2 (0)	-0.2, -0.1	<0.0001
Fesoterodine vs tolterodine ER	0 (0)	-0.0, 0.1	0.5972
Week 4	**n=311**	**n=631**	**n=627**
Baseline mean (SD)	3.4 (0.6)	3.4 (0.6)	3.4 (0.6)
Week 4 mean (SD)	3.2 (0.7)	3.0 (0.8)	3.0 (0.8)
Change from Baseline to Week 4			
LSMean (SE)	-0.2 (0)	-0.4 (0)	-0.5 (0)
95% CI for mean	-0.3, -0.1	-0.5, -0.4	-0.5, -0.4
p-Value[a]	<0.0001	<0.0001	<0.0001
Treatment difference[b]	LSMean difference (SE)	95% CI	p-value
Fesoterodine vs placebo	-0.3 (0)	-0.4, -0.2	<0.0001
Tolterodine ER vs placebo	-0.2 (0)	-0.3, -0.1	<0.0001
Fesoterodine vs tolterodine ER	-0.1 (0)	-0.1, 0	0.1267
Week 12	**n=311**	**n=631**	**n=628**
Baseline mean (SD)	3.4 (0.6)	3.4 (0.6)	3.4 (0.6)
Week 12 mean (SD)	3.0 (0.8)	2.8 (0.8)	2.8 (0.8)
Change from Baseline to Week 12			
LSMean (SE)	-0.4 (0)	-0.6 (0)	-0.7 (0)
95% CI for mean	-0.5, -0.3	-0.7, -0.5	-0.8, -0.6
p-Value[a]	<0.0001	<0.0001	<0.0001
Treatment difference[b]	LSMean difference (SE)	95% CI	p-value
Fesoterodine vs placebo	-0.3 (0.1)	-0.4, -0.2	<0.0001
Tolterodine ER vs placebo	-0.2 (0.1)	-0.3, -0.1	<0.0001
Fesoterodine vs tolterodine ER	-0.1 (0)	-0.2, -0	0.0289

CI = confidence interval; ER = extended-release formulation; LOCF = last observation carried forward; LSMean = least square of the mean; N = number of subjects in the respective treatment group; n = number of subjects with non-missing numerical change from Baseline to the respective postbaseline value (Week 1, Week 4 [LOCF], or Week 12 [LOCF]); SD = standard deviation; SE = standard error; USS = Urinary Sensation Scale; vs = versus.

a. Based on a paired t-test comparing baseline with postbaseline values.
b. Based on an analysis of covariance model with country and treatment as factors, and centered baseline value as a covariate.

The Frequency-Urgency Sum per 24 hours was comparable across the treatment groups at Baseline (score 40.4 to 41.0) and decreased in all 3 treatment arms at Weeks 1, 4, and 12 (Table 18). The reductions were statistically significantly greater in the active treatment groups compared with placebo at all postbaseline time-points (p<0.0001). At Week 12, the LSMean reduction was 13.2 in the fesoterodine group versus 12.1 in the tolterodine ER group; the difference was not statistically significant (p=0.1047).

Table 18. Change in Frequency-Urgency Sum per 24 Hours at Weeks 1, 4, and 12 Relative to Baseline – Full Analysis Set

Frequency-Urgency Sum per 24 Hours	Placebo N=334	Tolterodine ER N=684	Fesoterodine N=679
Week 1	**n=306**	**n=619**	**n=621**
Baseline mean (SD)	41.0 (14.4)	40.5 (13.7)	40.4 (13.5)
Week 1 mean (SD)	38.9 (15.7)	35.2 (15)	35.3 (15)
Change from Baseline to Week 1			
LSMean (SE)	-2.4 (0.7)	-5.7 (0.5)	-5.5 (0.5)
95% CI for mean	-3.2, -1	-6.2, -4.4	-6.0, -4.2
p-Value[a]	0.0003	<0.0001	<0.0001
Treatment difference[b]	LSMean difference (SE)	95% CI	p-value
Fesoterodine vs placebo	-3.1 (0.7)	-4.5, -1.7	<0.0001
Tolterodine ER vs placebo	-3.3 (0.7)	-4.7, -1.9	<0.0001
Fesoterodine vs tolterodine ER	0.2 (0.6)	-1, 1.4	0.7288
Week 4	**n=311**	**n=631**	**n=627**
Baseline mean (SD)	41.0 (14.3)	40.5 (13.8)	40.4 (13.4)
Week 4 mean (SD)	35.2 (15)	30.9 (14.5)	30.1 (14.1)
Change from Baseline to Week 4			
LSMean (SE)	-5.7 (0.8)	-9.7 (0.6)	-10.5 (0.6)
95% CI for mean	-7.2, -4.4	-10.6, -8.6	-11.3, -9.3
p-Value[a]	<0.0001	<0.0001	<0.0001
Treatment difference[b]	LSMean difference (SE)	95% CI	p-value
Fesoterodine vs placebo	-4.7 (0.8)	-6.3, -3.2	<0.0001
Tolterodine ER vs placebo	-4.0 (0.8)	-5.5, -2.4	<0.0001
Fesoterodine vs tolterodine ER	-0.7 (0.6)	-2, 0.5	0.2473
Week 12	**n=311**	**n=631**	**n=628**
Baseline mean (SD)	41.0 (14.3)	40.5 (13.8)	40.4 (13.4)
Week 12 mean (SD)	32.4 (15.4)	28.4 (14.1)	27.3 (14.4)
Change from Baseline to Week 12			
LSMean (SE)	-8.2 (0.8)	-12.1 (0.6)	-13.2 (0.6)
95% CI for mean	-10.1, -7	-13.1, -11	-14.2, -12.1
p-Value[a]	<0.0001	<0.0001	<0.0001
Treatment difference[b]	LSMean difference (SE)	95% CI	p-value
Fesoterodine vs placebo	-4.9 (0.8)	-6.6, -3.3	<0.0001
Tolterodine ER vs placebo	-3.8 (0.8)	-5.5, -2.2	<0.0001
Fesoterodine vs tolterodine ER	-1.1 (0.7)	-2.4, 0.2	0.1047

CI = confidence interval; ER = extended-release formulation; LOCF = last observation carried forward; LSMean = least square of the mean; N = number of subjects in the respective treatment group; n = number of subjects with non-missing numerical change from Baseline to the respective postbaseline value (Week 1, Week 4 [LOCF], or Week 12 [LOCF]); SD = standard deviation; SE = standard error; USS = Urinary Sensation Scale; vs = versus.

a. Based on a paired t-test comparing baseline with postbaseline values.
b. Based on an analysis of covariance model with country and treatment as factors, and centered baseline value as a covariate.

The distributions of the 6-point scale of PPBC were comparable across treatment groups at Baseline, eg, most subjects (88.9% to 90.5%) in every treatment group reported a score of 4 to 6 (moderate problems to many severe problems). The scores at Weeks 1, 4, and 12 were improved in all 3 treatment arms, ie, more subjects presented with score of 1 to 3 and less with score of 4 to 6, compared with Baseline.

In the 4-category analysis, individual responses were classified as 4 categories, ≥2 points improvement, 1 point improvement, no change, deterioration. The composition of the categorical changes of PPBC from Baseline was statistically significantly in favor of fesoterodine versus placebo at each postbaseline time-point (p<0.05; Table 19).

Table 19. Change in Patient Perception of Bladder Condition at Weeks 1, 4, and 12 Relative to Baseline (4-Category Analyses) – Full Analysis Set

PPBC Category[a]	Number (%)[b] of Subjects		
	Placebo N=334	Tolterodine ER N=684	Fesoterodine N=679
Change From Baseline to Week 1	**n=309**	**n=625**	**n=623**
4-category analysis			
>2 points improvement	32 (10.4)	79 (12.6)	102 (16.4)
1 point improvement	94 (30.4)	181 (29)	186 (29.9)
No change	147 (47.6)	306 (49)	286 (45.9)
Deterioration	36 (11.7)	59 (9.4)	49 (7.9)
p-Value, fesoterodine vs placebo[c]	0.0143		
Change From Baseline to Week 4	**n=313**	**n=632**	**n=629**
4-category analysis			
>2 points improvement	57 (18.2)	169 (26.7)	196 (31.2)
1 point improvement	95 (30.4)	201 (31.8)	224 (35.6)
No change	127 (40.6)	203 (32.1)	176 (28)
Deterioration	34 (10.9)	59 (9.3)	33 (5.2)
p-Value, fesoterodine vs placebo[c]	<0.0001	-	-
Change From Baseline to Week 12	**n=313**	**n=632**	**n=630**
4-category analysis			
>2 points improvement	67 (21.4)	210 (33.2)	254 (40.3)
1 point improvement	102 (32.6)	189 (29.9)	198 (31.4)
No change	111 (35.5)	171 (27.1)	148 (23.5)
Deterioration	33 (10.5)	62 (9.8)	30 (4.8)
p-Value, fesoterodine vs placebo[c]	<0.0001	-	-

ER = extended-release formulation; LOCF = last observation carried forward; N = number of subjects in the respective treatment group; n = number of subjects with non-missing numerical change from Baseline to the respective postbaseline value (Week 1, Week 4 [LOCF], or Week 12 [LOCF]); PPBC = Patient Perception of Bladder Condition; vs = versus.

a. ≥2 points improvement = score change is negative in magnitude of 2 or more; 1 point improvement = score change is negative in magnitude of 1; no change = score change is 0; deterioration = score change is positive.
b. Based on n.
c. Based on Cochran-Mantel-Haenszel test with modified ridit scoring and stratified by country.

The distribution of the 3-point scale of UPS at Baseline were comparable between the 2 active treatment groups, eg, about 36% of subjects in each group responded with score 1 (not able to hold urine). The raw score distribution was a slightly milder in the placebo group (42% of subjects with score 1). Compared with baseline scores were improved, eg, less subjects with score 1, in all 3 treatment arms at Weeks 1, 4, and 12 (Table 20).

In the 3-category analysis, individual responses were classified as 3 categories, ie improvement, no change, and deterioration. The distribution of the categorical changes of UPS from Baseline was statistically significantly in favor of fesoterodine compared to placebo at Week 4 (p=0.0017) and Week 12 (p=0.0008), but not at Week 1 (p=0.0773).

Table 20. Change in Urgency Perception Scale at Weeks 1, 4, and 12 Relative to Baseline (3-Category Analysis) – Full Analysis Set

UPS Score[a]	Number (%)[b] of Subjects		
	Placebo N=334	Tolterodine ER N=684	Fesoterodine N=679
Change From Baseline to Week 1	**n=309**	**n=627**	**n=624**
Improvement	68 (22)	162 (25.8)	171 (27.4)
No change	218 (70.6)	438 (69.9)	413 (66.2)
Deterioration	23 (7.4)	27 (4.3)	40 (6.4)
p-Value, fesoterodine vs placebo[c]	0.0773	-	-
Change From Baseline to Week 4	**n=313**	**n=633**	**n=629**
Improvement	98 (31.3)	238 (37.6)	256 (40.7)
No change	194 (62)	362 (57.2)	348 (55.3)
Deterioration	21 (6.7)	33 (5.2)	25 (4)
p-Value, fesoterodine vs placebo[c]	0.0017	-	-
Change From Baseline to Week 12	**n=313**	**n=633**	**n=630**
Improvement	112 (35.8)	254 (40.1)	291 (46.2)
No change	181 (57.8)	344 (54.3)	314 (49.8)
Deterioration	20 (6.4)	35 (5.5)	25 (4)
p-Value, fesoterodine vs placebo[c]	0.0008	-	-

Deterioration = negative score change; ER = extended-release formulation; improvement = positive score change; LOCF = last observation carried forward; N = number of subjects in the respective treatment group; n = number of subjects with non-missing numerical change from Baseline to the respective postbaseline value (Week 1, Week 4 [LOCF], or Week 12 [LOCF]), no change = score change is 0; SAP = statistical analysis plan; UPS = Urgency Perception Scale; vs = versus.

a. Formerly known as the Patient Perception of Urgency Scale, as used in the study protocol and SAP.
b. Based on n.
c. Based on Cochran-Mantel-Haenszel test with modified ridit scoring and stratified by country.

The scores of the Symptom Bother Scale and the HRQL Scale and its domains were comparable across the treatment groups at Baseline and improved in all 3 treatment arms from Baseline at Week 12. The improvement in each scale and domain in the fesoterodine group was statistically significantly greater compared with placebo ($p<0.001$). In addition, a numerically greater improvement on each scale and domain at Week 12 relative to Baseline was observed when comparing fesoterodine versus tolterodine ER and when comparing tolterodine versus placebo. However, the statistical tests were not pre-specified therefore not reported to verify the observed difference between these groups. Change in OAB-q at Week 12 relative to Baseline is summarized in Table 21.

Table 21. Change in Overactive Bladder Questionnaire at Week 12 Relative to Baseline – Full Analysis Set

HRQL Component	Placebo N=334	Tolterodine ER N=684	Fesoterodine N=679
HRQL Concern Domain	**n=289**	**n=589**	**n=572**
Baseline mean (SD)	52.4 (25)	51.5 (25.7)	54.6 (25.3)
Week 12 mean (SD)	67.9 (26.4)	73.1 (25.3)	77.9 (22.6)
Change from Baseline to Week 12			
LSMean (SE)	13.4 (1.5)	19.3 (1.1)	22.6 (1.2)
95% CI for mean	12.6, 18.5	19.4, 23.8	21.3, 25.3
p-Value[a]	<0.0001	<0.0001	<0.0001
Treatment difference[b]	LSMean difference (SE)	95% CI	p-value
Fesoterodine vs placebo	9.2 (1.6)	6.2, 12.3	<0.0001
HRQL Coping Domain	**n=289**	**n=589**	**n=572**
Baseline mean (SD)	48.2 (26.3)	48.0 (26.2)	52.2 (26.1)
Week 12 mean (SD)	64.8 (28.2)	69.0 (26.9)	75.2 (23.3)
Change from Baseline to Week 12			
LSMean (SE)	14.0 (1.5)	18.5 (1.2)	22.6 (1.2)
95% CI for mean	13.6, 19.6	18.9, 23.1	20.9, 25
p-Value[a]	<0.0001	<0.0001	<0.0001
Treatment difference[b]	LSMean difference (SE)	95% CI	p-value
Fesoterodine vs placebo	8.6 (1.6)	5.5, 11.7	<0.0001
HRQL Sleep Domain	**n=289**	**n=589**	**n=572**
Baseline mean (SD)	55.0 (26.1)	54.4 (26.5)	55.5 (25.4)
Week 12 mean (SD)	67.9 (25.4)	70.3 (24.3)	73.0 (23.2)
Change from Baseline to Week 12			
LSMean (SE)	12.2 (1.4)	15.1 (1.1)	17.3 (1.1)
95% CI for mean	9.9, 15.7	13.9, 18	15.5, 19.5
p-Value[a]	<0.0001	<0.0001	<0.0001
Treatment difference[b]	LSMean difference (SE)	95% CI	p-value
Fesoterodine vs placebo	5.0 (1.5)	2.1, 8.0	0.0008
HRQL Social Interaction Domain	**n=289**	**n=588**	**n=572**
Baseline mean (SD)	74.4 (24.4)	74.6 (23.6)	76.6 (23.1)
Week 12 mean (SD)	83.0 (20.8)	85.5 (20.2)	88.7 (17.6)
Change from Baseline to Week 12			
LSMean (SE)	6.8 (1.1)	9.4 (0.9)	11.6 (0.9)
95% CI for mean	6.1, 11.1	9.3, 12.6	10.4, 13.7
p-Value[a]	<0.0001	<0.0001	<0.0001
Treatment difference[b]	LSMean difference (SE)	95% CI	p-value
Fesoterodine vs placebo	4.8 (1.2)	2.5, 7.1	<0.0001
HRQL Scale Score Total	**n=289**	**n=588**	**n=572**
Baseline mean (SD)	56.0 (22.5)	55.6 (22.2)	58.4 (22.1)
Week 12 mean (SD)	69.9 (23.5)	73.8 (22.2)	78.2 (19.9)
Change from Baseline to Week 12			
LSMean (SE)	12.0 (1.3)	16.3 (1)	19.3 (1)
95% CI for mean	11.3, 16.5	16.4, 20	18.0, 21.5
p-Value[a]	<0.0001	<0.0001	<0.0001
Treatment difference[b]	LSMean difference (SE)	95% CI	p-value
Fesoterodine vs placebo	7.3 (1.3)	4.6, 9.9	<0.0001

Table 21. Change in Overactive Bladder Questionnaire at Week 12 Relative to Baseline – Full Analysis Set

HRQL Component	Placebo N=334	Tolterodine ER N=684	Fesoterodine N=679
Symptom Bother Score	**n=289**	**n=589**	**n=571**
Baseline mean (SD)	58.9 (19)	58.6 (19.5)	57.5 (20.3)
Week 12 mean (SD)	40.7 (23.4)	34.8 (22.7)	29.7 (20.3)
Change from Baseline to Week 12			
LSMean (SE)	-16.3 (1.4)	-22.5 (1.1)	-27.1 (1.1)
95% CI for mean	-21.0, -15.4	-25.8, -21.7	-29.7, -25.8
p-Value[a]	<0.0001	<0.0001	<0.0001
Treatment difference[b]	LSMean difference (SE)	95% CI	p-value
Fesoterodine vs placebo	-10.8 (1.5)	-13.7, -7.9	<0.0001

CI = confidence interval; ER = extended-release formulation; HRQL = health-related quality of life; LSMean = least square of the mean; N = number of subjects in the respective treatment group; n = number of subjects with non-missing numerical change from Baseline to Week 12; SD = standard deviation; SE = standard error; vs = versus.

a. Based on a paired t-test comparing baseline with postbaseline values.
b. Based on an analysis of covariance model with country and treatment as factors, and centered baseline value as a covariate.

Safety Results:

A summary of nonserious treatment-emergent adverse events (TEAEs) is provided in Table 22.

Table 22. Treatment-Emergent Non Serious Adverse Events (All Causalities) for Events Having a Frequency Rate ≥5%

Number (%) of Subjects with AEs by SOC MedDRA Preferred Term	Placebo n (%)	Tolterodine ER n (%)	Fesoterodine n (%)
Number (%) of subjects: evaluable for AEs	334	684	679
Number (%) of subjects: with AEs	34 (10.2)	141 (20.6)	226 (33.3)
Gastrointestinal Disorders	28 (8.4)	128 (18.7)	205 (30.2)
Constipation	10 (3)	28 (4.1)	37 (5.4)
Dry mouth	20 (6)	112 (16.4)	189 (27.8)
Nervous system disorders	8 (2.4)	23 (3.4)	38 (5.6)
Headache	8 (2.4)	23 (3.4)	38 (5.6)

Subjects were only counted once per treatment for each row.
Included data up to 7 days after last dose of study drug.
MedDRA (version 11.1) coding dictionary applied.
AEs = adverse events; MedDRA = Medical Dictionary for Regulatory Activities; n= number of subjects with AEs; SOC = system organ class.

The TEAEs considered treatment-related by the Investigator for events having a frequency rate ≥5% in every treatment group are summarized in Table 23.

Table 23. Treatment-Emergent Adverse Events by Body System (Treatment-Related) or Events Having a Frequency Rate ≥5% - Safety Analysis Set

Number (%) of Subjects with AEs by SOC MedDRA / Preferred Term	Placebo n (%)	Tolterodine ER n (%)	Fesoterodine n (%)
Number (%) of subjects: evaluable for AEs	334	684	679
Gastrointestinal disorders	37 (11.1)	137 (20)	222 (32.7)
Constipation	8 (2.4)	21 (3.1)	35 (5.2)
Dry mouth	20 (6)	108 (15.8)	188 (27.7)

Subjects were counted only once per treatment in each row. For the TESS algorithm any missing severities were imputed as severe unless the subject experienced another occurrence of the same event in a given treatment for which severity was recorded.
In this case, the reported severity was summarized. Missing baseline severities were imputed as mild.
Included data up to 7 days after last dose of study drug.
MedDRA (version 11.1) coding dictionary applied.
AEs and SAEs are not separated out in this table.
AEs = adverse events; MedDRA = Medical Dictionary for Regulatory Activities; n = number of subjects with AEs; SAEs = serious adverse events; SOC = system organ class.

SAEs are summarized in Table 24.

Table 24. Treatment-Emergent Serious Adverse Events (All Causalities)

Number (%) of Subjects with AEs by: SOC MedDRA / Preferred Term	Placebo n (%)	Tolterodine ER n (%)	Fesoterodine n (%)
Number (%) of Subjects: evaluable for AEs	334	684	679
Number (%) of Subjects: with AEs	8 (2.4)	9 (1.3)	15 (2.2)
Blood and lymphatic system disorders	0	0	1 (0.1)
Iron deficiency anaemia	0	0	1 (0.1)
Cardiac disorders	0	0	2 (0.3)
Hypertensive heart disease	0	0	1 (0.1)
Myocardial ischaemia	0	0	1 (0.1)
Gastrointestinal disorders	1 (0.3)	0	2 (0.3)
Abdominal pain	0	0	1 (0.1)
Appendicitis perforated	0	0	1 (0.1)
Nausea	1 (0.3)	0	0
Rectal haemorrhage	0	0	1 (0.1)
Vomiting	1 (0.3)	0	0
General disorders and administration site conditions	0	1 (0.1)	0
Chest pain	0	1 (0.1)	0
Hepatobiliary disorders	0	1 (0.1)	0
Biliary colic	0	1 (0.1)	0
Infections and infestations	1 (0.3)	2 (0.3)	1 (0.1)
Abdominal wall abscess	1 (0.3)	0	0
Bronchiectasis	0	0	1 (0.1)
Cystitis	0	1 (0.1)	0
Herpes zoster	0	1 (0.1)	0
Injury, poisoning and procedural complications	2 (0.6)	1 (0.1)	2 (0.3)
Hand fracture	1 (0.3)	0	0
Head injury	0	1 (0.1)	0
Seroma	1 (0.3)	0	0
Traumatic brain injury	0	0	1 (0.1)
Upper limb fracture	0	0	1 (0.1)
Musculoskeletal and connective tissue disorders	1 (0.3)	1 (0.1)	1 (0.1)
Cervical spinal stenosis	1 (0.3)	0	0
Intervertebral disc protrusion	0	1 (0.1)	1 (0.1)
Musculoskeletal pain	1 (0.3)	0	0
Pain in extremity	1 (0.3)	0	0
Spinal column stenosis	1 (0.3)	0	0
Neoplasms benign, malignant and unspecified (inclusive cysts and polyps)	2 (0.6)	2 (0.3)	2 (0.3)
Breast cancer	0	1 (0.1)	0
Hepatic neoplasm malignant	0	0	1 (0.1)
Lung cancer metastatic	1 (0.3)	0	0
Lymphoma	0	1 (0.1)	0
Neoplasm malignant	1 (0.3)	0	0
Prostate cancer	0	0	1 (0.1)
Skin cancer	1 (0.3)	0	0
Nervous system disorders	2 (0.6)	0	1 (0.1)
Dizziness	1 (0.3)	0	0
Haemorrhage intracranial	0	0	1 (0.1)
Vertebrobasilar insufficiency	1 (0.3)	0	0

Table 24. Treatment-Emergent Serious Adverse Events (All Causalities)

Number (%) of Subjects with AEs by: SOC MedDRA / Preferred Term	Placebo n (%)	Tolterodine ER n (%)	Fesoterodine n (%)
Psychiatric disorders	1 (0.3)	0	1 (0.1)
Mental status changes	1 (0.3)	0	0
Suicidal behaviour	0	0	1 (0.1)
Renal and urinary disorders	0	0	1 (0.1)
Urinary incontinence	0	0	1 (0.1)
Reproductive system and breast disorders	0	1 (0.1)	1 (0.1)
Breast mass	0	1 (0.1)	0
Uterine haemorrhage	0	0	1 (0.1)
Respiratory, thoracic and mediastinal disorders	1 (0.3)	1 (0.1)	0
Asthma	1 (0.3)	0	0
Dyspnoea exertional	0	1 (0.1)	0
Vascular disorders	1 (0.3)	0	0
Arteriosclerosis	1 (0.3)	0	0

Subjects were only counted once per treatment for each row.
Included data up to 7 days after last dose of study drug.
MedDRA (version 11.1) coding dictionary applied.
MedDRA = Medical Dictionary for Regulatory Activities; n = number of subjects with SAEs; SAEs = serious adverse events; SOC = system organ class.

TEAE that occurred during the double-blind treatment period and led to subject discontinuation from the study are summarized in Table 25.

Table 25. Most Frequent Treatment-Emergent Adverse Events That led to Permanent Discontinuation – Safety Analysis Set

MEdDRA Preferred Term[a,b,c]	Number (%) of Subjects					
	Placebo N=334		Tolterodine ER N=684		Fesoterodine N=679	
	All Causality	Treatment Related	All Causality	Treatment Related	All Causality	Treatment Related
Subjects evaluable for TEAEs	334		684		679	
Subjects discontinued from the study due to TEAE	6 (1.8%)	3 (0.9%)	28 (4.1%)	19 (2.8%)	42 (6.2%)[d]	33 (4.9%)
Subjects discontinued from the study due to severe TEAE	3 (0.9%)	1 (0.3%)	10 (1.5%)	6 (0.9%)	14 (2.1%)	12 (1.8%)
Subjects discontinued from the study due to TE SAE	1 (0.3%)	0	5 (0.7 %)	0	2 (0.3%)	0
Most frequent TEAEs that led to permanent discontinuation						
Dry mouth	1 (0.3)	1 (0.3)	6 (0.9)	6 (0.9)	14 (2.1)	14 (2.1)
Headache	0	0	1 (0.1)	1 (0.1)	7 (1.0)	7 (1.0)
Constipation	2 (0.6)	2 (0.6)	2 (0.3)	1 (0.1)	3 (0.4)	3 (0.4)
Vision blurred	0	0	1 (0.1)	1 (0.1)	3 (0.4)	3 (0.4)
Diarrhoea	0	0	0	0	3 (0.4)	2 (0.3)
Abdominal distension	0	0	0	0	2 (0.3)	2 (0.3)
Abdominal pain	0	0	0	0	2 (0.3)	2 (0.3)
Dizziness	1 (0.3)	0	1 (0.1)	1 (0.1)	2 (0.3)	2 (0.3)
Urinary tract infection	0	0	0	0	2 (0.3)	0
Hypertension	0	0	2 (0.3)	2 (0.3)	1 (0.1)	0
Anxiety	0	0	2 (0.3)	2 (0.3)	0	0
Micturition urgency	0	0	2 (0.3)	2 (0.3)	0	0

AEs and SAEs are not separated out in this table.
ER = extended-release formulation, MedDRA = Medical Dictionary for Regulatory Activities (version 11.1), N = number of subjects in the respective treatment group, TEAE = treatment-emergent adverse event (includes data up to 7 days after last dose of study drug), TE SAE = treatment-emergent serious adverse event.

a. Table includes only MedDRA preferred terms that led to discontinuation in at least 2 subjects in either active treatment group.
b. Sorted by descending frequency by TEAEs in the fesoterodine group (all causality).
c. Treatment discontinuation could be attributed to a single TEAE or to multiple events. Therefore, an individual subject may be counted more than once across the individual TEAEs.
d. Two subjects in the fesoterodine group were excluded as their TEAEs leading to discontinuation started prior to first administration of study drug.

The majority of TEAE-caused discontinuations were due to mild to moderate TEAEs. About one third of TEAE-caused discontinuations were due to severe TEAEs. The majority of these were treatment-related.

Few TEAE-caused discontinuations were due to treatment-emergent SAEs in any of the treatment groups. None of them were treatment-related.

There were no reports of dose reduction due to TEAEs. Temporary discontinuations of the study drug due to TEAEs are summarized in Table 26.

None of the temporary discontinuations of study drug caused by severe and/or serious TEAEs in the fesoterodine group were treatment-related and study treatments were resumed after improvements in those TEAEs.

Dyspepsia was the only TEAE leading to more than 1 case of temporary discontinuations of study drug in any treatment group. There were 2 subjects (0.3%) in the fesoterodine group who temporarily discontinued study treatment due to treatment-related mild dyspepsia.

Table 26. Dose Temporary Discontinuations Due to Treatment-Emergent Adverse Events – Safety Analysis Set

Variable	Number (%) of Subjects					
	Placebo N=334		Tolterodine ER N=684		Fesoterodine N=679	
	All Causality	Treatment Related	All Causality	Treatment Related	All Causality	Treatment Related
Subjects with temporary discontinuations due to TEAE[a]	5 (1.5%)	2 (0.6%)	5 (0.7%)	3 (0.4%)	10 (1.5%)	5 (0.7%)
Subjects with temporary discontinuations due to severe TEAE[a]	0	0	0	0	4 (0.6%)	0
Subjects with dose temporary discontinuations due to TE SAE[a]	0	0	0	0	3 (0.4%)	0

AEs and SAEs are not separated out in this table.
AEs = adverse events; ER = extended-release formulation, N = number of subjects in the respective treatment group, SAE = serious adverse events; TEAE = treatment-emergent AE (included data up to 7 days after last dose of study drug), TE SAE = treatment-emergent serious adverse event.
a. Calculated by author.

The treatment-emergent non-fatal SAEs were reported by 1.8%, 1.3%, and 2.1% of subjects in placebo, tolterodine ER and festerodine group, respectively. No SAE was reported by more than 1 subject in any treatment group.

Only 2 SAEs (iron deficiency anemia and urinary retention) in the fesoterodine group were considered by the investigators as treatment-related. Table 27 lists all SAEs for this study.

Table 27. Serious Adverse Events

Serial Number	SAE (MedDRA Preferred Term)	Dose at SAE Onset	SAE Start Day[a]	Drug Stop Day[a]	Action Taken Regarding Study Drug	Investigator Causality	Outcome at Last Data Entry
Placebo							
1	Musculoskeletal pain	N/A	6	33	No action taken	Not related	Recovered
	Pain in extremity	N/A	6	33	No action taken	Not related	Recovered
	Cervical spinal stenosis	N/A	7	33	No action taken	Not related	Recovered
	Spinal column stenosis	N/A	7	33	No action taken	Not related	Recovered
	Seroma	N/A	16	33	No action taken	Not related	Recovered
2	Abdominal wall abscess	N/A	58	84	No action taken	Not related	Recovered
3	Lung cancer metastatic	N/A	67	66	Permanently disc	Not related	Death
4	Arteriosclerosis	N/A	76	76	Permanently disc	Not related	Death
	Asthma	N/A	76	76	Permanently disc[b]	Not related	Death
5	Mental status changes	N/A	61	60	Permanently disc	Not related	Recovered
	Vomiting	N/A	61	60	Permanently disc	Not related	Recovered
	Nausea	N/A	61	60	Permanently disc	Not related	Recovered
	Dizziness	N/A	67	60	Permanently disc[b]	Not related	Recovered
	Mental status changes	N/A	67	60	Permanently disc[b]	Not related	Recovered
6	Skin cancer	N/A	106	105	No action taken	Not related	Recovered
7	Upper limb fracture[c]	N/A	25	88	No action taken	Not related	Recovered
8	Vertigo[d]	N/A	6	66	No action taken	Not related	Recovered
Tolterodine ER							
1	Herpes zoster	4 mg	50	91	No action taken	Not related	Recovered
2	Chest pain[e]	4 mg	35	35	Permanently disc	Not related	Recovered
	Chest discomfort[e]	4 mg	35	35	Permanently disc	Not related	Recovered
	Dyspnoea exertional	4 mg	35	35	Permanently disc	Not related	Recovered
3	Breast cancer	4 mg	5	28	Permanently disc	Not related	Ongoing
4	Intervertebral disc protrusion	4 mg	17	91	No action taken	Not related	Recovered
5	Breast mass	4 mg	67	84	No action taken	Not related	Recovered[f]
6	Lymphoma	4 mg	9	16	Permanently disc	Not related	Ongoing
7	Head injury	4 mg	3	21	Permanently disc	Not related	Recovered
8	Biliary colic	4 mg	47	54	Permanently disc	Not related	Recovered
9	Cystitis	4 mg	34	85	No action taken	Not related	Recovered
Fesoterodine							
1	Colitis[g]	8 mg	45	90	No action taken	Not related	Recovered
2	Haemorrhage intracranial	8 mg	53	84	Stopped temporarily	Not related	Recovered
3	Angina pectoris[h]	4 mg	8	8	Permanently disc	Not related	Recovered
4	Urinary retention[i]	4 mg	34	6	Permanently disc	Related	Recovered
5	Suicide attempt[j]	8 mg	84	94	No action taken	Not related	Recovered

Table 27. Serious Adverse Events

Serial Number	SAE (MedDRA Preferred Term)	Dose at SAE Onset	SAE Start Day[a]	Drug Stop Day[a]	Action Taken Regarding Study Drug	Investigator Causality	Outcome at Last Data Entry
6	Upper limb fracture	8 mg	62	91	No action taken	Not related	Recovered
7	Uterine haemorrhage	8 mg	60	75	No action taken	Not related	Recovered
8	Hypertensive heart disease	8 mg	56	77	No action taken	Not related	Ongoing
9	Iron deficiency anaemia	8 mg	57	88	No action taken	Related	Recovered
10	Hepatic neoplasm malignant	8 mg	9	99	No action taken	Not Related	Recovered
11	Bronchiectasis	8 mg	14	40	Stopped temporarily	Not Related	Recovered
12	Appendicitis perforated	4 mg	6	84	No action taken	Not Related	Recovered
13	Prostate cancer	8 mg	28	75	No action taken	Not Related	Ongoing
14	Death, cause unknown[i]	8 mg	111	97	No action taken	Not Related	Death
15	Intervertebral disc protrusion	8 mg	12	80	Stopped temporarily	Not Related	Recovered
16	Hiatus hernia[i,k]	8 mg	93	79	No action taken	Not Related	Recovered
17	Urinary incontinence[i]	8 mg	68	66	No action taken	Not Related	Recovered
18	Brain injury[l]	8 mg	79	79	Permanenty disc.	Not Related	Death

Disc. = discontinued, ER = extended-release formulation, MedDRA = Medical Dictionary for Regulatory Activities (version 11.1), N/A = not applicable, SAE = serious adverse event.

a. Day relative to start of study treatment; first day of study treatment = Day 1.
b. 'No action taken' in the study database.
c. 'Hand fracture' in the study database.
d. 'Vertebrobasilar insufficiency in the study database.
e. Only 'chest pain' in the study database based on Investigator term 'chest pain pressure'.
f. 'Still present' in the study database.
g. 'Abdominal pain' and 'rectal hemorrhage' (which were caused by colitis) in the study database.
h. 'Myocardial ischemia' in the study database.
i. Post-treatment SAE, ie, SAE occurred more than 7 days after last dose of study drug. All other listed SAEs were treatment-emergent, ie, SAE occurred up to 7 days after last dose of study drug.
j. 'Suicidal behavior' in the study database.
k. Not reported in the study database, as the SAE was a post-treatment event.
l. 'Traumatic brain injury' in the study database.

There were 4 deaths, 2 in the placebo group and 2 in the fesoterodine group; none was related to the study drug.

There were no clinically meaningful findings in either the fesoterodine or the tolterodine ER group in laboratory tests, vital signs, physical examinations, and ECGs.

CONCLUSIONS: This was a 12-week, randomized, double-blind, double-dummy, placebo-controlled study to compare the efficacy of fesoterodine to placebo and tolterodine ER in subjects with OAB.

- Fesoterodine and tolterodine ER demonstrated efficacy for treating OAB. At Week 12, both drugs were statistically significantly better than placebo on key bladder diary efficacy measures including those for UUI, micturition and urgency. Fesoterodine also showed statistically significantly greater improvements in all PRO measures, including HRQL domains of the OAB-q, over placebo.

- Fesoterodine 8 mg showed superior efficacy over tolterodine ER 4 mg on the primary endpoint, ie, statistically significantly greater reduction in UUI episodes from Baseline to Week 12, which was supported by a greater diary-dry rate at Week 12 (post-hoc analysis).

    - Fesoterodine 8 mg also showed statistically significantly greater effect than tolterodine ER 4 mg on the secondary diary endpoints of increase in mean voided volume per micturition and decrease in mean USS rating from Baseline to Week 12.

    - Fesoterodine 8 mg did not show statistically significantly greater effect than tolterodine ER 4 mg on the other secondary diary endpoints. However, those results were numerically in favor of fesoterodine except for nocturnal micturitions.

- Fesoterodine 4 mg, as the starting dose, showed a statistically significantly greater effect than placebo in improving key diary efficacy measures, including those for UUI, micturition and urgency, and PPBC at Week 1.

- Fesoterodine 8 mg for 11 weeks with starting dose of 4 mg for 1 week and tolterodine ER 4 mg for 12 weeks showed a good safety profile and were well tolerated.