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PROPRIETARY DRUG NAME®/GENERIC DRUG NAME: Detrol® LA / Tolterodine L-tartrate

PROTOCOL NO.: A6121127

PROTOCOL TITLE: A Randomized, Double-Blind, Placebo-Controlled Detrol LA "Add-On" to Alpha-Blocker Study in Men With Persistent Overactive Bladder Symptoms of Urinary Frequency and Urgency With/Without Urgency Incontinence After Previous Monotherapy With Alpha-Blocker

Study Centers: A total of 75 centers took part in the study and enrolled subjects. The study was conducted at 11 centers each in Canada and the United States; 8 centers in Germany; 6 centers in Spain; 5 centers in Slovakia; 4 centers each in the Republic of Korea, Mexico, South Africa, Taiwan, Turkey, and the United Kingdom; 3 centers each in Denmark and Sweden; and 2 centers each in Italy and Norway.

Study Initiation and Final Completion Dates: 06 March 2006 and 14 May 2007

Phase of Development: Phase 4

Study Objectives:

Primary Objective: To evaluate the additional benefit of 'Add-On' tolterodine L-tartrate extended release (ER), versus (vs) placebo, to alpha-blocker therapy in men with persistent overactive bladder (OAB) symptoms of urinary frequency and urgency with/without urgency incontinence as assessed by the change in the Patient Perception of Bladder Condition (PPBC) after 12 weeks of treatment.

Secondary Objectives:

- To evaluate the additional benefit of 'Add-On' tolterodine ER, vs. placebo, to alpha-blocker therapy in men with persistent OAB symptoms of urinary frequency and urgency with/without urgency incontinence:
  - On OAB symptoms as assessed by 5-day voiding bladder diaries including Urinary Sensation Scale (USS)
  - On lower urinary tract symptoms as assessed by the International Prostate Symptom Score (IPSS)

- On subject perception of treatment benefit as assessed by the Patient Perception of Treatment Benefit Questionnaire (PPTB)
- On proportion of subjects who experienced a change from Baseline in PPBC after 4 and 12 weeks of treatment
- On bothersome quality of life (QoL) symptoms as assessed by the Overactive Bladder Questionnaire (OAB-q)
- On sexual QoL as assessed by the International Consultation on Incontinence Modular Questionnaire – Male Sexual Matters Associated with Lower Urinary Tract Symptoms (ICIQ-MLUTSsex)
- On subject satisfaction with treatment as assessed by the Overactive Bladder Medication Satisfaction Questionnaires (OAB-S, pre-medication and medication assessments)
- On nocturia bothersome measure as assessed by the Nocturia Quality-of-Life Questionnaire (N-QoL)

- To evaluate the safety and tolerability of 'Add-On' tolterodine ER, vs. placebo, to alpha-blocker therapy in men with persistent OAB symptoms of urinary frequency and urgency with/without urgency incontinence.

METHODS

Study Design: This was a 12-week, randomized, double-blind, placebo-controlled, multi-national and multi-center, parallel group study of the addition of tolterodine ER vs placebo, to ongoing alpha-blocker therapy in men with persistent OAB symptoms of urinary frequency and urgency with or without urgency incontinence, who had been on a stable dose of an alpha-blocker therapy for a minimum of 1 month. The 2 treatment groups in the study were tolterodine ER plus alpha-blocker vs placebo plus alpha-blocker.

There was a Screening period of 1 week to assess baseline OAB symptoms with a 5-day micturition diary, which incorporated the USS. Subjects who had persistent OAB symptoms (defined as mean urinary frequency of ≥8 times in 24 hours, and mean number of micturition-related urgency episodes of ≥1 in 24 hours [ie, those episodes with a rating on the USS of ≥3]) with or without urinary urgency incontinence (UUI), who were bothered by their symptoms (defined by a PPBC rating ≥3), and who met all other entry criteria, were equally randomized (1:1) to receive either tolterodine ER or matching placebo, in addition to continuing on their currently prescribed alpha-blocker medication. The combined treatment was to continue for 12 weeks. Subjects were evaluated at 4 study visits: Screening/Visit 1, Baseline/Visit 2, and Treatment/Visits 3 and 4. There was no scheduled follow-up visit after Visit 4/Week 12. The schedule of activities is presented in Table 1.

Table 1. Schedule of Activities

Activities and Forms to Be Completed	Visit 1 Screening -5 to -7 Days	Visit 2 Baseline 0	Visit 3 End of Week 4 ±3 Days	Visit 4 End of Week 12 ±6 Days
Informed consent	X			
Inclusion/exclusion criteria	X	X		
Demographics	X			
Medical history	X			
Physical examination	X			
Sitting blood pressure and heart rate	X			X
Laboratory tests and urine dip stick	X			
Review of prohibited medication list	X	X reconfirm		
Ultrasound for post void residual volume (PVR) measurement	X		X	X
Flowmeter test measuring maximum urinary flow rate	X			X
Patient perception of bladder condition (PPBC)		X	X	X
Patient perception of treatment benefit including "Willingness to continue treatment question"[a]			X	X[a]
Overactive bladder questionnaire (OAB-q)		X	X	X
International prostate symptom score (I-PSS)		X	X	X
ICIQ-MLUTSsex questionnaire		X		X
OAB medication satisfaction questionnaire (pre-medication assessment) (OAB-S)		X		
OAB medication satisfaction questionnaire (medication assessment) (OAB-S)			X	X
Nocturia quality-of-life questionnaire		X		X
5-day micturition diary dispensing	X	X	X	
5-day micturition diary review		X	X	X
Drug dispensing		X	X	
Drug accountability and assessment of study drug compliance			X	X
Adverse events		X	X	X
Concomitant medication	X	X	X	X
Concomitant non-drug treatment/procedures	X	X	X	X
Subject summary				X

ICIQ-MLUTSsex = international consultation on incontinence modular questionnaire–male sexual matters associated with lower urinary tract symptoms; OAB = overactive bladder.
a. "Willingness to continue treatment" was done at Visit 4 only.

Number of Subjects (Planned and Analyzed): A total of 608 subjects (304 per group) were planned to be randomized in the study. A total of 652 subjects were assigned to study treatment; 329 subjects were randomized to the tolterodine ER plus alpha-blocker group and 323 subjects were randomized to the placebo plus alpha-blocker group. The subject enrollment by country and treatment group is presented in Table 2.

Table 2. Subject Enrollment by Country

	Tolterodine ER + Alpha-Blocker N=329	Placebo + Alpha-Blocker N=323
	n (%)	n (%)
Canada	42 (12.8)	38 (11.8)
Denmark	17 (5.2)	17 (5.3)
Germany	21 (6.4)	21 (6.5)
Italy/Spain	14 (4.3)	11 (3.4)
Republic of Korea	36 (10.9)	37 (11.5)
Mexico	25 (7.6)	23 (7.1)
Norway	10 (3.0)	11 (3.4)
Slovakia (Slovak Republic)	51 (15.5)	48 (14.9)
Sweden	26 (7.9)	25 (7.7)
Taiwan	30 (9.1)	30 (9.3)
Turkey	11 (3.3)	12 (3.7)
United Kingdom/South Africa	11 (3.3)	15 (4.6)
United States	35 (10.6)	35 (10.8)

ER = extended release; N = number of subjects in a treatment group; n = number of subjects per country.

Diagnosis and Main Criteria for Inclusion: The study included male subjects aged 40 years and above with symptoms of OAB (frequency more than 8 times per day and urgency more than 1 episode per day confirmed by bladder diary). Subjects with significant hepatic or renal disease, or history of radiation treatment were excluded from the study.

Study Treatment: The study treatments were tolterodine L-tartrate extended-release 4 mg capsules and matching placebo capsules. Subjects were instructed to take 1 study medication capsule orally once daily at night-time, for 12 weeks. Study medication was to be taken with fluids.

The subjects were to continue on their currently prescribed alpha-blocker medication for the duration of the study. The prescribed alpha-blocker was not supplied.

Efficacy and Safety Endpoints:

Primary Endpoint: The primary efficacy measure was the proportion of subjects who improved from Baseline in PPBC at Week 12.

Secondary Efficacy Endpoints:

- Micturition Diary:
    - Change in mean number of micturitions per 24 hours at Week 4 and Week 12 relative to Baseline
    - Change in mean number of daytime micturitions per day at Week 4 and Week 12 relative to Baseline
    - Change in mean number of nighttime micturitions per night at Week 4 and Week 12 relative to Baseline

- Change in the mean sensation rating on the USS at Week 4 and Week 12 relative to Baseline

- The number and percentage of subjects who improved at least 1 point in the average severity of the USS from Baseline

- Change in mean number of OAB micturition episodes (micturition-related urgency episodes) per 24 hours at Week 4 and Week 12 relative to Baseline

- Change in mean number of daytime OAB micturition episodes (micturition-related urgency episodes) at Week 4 and Week 12 relative to Baseline

- Change in mean number of nighttime OAB micturition episodes (micturition-related urgency episodes) at Week 4 and Week 12 relative to Baseline

- Change in mean number of severe OAB micturition episodes (severe micturition-related urgency episodes) per 24 hours at Week 4 and Week 12 relative to Baseline

- Change in mean number of daytime severe OAB micturition episodes (severe micturition-related urgency episodes) at Week 4 and Week 12 relative to Baseline

- Change in mean number of nighttime severe OAB micturition episodes (severe micturition-related urgency episodes) at Week 4 and Week 12 relative to Baseline

- PPBC

  - Proportion of subjects who improved from Baseline in PPBC at Week 4

    A binary post-baseline vs Baseline variable, defined the same as the primary endpoint, was derived at Week 4.

  - Proportion of subjects who experienced a change from Baseline in PPBC after 4 and 12 weeks of treatment

    Two post-baseline vs Baseline ordinal variables were derived at Week 4 and Week 12. The ordinal variables were defined as follows:

    (1) Deterioration, No Change, and Improvement

    Deterioration = Increase of 1 or more points in difference of scores

    No Change = Difference of scores was 0

    Improvement = Negative difference of scores

(2) Deterioration, No Change, Minor Improvement, and Major Improvement

Deterioration = Difference in scores was positive

No Change = Difference in scores was 0

Minor Improvement = Difference in scores was negative in magnitude of 1

Major Improvement = Difference in scores was negative in magnitude of 2 or more

- Change in the total score of OAB-q and change in total scores of each domain of OAB-q at Week 4 and Week 12 relative to Baseline

  The symptom bother/severity score and the Health-Related Quality of Life (HRQOL) score were analyzed based on transformed scores.

- International Prostate Symptom Score (IPSS)
  - Change in IPSS index score (Sum Q1 to Q7) at Week 4 and Week 12 relative to Baseline
  - Change in IPSS individual item scores (Q1, Q2, Q3, Q4, Q5, Q6, and Q7) at Week 4 and Week 12 relative to Baseline
  - Change in IPSS irritative or storage domain (Sum of Q2, Q4, and Q7) at Week 4 and Week 12 relative to Baseline
  - Change in IPSS obstructive or voiding domain (Sum of Q1, Q3, Q5, and Q6) at Week 4 and Week 12 relative to Baseline
  - Change in IPSS QoL score (Q8) at Week 4 and Week 12 relative to Baseline
- Change in the total scores of the ICIQ-MLUTSsex Questionnaire at Week 12 relative to Baseline
- Change in N-QoL measure at Week 12 relative to Baseline
- Overactive Bladder Medication Satisfaction Questionnaires (OAB-S)
  - Change in day-to-day life domain score at Weeks 4 and 12
  - Change in interruption in day-to-day life due to OAB at Weeks 4 and 12 relative to Baseline
  - Comparison of the satisfaction scale at Week 4 and Week 12
  - Comparison of overall satisfaction question at Week 4 and Week 12

- Patient Perception of Treatment Benefit Questionnaire (PPTB)
    - PPTB at Week 4 and Week 12
    - Willingness to continue with treatment at Week 12.

Safety Endpoints:

- Urinary retention requiring catheterization
- Voiding difficulties requiring study medication to be discontinued
- Urinary infection
- Incidence of prostate surgery
- Incidence, severity and relatedness to treatment of all reported and treatment emergent adverse events (AEs)
- Number of withdrawals from the study due to AEs
- Reporting of serious AEs (SAEs).

Safety Evaluations: Safety endpoints for this study included AEs, concomitant drug treatments, concomitant non-drug treatments, laboratory values, vital signs, physical examination, post void residual (PVR) volume measurements, and assessments of maximum urinary flow rates (Q_{max}).

Statistical Methods:

Efficacy: The primary efficacy endpoint was the proportion of subjects who improved from Baseline to Week 12 on the 6-point PPBC assessment (with "1= no problems at all" and "6= many severe problems"). A binary post-baseline vs Baseline variable was used in the primary analysis (Improvement = Negative change from Baseline, Non-improvement = Change from Baseline was 0 or more). The primary efficacy analysis methodology was a Cochran-Mantel-Haenszel (CMH) test stratified by country at the 5% level of significance. The number and percentage of the binary outcome, improvement/non-improvement, was summarized. The p-value for the treatment comparison, the odds ratio, and the 95% confidence interval (CI) of the odds ratio were presented.

Ordinal variables were analyzed using the CMH test with modified ridit scoring stratified by country. Summary statistics including cell counts and percentages were provided.

Testing for statistical difference between tolterodine ER plus alpha-blocker and placebo plus alpha-blocker was carried out at the 5% level of significance. Summary statistics for continuous variables were provided by treatment and included number of observations, mean, standard deviation, minimum, and maximum. Least squares (LS) mean and standard error were presented for variables analyzed using an analysis of covariance (ANCOVA)

model with terms for country, treatment, and baseline value of the variable being analyzed. An alpha-level of 0.10 was used to determine the statistical significance of interaction terms in the ANCOVA model. The interactions included treatment by Baseline and treatment by country, which were assessed at the 10% level of significance. For the OAB-S satisfaction scale, treatment by OAB Medication Expectation scale was assessed.

Safety: Safety variables PVR and Q_{max} were analyzed using ANCOVA with terms for country, treatment, treatment by country interaction, and the Baseline value as a covariate. All AE and medical history terms were coded using the Medical Dictionary for Regulatory Activities (MedDRA). Standard summaries and listings of AEs were generated using Clinical Data Analysis and Reporting System for the safety population.

RESULTS

Subject Disposition and Demography: A total of 652 subjects were assigned to study treatment; 329 subjects were randomized to the tolterodine ER plus alpha-blocker group and 323 subjects were randomized to the placebo plus alpha-blocker group. Subjects completing the study totaled 283 in the tolterodine ER plus alpha-blocker group and 292 in the placebo plus alpha-blocker group. A summary of subject dispositions is presented in Table 3.

Table 3. Subject Disposition and Subjects Analyzed

	Tolterodine ER + Alpha-Blocker N=329	Placebo + Alpha-Blocker N=323
	N	
Randomized to treatment	329	323
Received treatment	329	323
Discontinued study	46	31
Completed study	283	292
	n (%)	
Discontinuations[a]	46 (14.0)	31 (9.6)
Subject died[b]	1 (0.3)	1 (0.3)
Discontinuation related to study drug	19 (5.8)	10 (3.1)
Adverse event	13 (4.0)	8 (2.5)
Lack of efficacy	6 (1.8)	2 (0.6)
Discontinuation not related to study drug	26 (7.9)	20 (6.2)
Adverse event	2 (0.6)	2 (0.6)
Other	18 (5.5)	12 (3.7)
Subject defaulted	6 (1.8)	6 (1.9)
	N	
Efficacy Analysis		
Full Analysis Set[c]	329	323
FAS at Week 4 in Window[d]	306	306
FAS at Week 12 in Window[d,e]	307	306
Safety Analysis[f]	329	323

AE = adverse event; ER = extended release; FAS = full analysis set; N = number of subjects; n = number of subjects with reason for discontinuation.

a. The Investigator reported the reason for discontinuation for 1 tolterodine ER subject as "subject defaulted" and for another tolterodine ER subject as "insufficient clinical response," but reported "study medication discontinued" for both subjects on the AE page. In this table, these subjects were counted in the 'subject defaulted' group (not related to study drug) and the 'lack of efficacy' group (related to study drug), respectively. For 1 placebo subject, the Investigator reported the reason for discontinuation as "adverse event" but did not indicate "study med discontinued" on the AE page. In this table, this subject was counted in the 'adverse event' group (not related to study drug). For 1 placebo subject who discontinued due to death, the Investigator reported "study medication discontinued" on the AE page.
b. Both deaths in the study were considered by the Investigator to be not related to study drug.
c. FAS included subjects with at least 1 dose of study medication and an efficacy visit (Baseline or post-baseline).
d. Based upon primary efficacy endpoint.
e. Last Observation Carried Forward was used in the FAS analysis to impute missing values at Week 12 from Week 4.
f. Safety analysis set included all subjects who received at least 1 dose of study medication.

The demographic characteristics were similar between the 2 treatment groups. The average duration since first diagnosis of OAB (MedDRA preferred term hypertonic bladder) was 3.6 years for the tolterodine ER plus alpha-blocker group and 3.8 years for the placebo plus alpha-blocker group. A summary of demographic characteristics at enrollment is presented in Table 4.

Table 4. Demographic and Baseline Disease Characteristics – Safety Analysis Set

	Tolterodine ER + Alpha-Blocker N=329	Placebo + Alpha-Blocker N=323
Age (years), n (%)		
<18	0	0
18 – 44	4 (1.2)	6 (1.9)
45 – 64	137 (41.6)	151 (46.7)
≥65	188 (57.1)	166 (51.4)
Mean (SD)	65.6 (9.1)	64.8 (9.1)
Range	39–85	36–89
Race, n (%)		
White	229 (69.6)	227 (70.3)
Asian	69 (21.0)	70 (21.7)
Black	5 (1.5)	2 (0.6)
Other	26 (7.9)	24 (7.4)
Weight (kg)		
Mean (SD)	81.0 (15.9)	81.3 (14.1)
Range	49.9–150.0	50.0–131.5
Height (cm)		
Mean (SD)	172.4 (7.3)	173.0 (8.0)
Range	153.0–198.0	152.5–192.0
Duration since first diagnosis of hypertonic bladder (years)		
Mean	3.6	3.8
Range[a]	0.0–39.8	-0.1–34.8

ER = extended release; N = number of subjects; n = number of subjects with each character;
OAB = overactive bladder; SD = standard deviation.

a. One subject in the tolterodine ER plus alpha-blocker group had 0.03 year duration (listed as a minimum value of 0 due to rounding). One subject in the placebo plus alpha-blocker group received the specific diagnosis of OAB after enrollment into the study, thus a negative value was listed.

Efficacy and Safety Results:

Efficacy Results: The primary efficacy measure was the proportion of subjects who improved from Baseline in PPBC at Week 12 (last observation carried forward). This endpoint did not show a statistically significant difference between tolterodine ER plus alpha-blocker and placebo plus alpha-blocker therapy (p=0.6699). The number and percent of subjects at each category on the 6-point PPBC scale is presented in Table 5.

Table 5. Patient's Perception of Bladder Condition at Week 12

	Tolterodine ER + Alpha-Blocker N=329	Placebo + Alpha-Blocker N=323
	n (%)	
N[a]	305 (100)	305 (100)
Baseline		
No problems at all	0	0
Some very minor problems	1 (0.3)	1 (0.3)
Some minor problems	2 (0.7)	1 (0.3)
Some moderate problems	214 (70.2)	193 (63.3)
Severe problems	78 (25.6)	101 (33.1)
Many severe problems	10 (3.3)	9 (3.0)
Week 12		
No problems at all	16 (5.2)	13 (4.3)
Some very minor problems	46 (15.1)	43 (14.1)
Some minor problems	96 (31.5)	86 (28.2)
Some moderate problems	119 (39.0)	125 (41.0)
Severe problems	26 (8.5)	35 (11.5)
Many severe problems	2 (0.7)	3 (1.0)
Change from Baseline to Week 12		
Binary assessment		
Improvement[b]	194 (63.6)	188 (61.6)
No improvement[c]	111 (36.4)	117 (38.4)
95% CI	57.9, 69.0	55.9, 67.1
p-value[d]	0.6699	
Odds ratio (95% CI)	0.93 (0.66, 1.31)	

CI = confidence interval; ER = extended release; N = number of subjects; n = number of subjects meeting criteria.

a. Number of subjects with non-missing Baseline and Week 12 values.
b. Improvement was defined as a negative change from Baseline.
c. No improvement was defined as a change from Baseline ≥0.
d. The p-value was obtained from a Cochran-Mantel-Haenszel test stratified by country.

Secondary Efficacy Analysis:

Micturition Diary: Several of the secondary efficacy variables from the micturition diary (with a 5-point USS) demonstrated statistically significant improvements in subjects receiving add-on tolterodine ER treatment after previous mono-therapy with alpha-blockers.

Micturitions in a 24-hour Period: The ANCOVA showed a statistically significant difference between the groups tolterodine ER plus alpha-blocker and placebo plus alpha-blocker in mean changes from Baseline to Week 12 in the mean number of micturition episodes per 24 hours (p=0.0079). A statistically significant difference between the groups (tolterodine ER plus alpha-blocker and placebo plus alpha-blocker) was also observed in the percent change from Baseline to Week 12 (p=0.0012).

A similar analysis of the change from Baseline in the mean number of micturitions in 24 hours was also performed on data collected at Week 4. The difference between the groups was not statistically significant at this time point (p=0.9270). At Week 4, the difference between the groups (tolterodine ER plus alpha-blocker and placebo plus

alpha-blocker) in the percent change from Baseline also did not reach statistical significance (p=0.3043).

The mean number of micturitions in a 24 hour period at Baseline and at Weeks 4 and 12, and analysis of the numerical and percent change from Baseline are presented in Table 6.

Table 6. Change in Mean Number of Micturitions per 24 Hours at Weeks 4 and 12

	Tolterodine ER + Alpha-Blocker N=329	Placebo + Alpha-Blocker N=323
Week 4		
N[a]	302	303
Number of micturitions per 24 hours		
Baseline		
Mean (SD)	11.4 (2.9)	11.4 (2.9)
Median (range)	10.4 (7.4 to 24.0)	11.0 (7.2 to 29.2)
Week 4		
Mean (SD)	10.1 (2.8)	10.3 (2.9)
Median (range)	9.8 (5.0 to 24.0)	10.0 (4.4 to 26.2)
Numerical change from baseline to Week 4		
Mean (SD)	-1.3 (2.2)	-1.1 (2.4)
Median (range)	-1.2 (-10.2 to 5.2)	-0.8 (-13.0 to 5.6)
LS Mean (SE)	-1.2 (0.1)	-1.2 (0.1)
95% CI for mean, p-value[b]	-1.5, -1.0, <.0001	-1.4, -0.8, <.0001
Treatment difference in numerical change[c]	Tolterodine ER+alpha blocker versus placebo + alpha blocker	
LS mean difference (SE)	-0.0 (0.2)	
95% confidence interval	-0.4, 0.3	
p-value	0.927	
Percent change from Baseline to Week 4		
Mean (SD)	-10.3 (16.9)	-8.6 (18.2)
Median (range)	-11.9 (-50.6 to 45.6)	-8.2 (-65.5 to 57.1)
Treatment difference in percent change[d]	Tolterodine ER+alpha blocker versus placebo + alpha blocker	
p-value	0.3043	
Week 12		
N[a]	302	303
Number of micturitions per 24 hours		
Baseline		
Mean (SD)	11.4 (2.9)	11.4 (2.9)
Median (range)	10.4 (7.4 to 24.0)	11.0 (7.2 to 29.2)
Week 12		
Mean (SD)	9.7 (2.9)	10.3 (3.3)
Median (range)	9.2 (3.8 to 20.0)	9.8 (4.6 to 30.4)
Numerical change from Baseline to Week 12		
Mean (SD)	-1.7 (2.3)	-1.1 (2.6)
Median (range)	-1.6 (-9.0 to 7.2)	-0.8 (-15.0 to 11.6)
LS mean (SE)	-1.8 (0.1)	-1.2 (0.1)
95% CI for mean, p-value[b]	-1.9, -1.4, <0.0001	-1.4, -0.8, <0.0001
Treatment difference in numerical change[c]	Tolterodine ER+alpha blocker versus placebo + alpha blocker	
LS mean difference (SE)	-0.6 (0.2)	
95% CI	-1.0, -0.1	
p-value	0.0079	
Percent change from Baseline to Week 12		
Mean (SD)	-13.9 (18.2)	-9.1 (19.5)
Median (range)	-14.3 (-61.2 to 65.5)	-9.1 (-65.8 to 69.9)
Treatment difference in percent change[d]	Tolterodine ER+alpha blocker versus placebo + alpha blocker	
p-value	0.0012	

Table 6. Change in Mean Number of Micturitions per 24 Hours at Weeks 4 and 12

	Tolterodine ER + Alpha-Blocker N=329	Placebo + Alpha-Blocker N=323

ANCOVA = analysis of covariance; CI = confidence interval; ER = extended release; LS = least squares; N = number of subjects; SD = standard deviation; SE = standard error.

a. Number of subjects with non-missing numerical and percent change from Baseline.
b. The p-value was based on a paired t-test comparing Baseline with post-baseline values.
c. The treatment difference was based on an ANCOVA model with terms for country, treatment, treatment by country interaction, and the Baseline value as a covariate.
d. The treatment difference was based on a ranked ANCOVA model with the ranked value as the response, and terms for country, treatment, treatment by country interaction, and the Baseline value as a covariate.

Daytime and Nocturnal Micturitions: The mean number of daytime and nocturnal micturations at Baseline and Weeks 4 and 12, and analysis of the numerical change from Baseline to Weeks 4 and 12 for each category are presented in Table 7.

Table 7. Change in Mean Number of Daytime and Nocturnal Micturitions at Weeks 4 and 12

	Daytime Micturitions		Nocturnal Micturitions	
	Tolterodine ER + Alpha-Blocker N=329	**Placebo + Alpha-Blocker N=323**	**Tolterodine ER + Alpha-Blocker N=329**	**Placebo + Alpha-Blocker N=323**
Week 4				
N[a]	302	303	302	303
Mean number of micturitions per day				
Baseline				
Mean (SD)	9.1 (2.9)	9.1 (2.8)	1.7 (1.4)	1.7 (1.5)
Median (range)	8.4 (4.2 to 24.0)	8.6 (2.0 to 23.8)	1.4 (0.0 to 12.8)	1.4 (0.0 to 9.2)
Week 4				
Mean (SD)	8.1 (2.5)	8.3 (2.6)	1.5 (1.5)	1.4 (1.3)
Median	7.6 (2.6 to 17.6)	8.0 (3.6 to 23.4)	1.2 (0.0 to 8.4)	1.2 (0.0 to 7.0)
Numerical change from baseline to Week 4				
Mean (SD)	-1.0 (2.1)	-0.8 (2.2)	-0.2 (1.4)	-0.3 (1.3)
Median (range)	-0.8 (-11.4 to 6.4)	-0.8 (-12.8 to 7.2)	-0.2 (-10.8 to 8.0)	-0.2 (-7.6 to 5.2)
LS Mean (SE)	-1.0 (0.1)	-0.9 (0.1)	-0.2 (0.1)	-0.3 (0.1)
95% CI for mean, p-value[b]	-1.3, -0.8, <.0001	-1.0, -0.5, <.0001	-0.3, -0.0, 0.0404	-0.4, -0.1, 0.0001
Treatment difference in numerical change[c]	Tolterodine ER+alpha blocker versus placebo + alpha blocker			
LS mean difference (SE)	-0.1 (0.2)		0.1 (0.1)	
95% confidence interval	-0.4, 0.2		-0.1, 0.3	
p-value	0.5647		0.2267	
Week 12				
N[a]	302	303	302	303
Mean number of micturitions per day				
Baseline				
Mean (SD)	9.1 (2.9)	9.1 (2.8)	1.7 (1.4)	1.7 (1.5)
Median (range)	8.4 (4.2 to 24.0)	8.6 (2.0 to 23.8)	1.4 (0 to 12.8)	1.4 (0 to 9.2)
Week 12				
Mean (SD)	7.8 (2.4)	8.4 (2.8)	1.3 (1.3)	1.4 (1.7)
Median (range)	7.4 (2.6 to 17.0)	8.0 (3.4 to 25.2)	1.0 (0 to 8.6)	1.0 (0 to 14.6)
Numerical change from Baseline to Week 12				
Mean (SD)	-1.2 (2.2)	-0.7 (2.3)	-0.4 (1.4)	-0.3 (1.4)
Median (range)	-1.2 (-16.0 to 4.8)	-0.6 (-14.2 to 5.8)	-0.2 (-11.0 to 8.6)	-0.2 (-6.4 to 9.8)
LS mean (SE)	-1.3 (0.1)	-0.8 (0.1)	-0.4 (0.1)	-0.2 (0.1)
95% CI for mean, p-value[b]	-1.5, -1.0, <0.0001	-1.0, -0.5, <0.0001	-0.5, -0.2, <0.0001	-0.4, -0.1, 0.0013
Treatment difference in numerical change[c]	Tolterodine ER + alpha blocker versus placebo + alpha blocker			
LS mean difference (SE)	-0.4 (0.2)		-0.2 (0.1)	
95% CI	-0.8, -0.1		-0.4, 0.1	
p-value	0.0123		0.1740	

ANCOVA = analysis of covariance; CI = confidence interval; ER = extended release; LS = least squares; N = number of subjects; SD = standard deviation; SE = standard error.

a. Number of subjects with non-missing numerical change from baseline to Week 4/Week 12.
b. p-Value was based on paired t-test comparing baseline with post-baseline values.
c. Based on an ANCOVA model with terms for country, treatment and treatment by country interaction with baseline value as a covariate.

Mean Rating on the Urinary Sensation Scale: Subjects rated their feeling of urinary urgency associated with each micturition episode using the USS. This was a 5-point scale with an assessment of 1 indicative of no urgency and an assessment of 5 denoting urgency incontinence. The change in the mean rating at Weeks 4 and 12 relative to Baseline is shown in Table 8.

Table 8. Change in the Mean Sensation Rating on the Urinary Sensation Scale at Weeks 4 and 12

	Tolterodine ER + Alpha-Blocker N=329	Placebo + Alpha-Blocker N=323
Week 4		
N[a]	302	303
Baseline		
Mean (SD)	2.6 (0.5)	2.7 (0.6)
Median (range)	2.5 (1.3 to 4.0)	2.6 (1.3 to 5.0)
Week 4		
Mean (SD)	2.4 (0.6)	2.5 (0.6)
Median (range)	2.4 (1.0 to 4.4)	2.4 (1.0 to 4.9)
Numerical change from baseline to Week 4		
Mean (SD)	-0.2 (0.5)	-0.2 (0.5)
Median (range)	-0.1 (-2.1 to 1.3)	-0.1 (-2.8 to 1.0)
LS Mean (SE)	-0.2 (0.0)	-0.2 (0.0)
95% CI for mean, p-value[b]	-0.2, -0.1, <0.0001	-0.3, -0.1, <0.0001
Treatment difference in numerical change[c]	Tolterodine ER + alpha blocker versus placebo + alpha blocker	
LS mean difference (SE)	0.0 (0.0)	
95% confidence interval	-0.0, 0.1	
p-value	0.3869	
Week 12		
N[a]	302	303
Baseline		
Mean (SD)	2.6 (0.5)	2.7 (0.6)
Median (range)	2.5 (1.3 to 4.0)	2.6 (1.3 to 5.0)
Week 12		
Mean (SD)	2.3 (0.5)	2.4 (0.6)
Median (range)	2.2 (1.0 to 4.3)	2.3 (1.0 to 5.0)
Numerical change from baseline to Week 12		
Mean (SD)	-0.3 (0.6)	-0.3 (0.6)
Median (range)	-0.2 (-2.2 to 1.2)	-0.2 (-2.2 to 1.5)
LS Mean (SE)	-0.3 (0.0)	-0.3 (0.0)
95% CI for mean, p-value[b]	-0.4, -0.2, <0.0001	-0.3, -0.2, <0.0001
Treatment difference in numerical change[c]	Tolterodine ER + alpha blocker versus placebo + alpha blocker	
LS mean difference (SE)	-0.1 (0.0)	
95% confidence interval	-0.1, 0.0	
p-value	0.2060	

ANCOVA = analysis of covariance; CI = confidence interval; ER = extended release; LS = least squares; N = number of subjects; SD = standard deviation; SE = standard error.

a. Number of subjects with non-missing numerical change from baseline to Week 4/Week 12.
b. p-Value was based on paired t-test comparing baseline with post-baseline values.
c. Based on an ANCOVA model with terms for country, treatment and treatment by country interaction with baseline value as a covariate.

There was no significant difference in the percentage of subjects in the tolterodine ER plus alpha-blocker group who improved at least 1 point in the average severity of the USS from Baseline to Week 4 and Week 12 compared with subjects in the placebo plus alpha-blocker group. The number and percentage of subjects who improved at least 1 point from Baseline in the average severity of urinary urgency was also assessed and is presented in Table 9.

Table 9. Summary of Improvement in Rating on Urinary Sensation Scale at Week 4 and Week 12

	Tolterodine ER + Alpha-Blocker N=329	Placebo + Alpha-Blocker N=323
Week 4		
N[a]	302	303
Change from Baseline to Week 4, n (%)		
Improvement[b]	18 (6.0)	23 (7.6)
No improvement[c]	284 (94.0)	280 (92.4)
p-value[d]	0.3883	
Odds ratio	1.17	
95% CI	0.58, 2.37	
Week 12		
N[a]	302	303
Change from Baseline to Week 12, n (%)		
Improvement[b]	36 (11.9)	36 (11.9)
No improvement[c]	266 (88.1)	267 (88.1)
p-value[d]	0.9588	
Odds ratio	1.00	
95% CI	0.56, 1.77	

CI = confidence interval; ER = extended release; N = number of subjects.

a. Number of subjects with non-missing numerical change from baseline to Week 4/Week 12.
b. Improvement was defined as the difference in the average severity (post-baseline minus Baseline) of ≤-1.
c. No improvement was defined as difference in average severity > -1
d. The p-value was obtained from a Cochran-Mantel-Haenszel test stratified by country.

Micturition-Related Urgency Episodes in 24-hour Period: The mean number of micturition-related urgency episodes (ie, those with a USS rating of ≥3) per 24 hours was similar at Baseline in the tolterodine ER plus alpha-blocker and placebo plus alpha-blocker groups. LS mean changes from Baseline to Week 12 showed a statistically significant difference between the groups (p=0.0010). A statistically significant difference between the groups (tolterodine ER plus alpha-blocker and placebo plus alpha-blocker) was also observed in the percent change from Baseline to Week 12 (p=0.0420).

A similar analysis of the change from Baseline in the mean number of micturition-related urgency episodes in 24 hours was also performed on data collected at Week 4. The difference between the groups was not statistically significant at this time point (p=0.9197). The difference between the 2 groups (tolterodine ER plus alpha-blocker and placebo plus alpha-blocker) in the percent change from Baseline to Week 4 was not statistically significant (p=0.9613).

The mean number of micturition-related urgency episodes (ie, those with a USS rating of ≥3) recorded in a 24-hour period at Baseline and Weeks 4 and 12, and analysis of the numerical change from Baseline to Weeks 4 and 12 is presented in Table 10.

Table 10. Change in Mean Number of Micturition-related Urgency Episodes per 24 Hours at Week 4 and Week 12

	Tolterodine ER + Alpha-Blocker N=329	Placebo + Alpha-Blocker N=323
Week 4		
N[a]	302	303
Number of urgency episodes[b] per 24 hours		
Baseline		
Mean (SD)	6.4 (4.1)	6.8 (3.9)
Median (range)	5.6 (0.0 to 19.4)	6.0 (1.0 to 22.8)
Week 4		
Mean (SD)	4.6 (3.9)	5.1 (3.8)
Median (range)	3.6 (0.0 to 16.4)	4.2 (0.0 to 15.0)
Numerical change from Baseline to Week 4		
Mean (SD)	-1.8 (3.5)	-1.7 (3.5)
Median (range)	-1.2 (-15.2 to 7.4)	-1.4 (-16.8 to 8.5)
LS Mean (SE)	-1.8 (0.2)	-1.7 (0.2)
95% CI for mean, p-value[c]	-2.2, -1.4, <.0001	-2.1, -1.3, <.0001
Treatment difference in numerical change[d]	Tolterodine ER + alpha blocker versus placebo + alpha blocker	
LS mean difference (SE)	-0.0 (0.3)	
95% confidence interval	-0.6, 0.5	
p-value	0.9197	
Percent change from Baseline to Week 4		
Mean (SD)	-20.3 (66.5)	-18.5 (63.8)
Median (range)	-27.3 (-100.0 to 400.0)	-22.4 (-100.0 to 520.0)
Treatment difference in percent change[e]	Tolterodine ER + alpha blocker versus placebo + alpha blocker	
p-value	0.9613	
Week 12		
N[a]	302	303
Number of urgency episodes[b] per 24 hours		
Baseline		
Mean (SD)	6.4 (4.1)	6.8 (3.9)
Median (range)	5.6 (0.0 to 19.4)	6.0 (1.0 to 22.8)
Week 12		
Mean (SD)	3.8 (3.7)	4.9 (4.4)
Median (range)	2.6 (0.0 to 17.0)	3.8 (0.0 to 28.2)
Numerical change from baseline to Week 12		
Mean (SD)	-2.6 (4.2)	-1.9 (4.2)
Median (range)	-1.8 (-19.4 to 7.2)	-1.4 (-21.0 to 14.4)
LS Mean (SE)	-2.9 (0.2)	-1.8 (0.2)
95% CI for mean, p-value[c]	-3.1, -2.1, <0.0001	-2.4, -1.4, <0.0001
Treatment difference in numerical change[d]	Tolterodine ER + alpha blocker versus placebo + alpha blocker	
LS mean difference (SE)	-1.1 (0.3)	
95% confidence interval	-1.7, -0.4	
p-value	0.0010	
Percent change from Baseline to Week 12		
Mean (SD)	-28.0 (75.1)	-19.5 (88.6)
Median (range)	-45.0 (-100.0 to 380.0)	-26.7 (-100.0 to 800.0)
Treatment difference in percent change[e]	Tolterodine ER + alpha blocker versus placebo + alpha blocker	
p-value	0.0420	

Table 10. Change in Mean Number of Micturition-related Urgency Episodes per 24 Hours at Week 4 and Week 12

	Tolterodine ER + Alpha-Blocker N=329	Placebo + Alpha-Blocker N=323

ANCOVA = analysis of covariance; CI = confidence interval; ER = extended release; LS = least squares; N = number of subjects; SD = standard deviation; SE = standard error.

a. Number of subjects with non-missing numerical change from baseline to Week 4/Week 12.
b. Urgency episodes were those with a rating of ≥3 on the Urinary Sensation Scale.
c. p-Value was based on paired t-test comparing baseline with post-baseline values.
d. Based on an ANCOVA model with terms for country, treatment and treatment by country interaction with baseline value as a covariate.
e. Based on a ranked ANCOVA model with terms for country, treatment and treatment by country interaction with baseline value as a covariate.

Daytime and Nocturnal Micturition-Related Urgency Episodes: The mean number of daytime and nocturnal micturition-related urgency episodes at Baseline and Weeks 4 and 12, and analyses of the numerical changes from Baseline to Weeks 4 and 12 for each category are presented in Table 11.

Table 11. Change in Mean Number of Daytime and Nocturnal Micturition-Related Urgency Episodes at Week 4 and Week 12

	Daytime Urgency Episodes[a]		Nocturnal Urgency Episodes[a]	
	Tolterodine ER + Alpha-Blocker N=329	Placebo + Alpha-Blocker N=323	Tolterodine ER + Alpha-Blocker N=329	Placebo + Alpha-Blocker N=323
Week 4				
N[b]	302	303	302	303
Baseline				
Mean (SD)	4.9 (3.6)	5.1 (3.4)	1.1 (1.1)	1.2 (1.4)
Median (range)	4.2 (0.0 to 18.8)	4.6 (0.0 to 19.0)	0.8 (0.0 to 5.8)	0.8 (0.0 to 7.4)
Week 4				
Mean (SD)	3.5 (3.2)	3.8 (3.2)	0.8 (1.2)	0.9 (1.1)
Median (range)	2.7 (0.0 to 15.8)	3.0 (0.0 to 13.8)	0.4 (0.0 to 7.6)	0.4 (0.0 to 6.7)
Numerical change from baseline to Week 4				
Mean (SD)	-1.4 (2.9)	-1.3 (3.0)	-0.2 (1.1)	-0.4 (1.2)
Median (range)	-1.0 (-13.0 to 6.4)	-0.8 (-13.0 to 6.4)	-0.2 (-4.0 to 7.4)	-0.2 (-7.4 to 5.2)
LS Mean (SE)	-1.4 (0.2)	-1.3 (0.2)	-0.3 (0.1)	-0.3 (0.1)
95% CI for mean, p-value[c]	-1.7, -1.0, <0.0001	-1.6, -1.0, <0.0001	-0.4, -0.1, 0.0002	-0.5, -0.2, <0.0001
Treatment difference in numerical change[d]	Tolterodine ER + alpha blocker versus placebo + alpha blocker			
LS mean difference (SE)	-0.0 (0.2)		0.0 (0.1)	
95% confidence interval	-0.5, 0.4		-0.1, 0.2	
p-value	0.8846		0.6759	
Week 12				
N[b]	302	303	302	303
Baseline				
Mean (SD)	4.9 (3.6)	5.1 (3.4)	1.1 (1.1)	1.2 (1.4)
Median (range)	4.2 (0 to 18.8)	4.6 (0 to 19.0)	0.8 (0 to 5.8)	0.8 (0 to 7.4)
Week 12				
Mean (SD)	2.9 (3.0)	3.7 (3.6)	0.7 (1.0)	0.9 (1.4)
Median (range)	2.0 (0 to 15.4)	3.0 (0 to 15.2)	0.2 (0 to 8.2)	0.4 (0 to 13.0)
Numerical change from Baseline to Week 12				
Mean (SD)	-2.0 (3.6)	-1.4 (3.6)	-0.4 (1.1)	-0.4 (1.3)
Median (range)	-1.4 (-18.8 to 7.0)	-1.2 (-17.8 to 11.8)	-0.2 (-4.4 to 8.2)	-0.2 (-6.0 to 9.8)
LS mean (SE)	-2.2 (0.2)	-1.4 (0.2)	-0.5 (0.1)	-0.3 (0.1)
95% CI for mean, p-value[c]	-2.4, -1.6, <0.0001	-1.8, -1.0, <0.0001	-0.6, -0.3, <0.0001	-0.5, -0.2, <0.0001
Treatment difference in numerical change[d]	Tolterodine ER + alpha blocker versus placebo + alpha blocker			
LS mean difference (SE)	-0.8 (0.3)		-0.2 (0.1)	
95% CI	-1.3, -0.3		-0.4, 0	
p-value	0.0017		0.0378	

ANCOVA = analysis of covariance; CI = confidence interval; ER = extended release; LS = least squares; N = number of subjects; SD = standard deviation; SE = standard error.

a. Urgency episodes were those with a rating of ≥3 on the Urinary Sensation Scale.
b. Number of subjects with non-missing numerical change from Baseline to Week 4/Week 12.
c. The p-value was based on a paired t-test comparing Baseline with post-baseline values.
d. The treatment difference was based on an ANCOVA model with terms for country, treatment, treatment by country interaction, and the Baseline value as a covariate.

Severe Micturition-Related Urgency Episodes in a 24-Hour Period: The mean number of severe micturition-related urgency episodes (ie, those with a USS rating of ≥4) recorded in a 24-hour period at Baseline and Weeks 4 and 12, and analysis of the numerical change from Baseline to Weeks 4 and 12 is presented in Table 12.

Table 12. Change in Mean Number of Severe Micturition-Related Urgency Episodes per 24 Hours at Week 4 and Week 12

	Tolterodine ER + Alpha-Blocker N=329	Placebo + Alpha-Blocker N=323
Week 4		
N[a]	302	303
Number of severe micturition-related urgency episodes[b] per 24 hours		
Baseline		
Mean (SD)	1.6 (2.6)	1.7 (2.7)
Median (range)	0.6 (0.0 to 18.0)	0.6 (0.0 to 16.8)
Week 4		
Mean (SD)	0.9 (2.1)	1.0 (2.1)
Median (range)	0.0 (0.0 to 13.6)	0.0 (0.0 to 14.6)
Numerical change from Baseline to Week 4		
Mean (SD)	-0.7 (2.4)	-0.7 (2.4)
Median (range)	0.0 (-18.0 to 10.0)	0.0 (-16.8 to 9.8)
LS Mean (SE)	-0.7 (0.1)	-0.7 (0.1)
95% CI for mean, p-value[c]	-1.0, -0.4,<0.0001	-1.0, -0.4, <0.0001
Treatment difference in numerical change[c]	Tolterodine ER + alpha blocker versus placebo + alpha blocker	
LS mean difference (SE)	-0.0 (0.2)	
95% confidence interval	-0.3, 0.3	
p-value	0.9481	
Percent change from Baseline to Week 4		
Mean (SD)	-25.6 (188.0)	1.0 (335.1)
Median (range)	-82.1 (-100.0 to 1800.0)	-68.3 (-100.0 to 4300.0)
Treatment difference in percent change[d]	Tolterodine ER + alpha blocker versus placebo + alpha blocker	
p-value	0.7317	
Week 12		
N[a]	302	303
Number of severe micturition-related urgency episodes[b] per 24 hours		
Baseline		
Mean (SD)	1.6 (2.6)	1.7 (2.7)
Median (range)	0.6 (0 to 18.0)	0.6 (0 to 16.8)
Week 12		
Mean (SD)	0.6 (1.7)	0.9 (2.5)
Median (range)	0 (0 to 14.2)	0 (0 to 28.2)
Numerical change from baseline to Week 12		
Mean (SD)	-1.0 (2.4)	-0.8 (2.7)
Median (range)	-0.2 (-18.0 to 10.8)	-0.2 (-16.8 to 12.0)
LS Mean (SE)	-1.1 (0.1)	-0.7 (0.1)
95% CI for mean, p-value[c]	-1.3, -0.7, <0.0001	-1.1, -0.5, <0.0001
Treatment difference in numerical change[c]	Tolterodine ER + alpha blocker versus placebo + alpha blocker	
LS mean difference (SE)	-0.4 (0.2)	
95% confidence interval	-0.7, 0	
p-value	0.0495	
Percent change from Baseline to Week 12		
Mean (SD)	-38.8 (237.8)	-23.3 (351.5)
Median (range)	-100.0 (-100.0 to 2700.0)	-88.7 (-100.0 to 4800.0)
Treatment difference in percent change[d]	Tolterodine ER + alpha blocker versus placebo + alpha blocker	
p-value	0.0137	

Table 12. Change in Mean Number of Severe Micturition-Related Urgency Episodes per 24 Hours at Week 4 and Week 12

	Tolterodine ER + Alpha-Blocker N=329	Placebo + Alpha-Blocker N=323

ANCOVA = analysis of covariance; CI = confidence interval; ER = extended release; LS = least squares; N = number of subjects; SD = standard deviation; SE = standard error.

a. Number of subjects with non-missing numerical and percent change from Baseline to Week 4/Week 12.
b. Severe urgency episodes were those with a rating of ≥4 on the Urinary Sensation Scale.
c. The p-value was based on a paired t-test comparing Baseline with post-baseline values.
d. The treatment difference was based on an ANCOVA model with terms for country, treatment, treatment by country interaction, and the Baseline value as a covariate.

Daytime and Nocturnal Severe Micturition-Related Urgency Episodes: The mean number of daytime and nocturnal severe micturition-related urgency episodes at Baseline and Weeks 4 and 12, and analyses of the numerical changes from Baseline to Weeks 4 and 12 for each category are presented in Table 13.

Table 13. Change in Mean Number of Daytime and Nocturnal Severe Micturition-Related Urgency Episodes at Week 4 and Week 12

	Daytime Severe Urgency Episodes[a]		Nocturnal Severe Urgency Episodes[a]	
	Tolterodine ER + Alpha-Blocker N=329	Placebo + Alpha-Blocker N=323	Tolterodine ER + Alpha-Blocker N=329	Placebo + Alpha-Blocker N=323
Week 4				
N[b]	302	303	302	303
Baseline				
Mean (SD)	1.2 (2.1)	1.2 (2.1)	0.3 (0.6)	0.3 (0.8)
Median (range)	0.4 (0.0 to 15.6)	0.4 (0.0 to 15.6)	0.0 (0.0 to 4.2)	0.0 (0.0 to 6.0)
Week 4				
Mean (SD)	0.7 (1.6)	0.8 (1.7)	0.2 (0.6)	0.2 (0.5)
Median (range)	0.0 (0.0 to 9.0)	0.0 (0.0 to 11.0)	0.0 (0.0 to 5.8)	0.0 (0.0 to 5.2)
Numerical change from baseline to Week 4				
Mean (SD)	-0.5 (1.9)	-0.5 (1.8)	-0.1 (0.6)	-0.2 (0.8)
Median (range)	0.0 (-15.6 to 8.0)	0.0 (-10.8 to 9.8)	0.0 (-4.0 to 2.8)	0.0 (-6.0 to 5.2)
LS Mean (SE)	-0.5 (0.1)	-0.5 (0.1)	-0.1 (0.0)	-0.1 (0.0)
95% CI for mean, p-value[c]	-0.8, -0.3, <.0001	-0.7, -0.3, <.0001	-0.2, -0.0, 0.0106	-0.3, -0.1, 0.0001
Treatment difference in numerical change[d]	Tolterodine ER + alpha blocker versus placebo + alpha blocker			
LS mean difference (SE)	-0.0 (0.1)		0.0 (0.0)	
95% confidence interval	-0.3, 0.2		-0.1, 0.1	
p-value	0.7505		0.4680	
Week 12				
N[b]	302	303	302	303
Baseline				
Mean (SD)	1.2 (2.1)	1.2 (2.1)	0.3 (0.6)	0.3 (0.8)
Median (range)	0.4 (0 to 15.6)	0.4 (0 to 15.6)	0 (0 to 4.2)	0 (0 to 6.0)
Week 12				
Mean (SD)	0.5 (1.4)	0.7 (1.9)	0.1 (0.4)	0.2 (0.9)
Median (range)	0 (0 to 11.6)	0 (0 to 15.2)	0 (0 to 2.6)	0 (0 to 13.0)
Numerical change from Baseline to Week 12				
Mean (SD)	-0.8 (2.0)	-0.5 (2.0)	-0.2 (0.6)	-0.2 (1.0)
Median (range)	-0.2 (-15.6 to 9.6)	-0.2 (-10.8 to 9.6)	0 (-4.0 to 2.6)	0 (-6.0 to 10.2)
LS mean (SE)	-0.8 (0.1)	-0.5 (0.1)	-0.2 (0)	-0.1 (0)
95% CI for mean, p-value[c]	-1.0, -0.5, <0.0001	-0.8, -0.3, <0.0001	-0.2, -0.1, <0.0001	-0.3, -0.1, 0.0042
Treatment difference in numerical change[d]	Tolterodine ER + alpha blocker versus placebo + alpha blocker			
LS mean difference (SE)	-0.3 (0.1)		-0.1 (0.1)	
95% CI	-0.5, 0		-0.2, 0.1	
p-value	0.0443		0.2750	

ANCOVA = analysis of covariance; CI = confidence interval; ER = extended release; LS = least squares; N = number of subjects; SD = standard deviation; SE = standard error.

a. Severe urgency episodes were those with a rating of ≥4 on the Urinary Sensation Scale.
b. Number of subjects with non-missing numerical change from Baseline to Week 4/Week 12.
c. The p-value was based on a paired t-test comparing Baseline with post-baseline values.
d. The treatment difference was based on an ANCOVA model with terms for country, treatment, treatment by country interaction, and the Baseline value as a covariate.

Patient Perception of Bladder Condition at Week 4: The proportion of subjects who improved from Baseline in PPBC at Week 12 was the primary efficacy endpoint for this study, while an analysis of the PPBC data at Week 4 was included as a secondary endpoint. Analysis of the number and percent of subjects at each assessment on the 6-point PPBC scale at Week 4 is presented in Table 14.

Table 14. Patient's Perception of Bladder Condition at Week 4

	Tolterodine ER + Alpha-Blocker N=329	Placebo + Alpha-Blocker N=323
	n (%)	
N[a]	304 (100)	305 (100)
Baseline		
No problems at all	0	0
Some very minor problems	1 (0.3)	1 (0.3)
Some minor problems	2 (0.7)	1 (0.3)
Some moderate problems	213 (70.1)	193 (63.3)
Severe problems	78 (25.6)	101 (33.1)
Many severe problems	10 (3.3)	9 (3.0)
Week 4		
No problems at all	7 (2.3)	12 (3.9)
Some very minor problems	30 (9.9)	19 (6.2)
Some minor problems	88 (28.9)	76 (24.9)
Some moderate problems	138 (45.4)	151 (49.5)
Severe problems	37 (12.2)	44 (14.4)
Many severe problems	4 (1.3)	3 (1.0)
Change From Baseline to Week 4		
Binary assessment		
Improvement	172 (56.6)	162 (53.1)
No improvement	132 (43.4)	143 (46.9)
95% CI	50.8, 62.2	47.3, 58.8
p-value[b]	0.4609	
Odds ratio (95% CI)	0.88 (0.63, 1.23)	

CI = confidence interval; ER = extended release; N = number of subjects; n = number of subjects at each assessment.

a. Number of subjects with non-missing Baseline and Week 4 values.

b. The p-value was obtained from a Cochran-Mantel-Haenszel test stratified by country.

In addition to the binary assessment of improvement, 2 ordinal variables were analyzed at Week 4 and Week 12. The results are present in Table 15.

Table 15. Change in Ordinal Assessments for Patient's Perception of Bladder Condition

	Tolterodine ER + Alpha-Blocker N=329		Placebo + Alpha-Blocker N=323
	n (%)		
N[a]	304 (100)		305 (100)
Change from Baseline to Week 4			
Ordinal assessment			
Improvement	172 (56.6)		162 (53.1)
No change	111 (36.5)		129 (42.3)
Deterioration	21 (6.9)		14 (4.6)
p-value[b]		0.1560	
Major improvement	54 (17.8)		51 (16.7)
Minor improvement	118 (38.8)		111 (36.4)
No change	111 (36.5)		129 (42.3)
Deterioration	21 (6.9)		14 (4.6)
p-value[b]		0.1464	
N[a]	305 (100)		305 (100)
Change from Baseline to Week 12			
Ordinal assessment			
Improvement	194 (63.6)		188 (61.6)
No change	99 (32.5)		102 (33.4)
Deterioration	12 (3.9)		15 (4.9)
p-value[b]		0.9161	
Major improvement	84 (27.5)		81 (26.6)
Minor improvement	110 (36.1)		107 (35.1)
No change	99 (32.5)		102 (33.4)
Deterioration	12 (3.9)		15 (4.9)
p-value[b]		0.9731	

ER = extended release; N = number of subjects; n = number of subjects at each assessment.
a. Number of subjects with non-missing Baseline and Week 4 and Week 12 values.
b. The p-value was obtained from a Cochran-Mantel-Haenszel test with modified ridit scoring, stratified by country.

Overactive Bladder Questionnaire: The OAB-q assessed how much subjects were bothered by selected bladder symptoms during the previous 4 weeks. A set of 8 questions comprised the symptom severity/bother score. The other questions comprised the HRQOL component, which included domains for coping, concern, sleep, and social function. The change in the total score of OAB-q and changes in total scores of each domain of OAB-q at Week 4 and Week 12 relative to Baseline were analysed (Table 16).

Table 16. Change in the Total and Domain Scores of OAB-q at Weeks 4 and 12

	Tolterodine ER + Alpha-Blocker N=329	Placebo + Alpha-Blocker N=323	Tolterodine ER + Alpha-Blocker N=329	Placebo + Alpha-Blocker N=323	Tolterodine ER + Alpha-Blocker N=329	Placebo + Alpha-Blocker N=323
	OAB-q Total Symptom Bother Score		OAB-q Coping Domain Score		OAB-q Concern Domain Score	
Week 4						
N[a]	303	306	304	306	304	306
Baseline						
Mean (SD)	45.3 (16.0)	45.7 (16.1)	64.6 (21.8)	64.4 (22.3)	67.6 (19.3)	67.5 (18.7)
Median (range)	42.5 (5.0 to 90.0)	45.0 (10.0 to 92.5)	67.5 (5.0 to 100.0)	67.5 (2.5 to 100.0)	68.6 (14.3 to 100.0)	70.0 (5.7 to 100.0)
Week 4						
Mean (SD)	32.6 (16.5)	36.2 (16.1)	74.7 (21.8)	72.7 (20.6)	76.4 (19.0)	75.1 (18.1)
Median (range)	30.0 (0.0 to 97.5)	35.0 (0.0 to 90.0)	80.0 (7.5 to 100.0)	77.5 (7.5 to 100.0)	80.0 (11.4 to 100.0)	77.1 (20.0 to 100.0)
Numerical change from baseline to Week 4						
Mean (SD)	-12.7 (15.8)	-9.5 (16.6)	10.1 (15.0)	8.2 (16.5)	8.8 (15.4)	7.6 (16.6)
Median (range)	-10.0 (-75.0 to 32.5)	-7.5 (-72.5 to 37.5)	10.0 (-57.5 to 57.5)	7.5 (-45.0 to 72.5)	8.6 (-45.7 to 68.6)	5.7 (-45.7 to 71.4)
LS Mean (SE)	-12.9 (0.9)	-9.9 (0.9)	10.4 (0.9)	8.7 (0.9)	9.2 (0.9)	7.6 (0.9)
95% CI for mean, p-value[b]	-14.5, -11.0, <0.0001	-11.4, -7.6, <0.0001	8.4, 11.8, <0.0001	6.4, 10.1, <0.0001	7.1, 10.5, <0.0001	5.7, 9.4, <0.0001
Treatment difference in numerical change[c]	Tolterodine ER + alpha blocker versus placebo + alpha blocker					
LS mean difference (SE)	-3.0 (1.3)		1.7 (1.3)		1.5 (1.3)	
95% confidence interval	-5.5, -0.5		-0.8, 4.3		-1.0, 4.0	
p-value	0.0175		0.1829		0.2285	
Week 12						
N[a]	304	306	305	306	305	306
Baseline						
Mean (SD)	45.4 (16.0)	45.7 (16.1)	64.5 (21.8)	64.4 (22.3)	67.5 (19.3)	67.5 (18.7)
Median (range)	42.5 (5.0 to 90.0)	45.0 (10.0 to 92.5)	67.5 (5.0 to 100.0)	67.5 (2.5 to 100.0)	68.6 (14.3 to 100.0)	70.0 (5.7 to 100.0)
Week 12						
Mean (SD)	28.3 (15.6)	31.8 (15.7)	78.9 (20.6)	75.7 (21.3)	80.6 (18.7)	78.2 (18.5)
Median (range)	27.5 (2.5 to 75.0)	30.0 (0.0 to 92.5)	85.0 (7.5 to 100.0)	80.0 (2.5 to 100.0)	85.7 (8.6 to 100.0)	82.9 (8.6 to 100.0)
Numerical change from Baseline to Week 12						
Mean (SD)	-17.1 (17.4)	-13.9 (17.9)	14.4 (18.6)	11.3 (19.7)	13.1 (17.8)	10.6 (18.4)
Median (range)	-15.0 (-75.0 to 37.5)	-12.5 (-72.5 to 42.5)	10.0 (-52.5 to 90.0)	7.5 (-42.5 to 92.5)	11.4 (-42.9 to 74.3)	8.6 (-42.9 to 85.7)
LS mean (SE)	-17.9 (0.9)	-14.4 (0.9)	15.4 (1.1)	12.4 (1.0)	13.6 (1.0)	11.4 (1.0)
95% CI for mean, p-value[b]	-19.0, -15.1, <0.0001	-16.0, -11.9, <0.0001	12.3, 16.5, <0.0001	9.1, 13.5, <0.0001	11.1, 15.1, <0.0001	8.6, 12.7, <0.0001
Treatment difference in numerical change[c]	Tolterodine ER + alpha blocker versus placebo + alpha blocker					
LS mean difference (SE)	-3.5 (1.3)		2.9 (1.5)		2.2 (1.4)	
95% CI	-6.0, -0.9		0.0, 5.9		-0.6, 5.0	
p-value	0.0086		0.0491		0.1287	

Table 16. Change in the Total and Domain Scores of OAB-q at Weeks 4 and 12

	Tolterodine ER + Alpha-Blocker N=329	Placebo + Alpha-Blocker N=323	Tolterodine ER + Alpha-Blocker N=329	Placebo + Alpha-Blocker N=323	Tolterodine ER + Alpha-Blocker N=329	Placebo + Alpha-Blocker N=323
	OAB-q Sleep Domain Score		**OAB-q Social Interaction Domain Score**		**OAB-q Total HRQOL Score**	
Week 4						
N[a]	304	306	304	306	304	306
Baseline						
Mean (SD)	56.9 (20.8)	58.1 (21.5)	82.5 (18.2)	82.6 (18.6)	67.5 (17.1)	67.7 (17.4)
Median (range)	58.0 (8.0 to 100.0)	60.0 (4.0 to 100.0)	88.0 (20.0 to 100.0)	88.0 (12.0 to 100.0)	68.8 (15.2 to 99.2)	70.8 (8.0 to 98.4)
Week 4						
Mean (SD)	66.5 (21.4)	64.7 (21.1)	87.2 (15.7)	86.9 (16.5)	76.0 (17.2)	74.6 (16.4)
Median (range)	68.0 (0.0 to 100.0)	68.0 (4.0 to 100.0)	92.0 (20.0 to 100.0)	92.0 (12.0 to 100.0)	80.8 (10.4 to 100.0)	77.6 (16.8 to 100.0)
Numerical change from baseline to Week 4						
Mean (SD)	9.6 (17.4)	6.6 (16.9)	4.6 (13.1)	4.3 (13.8)	8.6 (12.8)	6.9 (13.9)
Median (range)	8.0 (-48.0 to 72.0)	4.0 (-48.0 to 72.0)	0.0 (-32.0 to 60.0)	0.0 (-32.0 to 88.0)	7.2 (-45.6 to 48.8)	5.2 (-34.4 to 73.6)
LS Mean (SE)	9.8 (1.0)	6.9 (1.0)	5.1 (0.7)	4.3 (0.7)	8.9 (0.8)	7.2 (0.8)
95% CI for mean, p-value[b]	7.6, 11.6, <0.0001	4.7, 8.5, <0.0001	3.1, 6.1, <0.0001	2.7, 5.9, <0.0001	7.1, 10.0, <0.0001	5.4, 8.5, <0.0001
Treatment difference in numerical change[c]	Tolterodine ER + alpha blocker versus placebo + alpha blocker					
LS mean difference (SE)	2.9 (1.4)		0.8 (1.0)		1.7 (1.1)	
95% confidence interval	0.1, 5.7		-1.2, 2.8		-0.4, 3.9	
p-value	0.0393		0.4091		0.1059	
Week 12						
N[a]	305	306	305	306	305	306
Baseline						
Mean (SD)	56.9 (20.8)	58.1 (21.5)	82.6 (18.2)	82.6 (18.6)	67.4 (17.1)	67.7 (17.4)
Median (range)	56.0 (8.0 to 100.0)	60.0 (4.0 to 100.0)	88.0 (20.0 to 100.0)	88.0 (12.0 to 100.0)	68.8 (15.2 to 99.2)	70.8 (8.0 to 98.4)
Week 12						
Mean (SD)	69.7 (21.7)	69.3 (20.1)	89.3 (15.7)	88.3 (16.6)	79.7 (17.2)	77.6 (16.8)
Median (range)	76.0 (4.0 to 100.0)	72.0 (4.0 to 100.0)	96.0 (0.0 to 100.0)	96.0 (8.0 to 100.0)	84.8 (10.4 to 100.0)	82.4 (12.0 to 100.0)
Numerical change from Baseline to Week 12						
Mean (SD)	12.9 (19.9)	11.2 (20.7)	6.8 (15.1)	5.7 (16.4)	12.2 (15.5)	10.0 (16.6)
Median (range)	12.0 (-52.0 to 76.0)	8.0 (-60.0 to 88.0)	4.0 (-36.0 to 80.0)	0.0 (-48.0 to 88.0)	10.4 (-26.4 to 78.4)	7.2 (-33.6 to 84.8)
LS mean (SE)	13.4 (1.2)	12.1 (1.1)	7.4 (0.8)	6.1 (0.8)	12.9 (0.9)	10.8 (0.9)
95% CI for mean, p-value[b]	10.6, 15.1, <0.0001	8.9, 13.5, <0.0001	5.1, 8.5, <0.0001	3.9, 7.6, <0.0001	10.5, 14.0, <0.0001	8.1, 11.8, <0.0001
Treatment difference in numerical change[c]	Tolterodine ER + alpha blocker versus placebo + alpha blocker					
LS mean difference (SE)	1.3 (1.6)		1.2 (1.2)		2.1 (1.3)	
95% CI	-1.9, 4.5		-1.1, 3.6		-0.4, 4.6	
p-value	0.4210		0.2983		0.1028	

Table 16. Change in the Total and Domain Scores of OAB-q at Weeks 4 and 12

	Tolterodine ER + Alpha-Blocker N=329	Placebo + Alpha-Blocker N=323	Tolterodine ER + Alpha-Blocker N=329	Placebo + Alpha-Blocker N=323	Tolterodine ER + Alpha-Blocker N=329	Placebo + Alpha-Blocker N=323

ANCOVA = analysis of covariance; CI = confidence interval; ER = extended release; HRQOL = health-related quality of life; LS = least squares; N = number of subjects; OAB-q = Overactive Bladder Questionnaire; SD = standard deviation; SE = standard error.

a. Number of subjects with non-missing numerical change from baseline to Week 4/Week 12.

b. p-Value was based on paired t-test comparing baseline with post-baseline values.

c. Based on an ANCOVA model with terms for country, treatment and treatment by country interaction with baseline value as a covariate.

International Prostate Symptom Score: The IPSS contains a 7-item Symptom index, on which subjects rated how frequently they were bothered by 3 storage symptoms (frequency, urgency, nocturia) and 4 voiding symptoms (straining, incomplete emptying, intermittency, weak stream).

The mean scores at Baseline and Weeks 4 and 12 for total IPSS and the storage and voiding subscales, and analyses of the numerical changes from Baseline to Weeks 4 and 12 for each are presented in Table 17.

Table 17. Change in IPSS Domain and Index Scores at Weeks 4 and 12

	Tolterodine ER + Alpha-Blocker N=329	Placebo + Alpha-Blocker N=323	Tolterodine ER + Alpha-Blocker N=329	Placebo + Alpha-Blocker N=323	Tolterodine ER + Alpha-Blocker N=329	Placebo + Alpha-Blocker N=323
	IPSS Index Score		IPSS Storage Domain		IPSS Voiding Domain	
Week 4						
N[a]	303	304	303	305	304	305
Baseline						
Mean (SD)	18.7 (6.5)	18.3 (6.4)	9.3 (2.6)	9.2 (2.6)	9.3 (5.0)	9.1 (4.9)
Median (range)	18.0 (3.0 to 35.0)	18.0 (2.0 to 35.0)	9.0 (3.0 to 15.0)	9.0 (2.0 to 15.0)	9.0 (0.0 to 20.0)	8.0 (0.0 to 20.0)
Week 4						
Mean (SD)	15.3 (6.6)	15.4 (6.3)	7.3 (3.0)	7.7 (2.8)	8.0 (4.7)	7.7 (4.5)
Median (range)	15.0 (2.0 to 33.0)	15.0 (3.0 to 34.0)	7.0 (1.0 to 15.0)	8.0 (2.0 to 15.0)	8.0 (0.0 to 20.0)	7.0 (0.0 to 20.0)
Numerical change from Baseline to Week 4						
Mean (SD)	-3.3 (5.4)	-3.0 (5.5)	-2.0 (2.8)	-1.5 (2.7)	-1.3 (3.5)	-1.4 (3.7)
Median (range)	-3.0 (-20.0 to 14.0)	-2.5 (-20.0 to 12.0)	-2.0 (-10.0 to 6.0)	-1.0 (-10.0 to 8.0)	-1.0 (-16.0 to 10.0)	-1.0 (-15.0 to 11.0)
LS Mean (SE)	-3.2 (0.3)	-3.3 (0.3)	-1.9 (0.2)	-1.6 (0.2)	-1.3 (0.2)	-1.7 (0.2)
95% CI for mean, p-value[b]	-3.9, -2.7, <0.0001	-3.6, -2.3, <0.0001	-2.3, -1.7, <0.0001	-1.8, -1.2, <0.0001	-1.7, -0.9, <0.0001	-1.9, -1.0, <0.0001
Treatment difference in numerical change[c]	Tolterodine ER + alpha blocker versus placebo + alpha blocker					
LS mean difference (SE)	0.0 (0.4)		-0.3 (0.2)		0.3 (0.3)	
95% confidence interval	-0.8, 0.9		-0.7, 0.1		-0.2, 0.9	
p-value	0.9156		0.1795		0.2498	
Week 12						
N[a]	305	305	305	306	305	305
Baseline						
Mean (SD)	18.7 (6.5)	18.3 (6.5)	9.3 (2.6)	9.2 (2.6)	9.4 (5.0)	9.1 (4.9)
Median (range)	18.0 (3.0 to 35.0)	18.0 (2.0 to 35.0)	9.0 (3.0 to 15.0)	9.0 (2.0 to 15.0)	9.0 (0.0 to 20.0)	8.0 (0.0 to 20.0)
Week 12						
Mean (SD)	14.2 (6.9)	14.5 (6.7)	6.7 (3.0)	7.3 (3.0)	7.5 (4.8)	7.2 (4.6)
Median (range)	14.0 (0.0 to 33.0)	14.0 (1.0 to 35.0)	6.0 (0.0 to 14.0)	7.0 (1.0 to 15.0)	7.0 (0.0 to 20.0)	7.0 (0.0 to 20.0)
Numerical change from Baseline to Week 12						
Mean (SD)	-4.5 (5.9)	-3.8 (6.7)	-2.6 (2.9)	-1.9 (3.2)	-1.8 (4.0)	-1.9 (4.3)
Median (range)	-4.0 (-26.0 to 10.0)	-3.0 (-24.0 to 17.0)	-2.0 (-11.0 to 6.0)	-2.0 (-12.0 to 8.0)	-1.0 (-17.0 to 7.0)	-1.0 (-16.0 to 14.0)
LS mean (SE)	-4.7 (0.4)	-4.3 (0.4)	-2.6 (0.2)	-2.1 (0.2)	-2.0 (0.2)	-2.1 (0.2)
95% CI for mean, p-value[b]	-5.1, -3.8, <0.0001	-4.6, -3.1, <0.0001	-3.0, -2.3, <0.0001	-2.3, -1.6, <0.0001	-2.3, -1.4, <0.0001	-2.4, -1.4, <0.0001
Treatment difference in numerical change[c]	Tolterodine ER + alpha blocker versus placebo + alpha blocker					
LS mean difference (SE)	-0.4 (0.5)		-0.5 (0.2)		0.1 (0.3)	
95% CI	-1.4, 0.6		-1.0, -0.0		-0.5, 0.7	
p-value	0.4223		0.0370		0.7655	

Table 17. Change in IPSS Domain and Index Scores at Weeks 4 and 12

	Tolterodine ER + Alpha-Blocker N=329	Placebo + Alpha-Blocker N=323	Tolterodine ER + Alpha-Blocker N=329	Placebo + Alpha-Blocker N=323	Tolterodine ER + Alpha-Blocker N=329	Placebo + Alpha-Blocker N=323
	IPSS Index Score		IPSS Storage Domain		IPSS Voiding Domain	

ANCOVA = analysis of covariance; CI = confidence interval; ER = extended release; IPSS = International Prostate Symptom Score; LS = least squares; N = number of subjects; SD = standard deviation; SE = standard error.

a. Number of subjects with non-missing numerical change from baseline to Week 4/Week 12.

b. p-Value was based on paired t-test comparing baseline with post-baseline values.

c. Based on an ANCOVA model with terms for country, treatment and treatment by country interaction with baseline value as a covariate.

The changes in score for each item (questions 1 through 7) in the IPSS at Week 4 and Week 12 relative to Baseline were analyzed. Responses to the QoL question (question 8) that assessed the impact of urinary symptoms on the QoL were also evaluated. The results from the analyses of these individual items are summarized in Table 18.

Table 18. Change in IPSS Individual Item and QoL Scores at Weeks 4 and 12

	Tolterodine ER + Alpha-Blocker N=329	Placebo + Alpha-Blocker N=323	Tolterodine ER + Alpha-Blocker N=329	Placebo + Alpha-Blocker N=323	Tolterodine ER + Alpha-Blocker N=329	Placebo + Alpha-Blocker N=323
	IPSS Not Emptying Item		IPSS Urinating Again Item		IPSS Stop/Start Item	
Week 4						
N[a]	304	306	304	306	304	306
Baseline						
Mean (SD)	2.6 (1.5)	2.5 (1.6)	3.4 (1.2)	3.4 (1.3)	2.4 (1.7)	2.3 (1.6)
Median (range)	3.0 (0.0 to 5.0)	3.0 (0.0 to 5.0)	3.0 (0.0 to 5.0)	3.0 (0.0 to 5.0)	2.0 (0.0 to 5.0)	2.0 (0.0 to 5.0)
Week 4						
Mean (SD)	2.2 (1.5)	2.2 (1.5)	2.7 (1.4)	2.8 (1.3)	2.1 (1.5)	1.9 (1.4)
Median (range)	2.0 (0.0 to 5.0)	2.0 (0.0 to 5.0)	3.0 (0.0 to 5.0)	3.0 (0.0 to 5.0)	2.0 (0.0 to 5.0)	2.0 (0.0 to 5.0)
Numerical change from baseline to Week 4						
Mean (SD)	-0.4 (1.4)	-0.3 (1.5)	-0.7 (1.4)	-0.6 (1.3)	-0.3 (1.4)	-0.4 (1.4)
Median (range)	0.0 (-5.0 to 3.0)	0.0 (-4.0 to 5.0)	-1.0 (-5.0 to 4.0)	0.0 (-5.0 to 3.0)	0.0 (-5.0 to 4.0)	0.0 (-5.0 to 4.0)
LS Mean (SE)	-0.4 (0.1)	-0.4 (0.1)	-0.7 (0.1)	-0.6 (0.1)	-0.3 (0.1)	-0.5 (0.1)
95% CI for mean, p-value[b]	-0.6, -0.2, <0.0001	-0.5, -0.2, <0.0001	-0.8, -0.5, <0.0001	-0.7, -0.4, <0.0001	-0.5, -0.2, <0.0001	-0.6, -0.2, <0.0001
Treatment difference in numerical change[c]	Tolterodine ER + alpha blocker versus placebo + alpha blocker					
LS mean difference (SE)	0.0 (0.1)		-0.1 (0.1)		0.2 (0.1)	
95% confidence interval	-0.2, 0.3		-0.3, 0.1		-0.0, 0.4	
p-value	0.7823		0.5076		0.0558	
Week 12						
N[a]	305	306	305	306	305	306
Baseline						
Mean (SD)	2.6 (1.5)	2.5 (1.6)	3.4 (1.2)	3.4 (1.3)	2.4 (1.7)	2.3 (1.6)
Median (range)	3.0 (0.0 to 5.0)	3.0 (0.0 to 5.0)	3.0 (0.0 to 5.0)	3.0 (0.0 to 5.0)	2.0 (0.0 to 5.0)	2.0 (0.0 to 5.0)
Week 12						
Mean (SD)	2.0 (1.4)	1.9 (1.4)	2.4 (1.3)	2.7 (1.4)	2.0 (1.5)	1.8 (1.5)
Median (range)	2.0 (0.0 to 5.0)	2.0 (0.0 to 5.0)	2.0 (0.0 to 5.0)	3.0 (0.0 to 5.0)	2.0 (0.0 to 5.0)	2.0 (0.0 to 5.0)
Numerical change from Baseline to Week 12						
Mean (SD)	-0.6 (1.5)	-0.7 (1.5)	-0.9 (1.3)	-0.7 (1.4)	-0.5 (1.4)	-0.4 (1.5)
Median (range)	0.0 (-5.0 to 4.0)	-1.0 (-5.0 to 5.0)	-1.0 (-4.0 to 3.0)	-1.0 (-4.0 to 4.0)	0.0 (-5.0 to 4.0)	0.0 (-5.0 to 3.0)
LS mean (SE)	-0.6 (0.1)	-0.7 (0.1)	-1.0 (0.1)	-0.8 (0.1)	-0.5 (0.1)	-0.5 (0.1)
95% CI for mean, p-value[b]	-0.7, -0.4, <0.0001	-0.8, -0.5, <0.0001	-1.1, -0.8, <0.0001	-0.9, -0.6, <0.0001	-0.6, -0.3, <0.0001	-0.6, -0.3, <0.0001
Treatment difference in numerical change[c]	Tolterodine ER + alpha blocker versus placebo + alpha blocker					
LS mean difference (SE)	0.1 (0.1)		-0.2 (0.1)		0.0 (0.1)	
95% CI	-0.1, 0.3		-0.4, 0.0		-0.2, 0.2	
p-value	0.3962		0.0840		0.9021	

Table 18. Change in IPSS Individual Item and QoL Scores at Weeks 4 and 12

	Tolterodine ER + Alpha-Blocker N=329	Placebo + Alpha-Blocker N=323	Tolterodine ER + Alpha-Blocker N=329	Placebo + Alpha-Blocker N=323	Tolterodine ER + Alpha-Blocker N=329	Placebo + Alpha-Blocker N=323
	IPSS Postpone Item		IPSS Weak Stream Item		IPSS Push/Strain Item	
Week 4						
N[a]	304	305	304	305	304	306
Baseline						
Mean (SD)	3.0 (1.4)	3.0 (1.4)	2.8 (1.6)	2.8 (1.6)	1.6 (1.5)	1.6 (1.5)
Median (range)	3.0 (0.0 to 5.0)	3.0 (0.0 to 5.0)	3.0 (0.0 to 5.0)	3.0 (0.0 to 5.0)	1.0 (0.0 to 5.0)	1.0 (0.0 to 5.0)
Week 4						
Mean (SD)	2.2 (1.4)	2.4 (1.4)	2.4 (1.6)	2.4 (1.6)	1.4 (1.4)	1.3 (1.3)
Median (range)	2.0 (0.0 to 5.0)	2.0 (0.0 to 5.0)	2.0 (0.0 to 5.0)	2.0 (0.0 to 5.0)	1.0 (0.0 to 5.0)	1.0 (0.0 to 5.0)
Numerical change from baseline to Week 4						
Mean (SD)	-0.8 (1.4)	-0.6 (1.4)	-0.4 (1.3)	-0.4 (1.4)	-0.2 (1.2)	-0.3 (1.1)
Median (range)	-1.0 (-5.0 to 4.0)	0.0 (-5.0 to 3.0)	0.0 (-5.0 to 5.0)	0.0 (-5.0 to 5.0)	0.0 (-5.0 to 4.0)	0.0 (-4.0 to 3.0)
LS Mean (SE)	-0.8 (0.1)	-0.6 (0.1)	-0.4 (0.1)	-0.4 (0.1)	-0.2 (0.1)	-0.3 (0.1)
95% CI for mean, p-value[b]	-0.9, -0.6, <0.0001	-0.7, -0.4, <0.0001	-0.5, -0.3, <0.0001	-0.5, -0.2, <0.0001	-0.4, -0.1, 0.0026	-0.4, -0.2, <0.0001
Treatment difference in numerical change[c]	Tolterodine ER + alpha blocker versus placebo + alpha blocker					
LS mean difference (SE)	-0.2 (0.1)		-0.0 (0.1)		0.1 (0.1)	
95% confidence interval	-0.4, 0.0		-0.2, 0.2		-0.1, 0.3	
p-value	0.0736		0.8805		0.2157	
Week 12						
N[a]	305	306	305	305	305	306
Baseline						
Mean (SD)	3.0 (1.4)	3.0 (1.4)	2.8 (1.6)	2.8 (1.6)	1.6 (1.5)	1.6 (1.5)
Median (range)	3.0 (0.0 to 5.0)	3.0 (0.0 to 5.0)	3.0 (0.0 to 5.0)	3.0 (0.0 to 5.0)	1.0 (0.0 to 5.0)	1.0 (0.0 to 5.0)
Week 12						
Mean (SD)	2.0 (1.4)	2.2 (1.4)	2.2 (1.5)	2.3 (1.5)	1.3 (1.4)	1.3 (1.3)
Median (range)	2.0 (0.0 to 5.0)	2.0 (0.0 to 5.0)	2.0 (0.0 to 5.0)	2.0 (0.0 to 5.0)	1.0 (0.0 to 5.0)	1.0 (0.0 to 5.0)
Numerical change from Baseline to Week 12						
Mean (SD)	-1.0 (1.4)	-0.8 (1.6)	-0.6 (1.3)	-0.5 (1.4)	-0.2 (1.3)	-0.3 (1.3)
Median (range)	-1.0 (-5.0 to 4.0)	-1.0 (-5.0 to 4.0)	0.0 (-5.0 to 4.0)	0.0 (-4.0 to 5.0)	0.0 (-5.0 to 5.0)	0.0 (-5.0 to 5.0)
LS mean (SE)	-1.0 (0.1)	-0.8 (0.1)	-0.6 (0.1)	-0.5 (0.1)	-0.2 (0.1)	-0.4 (0.1)
95% CI for mean, p-value[b]	-1.1, -0.8, <0.0001	-0.9, -0.6, <0.0001	-0.7, -0.4, <0.0001	-0.7, -0.3, <0.0001	-0.4, -0.1, 0.0024	-0.5, -0.2, <0.0001
Treatment difference in numerical change[c]	Tolterodine ER + alpha blocker versus placebo + alpha blocker					
LS mean difference (SE)	-0.1 (0.1)		-0.1 (0.1)		0.1 (0.1)	
95% CI	-0.4, 0.1		-0.3, 0.1		-0.1, 0.3	
p-value	0.2497		0.3370		0.2816	

Table 18. Change in IPSS Individual Item and QoL Scores at Weeks 4 and 12

	Tolterodine ER + Alpha-Blocker N=329	Placebo + Alpha-Blocker N=323	Tolterodine ER + Alpha-Blocker N=329	Placebo + Alpha-Blocker N=323	Tolterodine ER + Alpha-Blocker N=329	Placebo + Alpha-Blocker N=323
	IPSS Nocturia Item		IPSS Quality of Life Item			
Week 4						
N[a]	303	306	304	306		
Baseline						
Mean (SD)	3.0 (1.2)	2.8 (1.2)	4.2 (1.2)	4.2 (1.1)		
Median (range)	3.0 (0.0 to 5.0)	3.0 (0.0 to 5.0)	4.0 (0.0 to 6.0)	4.0 (1.0 to 6.0)		
Week 4						
Mean (SD)	2.4 (1.3)	2.4 (1.2)	3.5 (1.3)	3.6 (1.3)		
Median (range)	2.0 (0.0 to 5.0)	2.0 (0.0 to 5.0)	3.5 (1.0 to 6.0)	4.0 (0.0 to 6.0)		
Numerical change from baseline to Week 4						
Mean (SD)	-0.5 (1.1)	-0.4 (1.2)	-0.6 (1.1)	-0.6 (1.2)		
Median (range)	0.0 (-4.0 to 4.0)	0.0 (-4.0 to 3.0)	-1.0 (-4.0 to 4.0)	0.0 (-4.0 to 3.0)		
LS Mean (SE)	-0.5 (0.1)	-0.4 (0.1)	-0.6 (0.1)	-0.6 (0.1)		
95% CI for mean, p-value[b]	-0.7, -0.4, <0.0001	-0.5, -0.2, <0.0001	-0.8, -0.5, <0.0001	-0.7, -0.4, <0.0001		
Treatment difference in numerical change[c]	Tolterodine ER + alpha blocker versus placebo + alpha blocker					
LS mean difference (SE)	-0.1 (0.1)		-0.1 (0.1)			
95% confidence interval	-0.2, 0.1		-0.3, 0.1			
p-value	0.5655		0.4879			
Week 12						
N[a]	305	306	305	306		
Baseline						
Mean (SD)	3.0 (1.2)	2.8 (1.2)	4.2 (1.2)	4.2 (1.1)		
Median (range)	3.0 (0.0 to 5.0)	3.0 (0.0 to 5.0)	4.0 (0.0 to 6.0)	4.0 (1.0 to 6.0)		
Week 12						
Mean (SD)	2.2 (1.3)	2.4 (1.2)	3.1 (1.4)	3.3 (1.4)		
Median (range)	2.0 (0.0 to 5.0)	2.0 (0.0 to 5.0)	3.0 (0.0 to 6.0)	3.0 (0.0 to 6.0)		
Numerical change from Baseline to Week 12						
Mean (SD)	-0.7 (1.3)	-0.4 (1.3)	-1.1 (1.5)	-0.8 (1.4)		
Median (range)	-1.0 (-5.0 to 4.0)	0.0 (-4.0 to 3.0)	-1.0 (-6.0 to 4.0)	-1.0 (-6.0 to 2.0)		
LS mean (SE)	-0.7 (0.1)	-0.5 (0.1)	-1.1 (0.1)	-0.9 (0.1)		
95% CI for mean, p-value[b]	-0.9, -0.6, <0.0001	-0.6, -0.3, <0.0001	-1.2, -0.9, <0.0001	-1.0, -0.7, <0.0001		
Treatment difference in numerical change[c]	Tolterodine ER + alpha blocker versus placebo + alpha blocker					
LS mean difference (SE)	-0.2 (0.1)		-0.2 (0.1)			
95% CI	-0.4, 0.0		-0.4, 0.0			
p-value	0.0542		0.0762			

Table 18. Change in IPSS Individual Item and QoL Scores at Weeks 4 and 12

	Tolterodine ER + Alpha-Blocker N=329	Placebo + Alpha-Blocker N=323	Tolterodine ER + Alpha-Blocker N=329	Placebo + Alpha-Blocker N=323	Tolterodine ER + Alpha-Blocker N=329	Placebo + Alpha-Blocker N=323

ANCOVA = analysis of covariance; CI = confidence interval; ER = extended release; IPSS = International Prostate Symptom Score; LS = least squares; N = number of subjects; QoL = quality of life; SD = standard deviation; SE = standard error.

a. Number of subjects with non-missing numerical change from baseline to Week 4/Week 12.

b. p-Value was based on paired t-test comparing baseline with post-baseline values.

c. Based on an ANCOVA model with terms for country, treatment and treatment by country interaction with baseline value as a covariate.

International Consultation on Incontinence Modular Questionnaire–Male Sexual Matters Associated with Lower Urinary Tract Symptoms: The ICIQ-MLUTSsex questionnaire was composed of 5 items to assess the subject's perception of sexual matters related to urinary symptoms before and after treatment. An analysis of the change in the total score at Week 12 relative to Baseline is presented in Table 19.

Table 19. Change in Total Score on the ICIQ-MLUTSsex Questionnaire at Week 12

	Tolterodine ER + Alpha-Blocker N=329	Placebo + Alpha-Blocker N=323
N[a]	287	291
Baseline		
Mean (SD)	3.0 (2.1)	3.0 (2.2)
Median (range)	3.0 (0 to 9.0)	3.0 (0 to 9.0)
Week 12		
Mean (SD)	3.0 (2.0)	2.8 (2.1)
Median (range)	3.0 (0 to 9.0)	3.0 (0 to 9.0)
Numerical change from Baseline to Week 12		
Mean (SD)	0 (1.3)	-0.1 (1.5)
Median (range)	0 (-5.0 to 3.5)	0 (-6.0 to 5.0)
LS mean (SE)	-0.1 (0.1)	-0.1 (0.1)
95% CI for mean, p-value[b]	-0.2, 0.1, 0.7074	-0.3, 0, 0.1513
Treatment difference in numerical change[c]		
LS mean difference (SE)	0 (0.1)	
95% CI	-0.2, 0.3	
p-value	0.9827	

ANCOVA = analysis of covariance; CI = confidence interval; ER = extended release; ICIQ-MLUTSsex = International Consultation on Incontinence Modular Questionnaire–Male Sexual Matters Associated with Lower Urinary Tract Symptoms; LS = least squares; N = number of subjects; SD = standard deviation; SE = standard error.

a. Number of subjects with non-missing numerical change from Baseline to Week 12.
b. The p-value was based on a paired t-test comparing Baseline with Week 12 values.
c. The treatment difference was based on an ANCOVA model with terms for country, treatment, treatment by country interaction, and the Baseline value as a covariate.

Nocturia Quality-of-Life: The impact of nocturia on QoL was assessed with the N-QoL questionnaire. An analysis of the change in N-QoL measures, including the subscales and overall score, from Baseline to Week 12 is shown in Table 20.

Table 20. Change in Mean N-QoL Scores at Week 12

	Tolterodine ER + Alpha-Blocker N=329	Placebo + Alpha-Blocker N=323
N-QoL Sleep/Energy Domain		
N[a]	290	299
Baseline Mean (SD)	20.4 (5.1)	20.1 (5.4)
Week 12 Mean (SD)	22.9 (5.2)	22.8 (4.8)
Numerical change from Baseline to Week 12		
Mean (SD)	2.5 (4.9)	2.7 (4.9)
LS mean (SE)	2.8 (0.3)	2.8 (0.3)
95% CI for mean, p-value[b]	2.0, 3.1, <0.0001	2.1, 3.3, <0.0001
N-QoL Bother/Concern Domain		
N[a]	290	299
Baseline Mean (SD)	18.2 (4.0)	18.2 (3.8)
Week 12 Mean (SD)	20.4 (4.0)	20.4 (3.8)
Numerical change from Baseline to Week 12		
Mean (SD)	2.3 (4.4)	2.2 (4.2)
LS mean (SE)	2.5 (0.2)	2.4 (0.2)
95% CI for mean, p-value[b]	1.8, 2.8, <0.0001	1.7, 2.7, <0.0001
N-QoL Overall Nocturia Score		
N[a]	290	299
Baseline Mean (SD)	38.6 (8.3)	38.4 (8.3)
Week 12 Mean (SD)	43.4 (8.6)	43.3 (7.8)
Numerical change from Baseline to Week 12		
Mean (SD)	4.8 (8.2)	4.9 (8.3)
LS mean (SE)	5.4 (0.5)	5.1 (0.5)
95% CI for mean, p-value[b]	3.8, 5.7, <0.0001	3.9, 5.8, <0.0001

CI = confidence interval; ER = extended release; LS = least squares; N = number of subjects; N-QoL = Nocturia Quality-of-Life questionnaire; SD = standard deviation; SE = standard error.

a. Number of subjects with non-missing numerical change from Baseline to Week 12.

b. The p-value was based on a paired t-test comparing Baseline with Week 12 values.

Overactive Bladder Treatment Satisfaction Questionnaire: The OAB-S evaluated OAB medication expectations, impact on daily life with OAB, and satisfaction with OAB control. There were no consistent statistically significant differences between the groups (tolterodine ER plus alpha-blocker and placebo plus alpha-blocker) in the responses on the OAB-S questionnaire. A summary of the analysis of change in the day-to-day life module and interruption with day-to-day life questions from Baseline to Weeks 4 and 12 is presented in Table 21. This table also includes assessment of the subjects' satisfaction with their OAB medication at Weeks 4 and 12.

Table 21. Results of Analyses of OAB-S Scores at Week 4 and 12

	Tolterodine ER + Alpha-Blocker N=329	Placebo + Alpha-Blocker N=323
Change in OAB-S Day-to-Day Life Domain Score		
Week 4		
N[a]	305	307
Baseline		
Mean (SD)	60.5 (24.2)	59.1 (24.7)
Median (range)	60.0 (0.0 to 100.0)	62.5 (0.0 to 100.0)
Week 4		
Mean (SD)	68.9 (23.2)	66.9 (23.0)
Median (range)	72.5 (0.0 to 100.0)	70.0 (2.5 to 100.0)
Numerical change from baseline to Week 4		
Mean (SD)	8.4 (27.9)	7.8 (24.8)
Median (range)	7.5 (-100.0 to 100.0)	7.5 (-92.5 to 75.0)
LS Mean (SE)	9.8 (1.4)	7.1 (1.3)
95% CI for mean, p-value[b]	5.2, 11.5,<.0001	5.0, 10.6,<.0001
Treatment difference in numerical change[c]	Tolterodine ER + alpha blocker versus placebo + alpha blocker	
LS mean difference (SE)	2.7 (1.9)	
95% confidence interval	-1.1, 6.5	
p-value	0.1610	
Week 12		
N[a]	306	307
Baseline		
Mean (SD)	60.4 (24.2)	59.1 (24.7)
Median (range)	60.0 (0.0 to 100.0)	62.5 (0.0 to 100.0)
Week 12		
Mean (SD)	73.2 (23.7)	69.5 (24.4)
Median (range)	77.5 (0.0 to 100.0)	75.0 (0.0 to 100.0)
Numerical change from baseline to Week 12		
Mean (SD)	12.7 (28.4)	10.4 (28.3)
Median (range)	9.9 (-85.0 to 100.0)	7.5 (-80.0 to 90.0)
LS Mean (SE)	14.1 (1.5)	10.2 (1.5)
95% CI for mean, p-value[b]	9.5, 15.9,<.0001	7.2, 13.6,<.0001
Treatment difference in numerical change[c]	Tolterodine ER + alpha blocker versus placebo + alpha blocker	
LS mean difference (SE)	3.9 (2.1)	
95% confidence interval	-0.2, 8.0	
p-value	0.0625	
Change in OAB-S Interruption of Day-to-Day Life		
Week 4		
N[a]	304	307
Baseline		
Mean (SD)	2.4 (1.0)	2.4 (1.0)
Median (range)	2.0 (1.0 to 5.0)	2.0 (1.0 to 5.0)
Week 4		
Mean (SD)	3.0 (1.1)	2.9 (1.0)
Median (range)	3.0 (1.0 to 5.0)	3.0 (1.0 to 5.0)
Numerical change from baseline to Week 4		
Mean (SD)	0.6 (1.1)	0.5 (1.1)
Median (range)	1.0 (-3.0 to 4.0)	0.0 (-3.0 to 4.0)
LS Mean (SE)	0.6 (0.1)	0.4 (0.1)
95% CI for mean, p-value[b]	0.5, 0.7,<.0001	0.4, 0.6,<.0001

Table 21. Results of Analyses of OAB-S Scores at Week 4 and 12

	Tolterodine ER + Alpha-Blocker N=329	Placebo + Alpha-Blocker N=323
Treatment difference in numerical change[c]	Tolterodine ER + alpha blocker versus placebo + alpha blocker	
LS mean difference (SE)	0.2 (0.1)	
95% confidence interval	0.0, 0.3	
p-value	0.0417	
Week 12		
N[a]	305	307
Baseline		
Mean (SD)	2.4 (1.0)	2.4 (1.0)
Median (range)	2.0 (1.0 to 5.0)	2.0 (1.0 to 5.0)
Week 12		
Mean (SD)	3.1 (1.1)	3.0 (1.1)
Median (range)	3.0 (1.0 to 5.0)	3.0 (1.0 to 5.0)
Numerical change from baseline to Week 12		
Mean (SD)	0.7 (1.2)	0.6 (1.2)
Median (range)	1.0 (-3.0 to 4.0)	1.0 (-3.0 to 4.0)
LS Mean (SE)	0.8 (0.1)	0.6 (0.1)
95% CI for mean, p-value[b]	0.6, 0.8,<.0001	0.5, 0.8,<.0001
Treatment difference in numerical change[c]	Tolterodine ER + alpha blocker versus placebo + alpha blocker	
LS mean difference (SE)	0.1 (0.1)	
95% confidence interval	-0.0, 0.3	
p-value	0.1254	
OAB-S Satisfaction of OAB Medication Scales		
Week 4		
N[d]	304	307
OAB-S medication expectation at Baseline		
Mean (SD)	77.1 (14.9)	76.9 (14.9)
Median (range)	77.5 (32.5 to 100.0)	77.5 (30.0 to 100.0)
OAB-S medication satisfaction at Week 4		
Mean (SD)	3.3 (1.2)	3.2 (1.2)
Median (range)	4.0 (1.0 to 5.0)	4.0 (1.0 to 5.0)
LS Mean (SE)[e]	3.3 (0.1)	3.2 (0.1)
Treatment difference[e]	Tolterodine ER + alpha blocker versus placebo + alpha blocker	
LS mean difference (SE)	0.1 (0.1)	
95% confidence interval	-0.1, 0.3	
p-value	0.3113	
Week 12		
N[d]	305	307
OAB-S medication expectation at Baseline		
Mean (SD)	77.1 (14.9)	76.9 (14.9)
Median (range)	77.5 (32.5 to 100.0)	77.5 (30.0 to 100.0)
OAB-S medication satisfaction at Week 12		
Mean (SD)	3.4 (1.3)	3.3 (1.3)
Median (range)	4.0 (1.0 to 5.0)	4.0 (1.0 to 5.0)
LS Mean (SE)[e]	3.4 (0.1)	3.3 (0.1)
Treatment difference[e]	Tolterodine ER + alpha blocker versus placebo + alpha blocker	
LS mean difference (SE)	0.1 (0.1)	
95% confidence interval	-0.1, 0.3	
p-value	0.5143	

Table 21. Results of Analyses of OAB-S Scores at Week 4 and 12

	Tolterodine ER + Alpha-Blocker N=329	Placebo + Alpha-Blocker N=323

ANCOVA = analysis of covariance; CI = confidence interval; ER = extended release; LS = least squares; N = number of subjects; OAB-S = Overactive Bladder Treatment Satisfaction Questionnaires; SD = standard deviation; SE = standard error.

a. Number of subjects with non-missing numerical change from Baseline to Week 4/Week 12
b. p-Value was based on paired t-test comparing baseline with post-Baseline values.
c. Based on an ANCOVA model with terms for country, treatment and treatment by country interaction with Baseline value as a covariate.
d. Number of subjects with non-missing OAB-S medication expectation at Baseline.
e. Based on an ANCOVA model with terms for country, treatment and treatment by country interaction with OAB-S Medication Expectation as a covariate.

An analysis was also performed to compare the subjects' overall satisfaction with their OAB medication. The number and percent of subjects at each assessment at Week 4 and 12 is presented in Table 22.

Table 22. OAB-S Overall Satisfaction at Weeks 4 and 12

Overall Satisfaction with OAB Medication	Tolterodine ER + Alpha-Blocker N=329 n (%)	Placebo + Alpha-Blocker N=323 n (%)
Week 4		
N[a]	307 (100)	307 (100)
Very dissatisfied	36 (11.7)	40 (13.0)
Somewhat dissatisfied	32 (10.4)	41 (13.4)
Neither dissatisfied nor satisfied	75 (24.4)	69 (22.5)
Somewhat satisfied	126 (41.0)	121 (39.4)
Very satisfied	38 (12.4)	36 (11.7)
p-value CMH test[b]	0.3886	
Week 12		
N[a]	308 (100)	307 (100)
Very dissatisfied	37 (12.0)	42 (13.7)
Somewhat dissatisfied	37 (12.0)	43 (14.0)
Neither dissatisfied nor satisfied	62 (20.1)	51 (16.6)
Somewhat satisfied	115 (37.3)	116 (37.8)
Very satisfied	57 (18.5)	55 (17.9)
p-value CMH test[b]	0.4818	

CMH = Cochran-Mantel-Haenszel; ER = extended release; N = number of subjects; n = number of subjects in each category; OAB-S = Overactive Bladder Treatment Satisfaction Questionnaires.

a. Number of subjects with non-missing value at Week 4/Week 12.
b. The p-value was obtained from a Cochran-Mantel-Haenszel test with modified ridit scoring, stratified by country.

Patient Perception of Treatment Benefit: The PPTB questionnaire assessed the subjects' perception of treatment benefit and their satisfaction with the assigned treatment. Both a binary and an ordinal assessment were utilized for treatment benefit. Subjects were also surveyed for their willingness to continue with the assigned treatment. A binary analysis of the number and percentage of subjects responding to the questionnaire is presented in Table 23.

Table 23. Patient Perception of Treatment Benefit, Satisfaction and Willingness to Continue (Binary) at Weeks 4 and 12

	Tolterodine ER + Alpha-Blocker N=329		Placebo + Alpha-Blocker N=323
	n (%)		n (%)
Patient Perception of Treatment Benefit			
Week 4			
N[a]	302 (100)		304 (100)
Benefit	221 (73.2)		209 (68.8)
No Benefit	81 (26.8)		95 (31.3)
p-value CMH test[b] by country		0.2323	
Odds Ratio (95% CI)		0.73 (0.49, 1.07)	
Week 12			
N[a]	307 (100)		306 (100)
Benefit	219 (71.3)		221 (72.2)
No Benefit	88 (28.7)		85 (27.8)
p-value CMH test[b] by country		0.7710	
Odds Ratio (95% CI)		1.03 (0.71, 1.49)	
Treatment Satisfaction			
Week 4			
N[a]	290 (100)		293 (100)
Yes	214 (73.8)		201 (68.6)
No	76 (26.2)		92 (31.4)
p-value CMH test[b] by country		0.1898	
Odds Ratio (95% CI)		1.32 (0.90, 1.93)	
Week 12			
N[a]	305 (100)		304 (100)
Yes	215 (70.5)		205 (67.4)
No	90 (29.5)		99 (32.6)
p-value CMH test[b] by country		0.4531	
Odds Ratio (95% CI)		1.17 (0.81, 1.69)	
Willing to Continue Treatment			
Week 12			
N[a]	284 (100)		285 (100)
Willing	201 (70.8)		189 (66.3)
Not Willing	83 (29.2)		96 (33.7)
p-value CMH test[b] by country		0.3121	
Odds Ratio (95% CI)		0.85 (0.58, 1.24)	

CI = confidence interval; CMH = Cochran-Mantel-Haenszel; ER = extended release; N = number of subjects; n = number of subjects in each category.

a. Number of subjects with non-missing Week 4/Week 12 values.

b. The p-value was obtained from a Cochran-Mantel-Haenszel test stratified by country.

An ordinal analysis of the number and percentage of subjects responding to the questionnaire is presented in Table 24.

Table 24. Patient Perception of Treatment Benefit (Ordinal) at Weeks 4 and 12

Patient Perception of Treatment Benefit	Tolterodine ER + Alpha-Blocker N=329	Placebo + Alpha-Blocker N=323
	n (%)	n (%)
Week 4		
N[a]	302 (100)	304 (100)
Much Benefit	69 (22.8)	66 (21.7)
Little Benefit	152 (50.3)	143 (47.0)
No Benefit	81 (26.8)	95 (31.3)
p-value CMH test[b]	0.2678	
Week 12		
N[a]	307 (100)	306 (100)
Much Benefit	101 (32.9)	89 (29.1)
Little Benefit	118 (38.4)	132 (43.1)
No Benefit	88 (28.7)	85 (27.8)
p-value CMH test[b]	0.3065	

CMH = Cochran-Mantel-Haenszel; ER = extended release; N = number of subjects; n = number of subjects in each category.

a. Number of subjects with non-missing change from baseline to Week 12.
b. The p-value was obtained from a Cochran-Mantel-Haenszel test with modified ridit scoring, stratified by country.

Safety Results: An overview of treatment-emergent AEs, all causalities and treatment-related, is presented in Table 25.

Table 25. Treatment-Emergent Adverse Events

	Tolterodine ER + Alpha-Blocker N=329		Placebo + Alpha-Blocker N=323	
	All Causalities n (%)	Treatment-Related n (%)	All Causalities n (%)	Treatment-Related n (%)
Number of AEs	224	134	153	71
Subjects with AEs	114 (34.7)	75 (22.8)	89 (27.6)	43 (13.3)
Subjects with SAEs	10 (3.0)	1 (0.3)	5 (1.5)	1 (0.3)
Subjects with severe AEs	15 (4.6)	8 (2.4)	4 (1.2)	2 (0.6)
Subjects discontinued due to AEs	17 (5.2)	14 (4.3)	10 (3.1)	8 (2.5)
Subjects with dose reduced or temporary discontinuation due to AEs	7 (2.1)	4 (1.2)	6 (1.9)	3 (0.9)

AEs and SAEs are not separated out.
The Investigator reported the reason for discontinuation for 1 tolterodine ER subject as "subject defaulted" and for another tolterodine ER subject as "insufficient clinical response," but reported "study medication discontinued" for both subjects on the AE page. For 1 placebo subject, the Investigator reported the reason for discontinuation as "adverse event" but did not indicate "study medication discontinued" on the AE page. For 1 placebo subject who discontinued due to death, the investigator reported "study medication discontinued" on AE page. One subject, randomized to tolterodine ER, had an Investigator-reported SAE that was not considered an SAE, per protocol and was not counted as an SAE.
AEs = adverse events; ER = extended release; N = number of subjects; n = number of subjects in each category; SAE = serious adverse events.

Treatment-emergent AEs occurring in ≥1% of subjects in either treatment group are presented in Table 26.

Table 26. Treatment-Emergent Adverse Events Occurring in ≥1% of Subjects in Either Treatment Group (All Causalities)

System Organ Class Preferred term	Tolterodine ER + Alpha-Blocker N=329	Placebo + Alpha-Blocker N=323
Eye disorders		
Vision blurred	5 (1.5)	1 (0.3)
Gastrointestinal disorders		
Constipation	14 (4.3)	3 (0.9)
Diarrhea	3 (0.9)	6 (1.9)
Dry mouth	32 (9.7)	18 (5.6)
Infections and infestations		
Nasopharyngitis	7 (2.1)	7 (2.2)
Investigations		
Residual urine volume	4 (1.2)	1 (0.3)
Nervous system disorders		
Dizziness	6 (1.8)	3 (0.9)
Headache	12 (3.6)	3 (0.9)
Somnolence	2 (0.6)	4 (1.2)
Renal and urinary disorders		
Dysuria	11 (3.3)	4 (1.2)
Urinary hesitation	6 (1.8)	1 (0.3)

AEs and SAEs are not separated out.
AEs = adverse events; ER = extended release; N = number of subjects; n = number of subjects in each category; SAE = serious adverse events.

Treatment-related AEs occurring in ≥1% of subjects in either treatment group are presented in Table 27.

Table 27. Treatment-Related Adverse Events Occurring in ≥1% of Subjects in Either Treatment Group

System Organ Class Preferred term	Tolterodine ER + Alpha-Blocker N=329	Placebo + Alpha-Blocker N=323
Eye disorders		
Vision blurred	5 (1.5)	1 (0.3)
Gastrointestinal disorders		
Constipation	13 (4.0)	3 (0.9)
Dry mouth	31 (9.6)	18 (5.6)
Nervous system disorders		
Dizziness	6 (1.8)	2 (0.6)
Headache	9 (2.7)	2 (0.6)
Somnolence	1 (0.3)	4 (1.2)
Renal and urinary disorders		
Dysuria	10 (3.0)	3 (0.9)
Urinary hesitation	6 (1.8)	1 (0.3)

AEs and SAEs are not separated out.
AEs = adverse events; ER = extended release; N = number of subjects; n = number of subjects in each category; SAE = serious adverse events.

There were 2 deaths in this study, 1 each in the tolterodine ER plus alpha-blocker and placebo plus alpha-blocker groups. The subject in the tolterodine ER plus alpha-blocker group died of acquired immunodeficiency syndrome on Study Day 63 and the Investigator

considered the causality of the event to be not related to the study drug. The subject in the placebo plus alpha-blocker group died of pneumonia on Study Day 92 and the Investigator considered the causality of the event to be a *Staphylococcus aureus* infection, and not related to study drug.

Nine subjects from the tolterodine ER plus alpha-blocker group and 5 subjects from the placebo plus alpha-blocker group experienced SAEs during this study. The non-fatal, treatment-emergent SAEs are presented in Table 28. An additional case of drug exposure during partner pregnancy was reported for a subject in the tolterodine ER plus alpha-blocker group. This event was noted as an SAE by the Investigator, but was not considered an SAE per protocol and was not included in the SAE table. One SAE in each treatment group was considered related to study drug; an event of drug exposure during a partner pregnancy in the tolterodine ER plus alpha-blocker group and urinary retention in the placebo plus alpha-blocker group.

There were 3 other subjects with SAEs that were included in the safety database. Prior to randomization, 2 subjects experienced SAEs of hematuria and gastritis, respectively, and 1 subject had a post-treatment SAE of nephrolithiasis.

Table 28. Non-fatal Treatment-Emergent Serious Adverse Events

S. No.	Adverse Event	Treatment (in Addition to Alpha-Blocker)	Action Taken[a]	Causality
1	Coronary artery disease	Tolterodine ER	No action taken	Tobacco abuse, hypertension
2	Melaena	Tolterodine ER	Study drug stopped temporarily	Duodenitis
3	Coronary artery disease	Tolterodine ER	No action taken	Medical history of coronary artery disease
4	Chronic obstructive pulmonary disease (COPD)	Tolterodine ER	Study drug stopped temporarily	Exacerbation of COPD
5	Haemorrhoidal haemorrhage	Tolterodine ER	No action taken	Internal hemorrhoids
6	Cerebrovascular accident	Tolterodine ER	No action taken	Hypertension
7	Lung neoplasm malignant	Tolterodine ER	Discontinued	Pre-existing nodules, scarring of the lung
8	Faecaloma	Tolterodine ER	No action taken	History of constipation
	Urinary retention		No action taken	History of constipation
9	Vertigo	Placebo	No action taken	History of vertigo
10	Urinary retention	Placebo	Discontinued	Study drug
11	Cataract operation complication	Placebo	No action taken	Other
12	Calculus bladder	Placebo	No action taken	Benign prostatic hyperplasia complication

COPD = chronic obstructive pulmonary disease; ER = extended release; S. No. = serial number.
a. Column refers to action taken with the study medication.

The permanent discontinuations due to treatment-related AEs are presented in Table 29. AEs leading to discontinuation that were not considered related to study drug included events of malignant lung neoplasm and dry mouth in the tolterodine ER plus alpha-blocker group, and cough and dysuria in the placebo plus alpha-blocker group.

Table 29. Permanent Discontinuations Due to Treatment-Related Adverse Events

S. No.	Adverse Event	Treatment (in Addition to Alpha-blocker)	Severity	Outcome
1	Prostatic specific antigen abnormal	Tolterodine ER	Moderate	Resolved
	Urinary tract disorder		Moderate	Resolved
2	Constipation	Tolterodine ER	Moderate	Resolved
	Urinary hesitation		Moderate	Resolved
3	Dry mouth	Tolterodine ER	Mild	Resolved
	Headache		Mild	Resolved
	Nervousness		Mild	Resolved
	Benign prostatic hyperplasia		Moderate	Resolved
4	Urinary retention	Tolterodine ER	Moderate	Still present
5	Visual disturbance	Tolterodine ER	Moderate	Resolved
6	Constipation			Still present
	Dysuria		Severe	Resolved
7	Abdominal discomfort	Tolterodine ER	Mild	Still present
8	Dizziness	Tolterodine ER	Mild	Resolved
	Headache		Mild	Resolved
9	Constipation	Tolterodine ER	Moderate	Resolved
10	Dry mouth	Tolterodine ER	Moderate	Resolved
11	Dizziness	Tolterodine ER	Severe	Resolved
12	Urinary retention	Tolterodine ER	Mild	Resolved
13	Dysuria	Tolterodine ER	Severe	Resolved
	Hypertonic bladder		Severe	Resolved
	Urinary hesitation		Severe	Resolved
	Urinary incontinence		Severe	Resolved
14	Abdominal distension	Placebo	Mild	Resolved
15	Constipation	Placebo	Moderate	Still present
	Dry mouth		Moderate	Still present
	Dysphagia		Moderate	Still present
	Muscle stiffness		Moderate	Still present
	Dysphonia		Moderate	Still present
16	Vision blurred	Placebo	Mild	Resolved
	Abdominal distension		Mild	Resolved
	Diarrhoea		Mild	Resolved
	Flatulence		Mild	Resolved
	Nausea		Mild	Resolved
	Somnolence		Mild	Resolved
	Anxiety		Mild	Resolved
	Dysuria		Mild	Resolved
	Urinary retention		Mild	Resolved
17	Urinary retention	Placebo	Severe	Resolved
18	Fatigue	Placebo	Moderate	Resolved
19	Dysuria	Placebo	Mild	Still present
	Pollakiuria		Mild	Still present
	Residual urine		Moderate	Still present
	Urine flow decreased		Mild	Still present
20	Headache	Placebo	Moderate	Resolved
21	Urinary tract disorder	Placebo	Moderate	Resolved

ER = extended release; S.No. = serial number.

Seven (2.1%) subjects in the tolterodine ER plus alpha-blocker group temporarily discontinued study drug due to AEs; 4 of these events were considered to be related to study drug. Six (1.9%) subjects in the placebo plus alpha-blocker group temporarily discontinued study drug due to AEs; 3 of the events were considered treatment-related. Most events experienced by subjects in either group were moderate in severity.

The temporary discontinuations due to AEs are presented in Table 30.

Table 30. Temporary Discontinuations Due to Adverse Events

S. No.	Adverse Event	Treatment (in Addition to Alpha-Blocker)	Severity	Causality
1	Melaena	Tolterodine ER	Severe	Duodenitis
2	Headache	Tolterodine ER	Moderate	Study drug
3	Chronic obstructive pulmonary disease	Tolterodine ER	Moderate	Exacerbation of COPD
4	Headache	Tolterodine ER	Moderate	Study drug
5	Gastroenteritis	Tolterodine ER	Mild	Study drug
6	Constipation	Tolterodine ER	Moderate	Study drug
7	Abdominal discomfort	Tolterodine ER	Moderate	Indigestion
	Wheezing		Moderate	Smoking
8	Chest pain	Placebo	Mild	Muscular pain
9	Diarrhoea	Placebo	Mild	High fat diet
10	Headache	Placebo	Moderate	Study drug
11	Hypertension	Placebo	Moderate	Worsening hypertension
12	Dysuria	Placebo	Severe	Study drug
13	Upper respiratory tract infection	Placebo	Moderate	Study drug

COPD = Chronic obstructive pulmonary disease; ER = extended release.

Post Void Residual Volume: PVR measurements were obtained by ultrasound and analyzed for the change in mean volume from Baseline to Week 4 and to Week 12. These results are presented in Table 31.

Table 31. Change in Mean Post Void Residual Volume at Week 4 and Week 12

	Tolterodine ER + Alpha-Blocker N=329	Placebo + Alpha-Blocker N=323
Week 4		
N[a]	294	299
Baseline		
Mean (SD)	46.0 (48.0)	47.7 (51.6)
Median (range)	30.0 (0 to 200.0)	30.0 (0 to 331.0)
Week 4		
Mean (SD)	52.3 (71.3)	39.3 (45.2)
Median (range)	30.0 (0 to 709.0)	27.0 (0 to 247.0)
Numerical change from baseline to Week 4		
Mean (SD)	6.2 (61.8)	-8.4 (45.2)
Median (range)	0 (-150.0 to 515.0)	0 (-329.0 to 111.0)
LS Mean (SE)	3.8 (3.4)	-8.0 (3.3)
95% CI for mean, p-value[b]	-0.8, 13.3, 0.0838	-13.6, -3.3, 0.0014
Treatment difference in numerical change[c]		
LS mean difference (SE)	11.8 (4.7)	
95% confidence interval	2.5, 21.1	
p-value	0.0130	
Week 12		
N[a]	289	293
Baseline		
Mean (SD)	45.1 (46.8)	45.7 (49.9)
Median (range)	30.0 (0 to 200.0)	30.0 (0 to 331.0)
Week 12		
Mean (SD)	59.4 (79.4)	48.6 (57.9)
Median (range)	36.0 (0 to 686.0)	30.0 (0 to 344.0)
Numerical change from baseline to Week 12		
Mean (SD)	14.3 (68.6)	2.9 (51.6)
Median (range)	0 (-150.0 to 622.0)	0 (-305.0 to 334.0)
LS Mean (SE)	13.6 (4.0)	1.0 (3.8)
95% CI for mean, p-value[b]	6.4, 22.2, 0.0005	-3.0, 8.8, 0.3398
Treatment difference in numerical change[c]		
LS mean difference (SE)	12.6 (5.5)	
95% confidence interval	1.7, 23.5	
p-value	0.0231	

ANCOVA = analysis of covariance; CI = confidence interval; ER = extended release; LS = least squares; N = number of subjects; SD = standard deviation; SE = standard error.

a. Number of subjects with non-missing numerical and percent change from Baseline to Week 4 and Week 12.
b. The p-value was based on a paired t-test comparing Baseline with post-baseline values.
c. The treatment difference was based on an ANCOVA model with terms for country, treatment, treatment by country interaction, and the Baseline value as a covariate.

One subject in the tolterodine ER plus alpha-blocker group and 2 subjects in the placebo plus alpha-blocker group experienced symptoms of urinary retention requiring catherization.

Q_{max} measurements were obtained by a flowmeter and analyzed for the change in mean volume from Baseline to Week 12. These results are presented in Table 32.

Table 32. Change in Mean Peak Flow at Week 12

	Tolterodine ER + Alpha-Blocker N=329	Placebo + Alpha-Blocker N=323
N[a]	289	291
Baseline		
Mean (SD)	12.2 (6.0)	12.3 (5.7)
Median (range)	11.0 (1.9 to 39.1)	11.4 (2.5 to 40.4)
Week 12		
Mean (SD)	11.9 (6.2)	12.7 (9.2)
Median (range)	10.5 (1.0 to 40.9)	11.5 (1.6 to 136.0)
Numerical change from baseline to Week 12		
Mean (SD)	-0.3 (5.3)	0.4 (8.8)
Median (range)	-0.3 (-18.4 to 24.1)	-0.1 (-15.8 to 121.8)
LS Mean (SE)	-0.2 (0.5)	0.8 (0.5)
95% CI for mean, p-value[b]	-0.9, 3.0, 0.3687	-0.6, 1.5, 0.3957
Treatment difference in numerical change[c]		
LS mean difference (SE)	-1.0 (0.7)	
95% confidence interval	-2.3, 0.3	
p-value	0.1420	

ANCOVA = analysis of covariance; ER = extended release; LS = least squares; N = number of subjects; SD = standard deviation; SE = standard error.

a. Number of subjects with non-missing numerical and percent change from Baseline to Week 12.
b. The p-value was based on a paired t-test comparing Baseline with post-baseline values.
c. The treatment difference was based on an ANCOVA model with terms for country, treatment, treatment by country interaction, and the Baseline value as a covariate.

CONCLUSIONS: In men with persistent OAB symptoms after receiving alpha-blocker mono-therapy, 12 weeks of add-on treatment with tolterodine ER plus alpha-blocker did not show significantly more improvement in the subjects' perception of their bladder condition based on the PPBC questionnaire relative to the placebo plus alpha-blocker arm (p=0.6699).

There was, however, a statistically significant treatment effect of add-on tolterodine ER with respect to several key OAB symptoms such as 24-hour reductions of micturition frequency, micturition-related urgency, and severe micturition-related urgency (p=0.0079, p=0.0010, and p=0.0495, respectively). Tolterodine ER plus alpha-blocker also showed significantly greater improvement in storage subscale of the IPSS relative to placebo plus alpha-blocker at Week 12 (p=0.0370).

Data from the micturition diary that did not show a statistically significant difference from placebo in change from Baseline included the mean rating on the USS and the number of UUI episodes. The total IPSS and the voiding subscale scores of the IPSS were not statistically different between tolterodine ER plus alpha-blocker and placebo plus alpha-blocker. Results from the other patient-reported outcome questionnaires (OAB-q, ICIQ-MLUTSsex, N-QoL, OAB-S, and PPTB) did not show statistically significant differences between the 2 treatment groups.

Tolterodine ER plus alpha-blocker was well-tolerated by the population. No serious safety concerns were identified. There were 2 fatal outcomes in this study, 1 in each of the treatment groups. Neither case was considered by the Investigator to be related to study drug. Fifteen subjects experienced SAEs, the majority of which were not related to study

drug. One subject in each treatment group experienced an SAE considered to be treatment-related. Dry mouth was the most commonly occurring treatment-emergent AE in both treatment groups.

There was no increase in the incidence of acute urinary retention, acute urinary retention requiring catherization, or study drug discontinuation in the tolterodine ER plus alpha-blocker group compared to the placebo plus alpha-blocker group. There was a statistically significant increase in PVR between the tolterodine ER plus alpha-blocker and placebo plus alpha-blocker groups (+13.6 mL from 45.1 mL Baseline in the tolterodine ER group vs +1.0 mL from 45.7 mL in the placebo group, p=0.0231). Importantly, there was no significant decrease in Q_{max} between the tolterodine ER plus alpha-blocker and the placebo plus alpha-blocker groups.