SYNOPSIS

Title of Study:

A randomized, double-blind, double-dummy, placebo-controlled study to evaluate the efficacy and safety of solifenacin succinate (5 and 10 mg once daily) against placebo and oxybutynin hydrochloride (5 mg three times daily) in the treatment of subjects with neurogenic detrusor overactivity.

Investigators/Coordinating Investigator:

[redacted] MD, [redacted] Belgium.

Study Centers:

This was a multi-center study performed in 45 centers in 11 countries (Australia, Belgium, Czech Republic, France, Germany, Hungary, Italy, the Netherlands, Spain, United Kingdom, Russia).

Publication (reference):

Not applicable.

Study Period:

Date of first enrollment (Study initiation date): 14 March 2008

Date of last evaluation (Study completion date): 28 January 2011

Phase of Development: Phase 3B/4

Objectives:

The primary objective was to assess the efficacy of solifenacin 10 mg compared to placebo in subjects with neurogenic detrusor overactivity.

The secondary objectives were:

- To assess the efficacy of solifenacin 5 mg compared to placebo in subjects with neurogenic detrusor overactivity
- To assess the efficacy of solifenacin compared to oxybutynin in subjects with neurogenic detrusor overactivity
- To assess the safety and tolerability of solifenacin compared to placebo in subjects with neurogenic detrusor overactivity
- To assess the safety and tolerability of solifenacin compared to oxybutynin in subjects with neurogenic detrusor overactivity

Methodology:

This was a prospective, randomized, multi-center, multi-national Phase 3b/4 parallel-group study with a single-blind placebo run-in period of 2 weeks, followed by a randomized, double-blind, placebo- and active-controlled treatment period of 4 weeks to evaluate the efficacy and safety of solifenacin for treatment of neurogenic detrusor overactivity.

Subjects satisfying all selection criteria at the end of the placebo run-in period (Visit 2) were randomized to receive 5 mg or 10 mg solifenacin once daily, 5 mg oxybutynin 3 times daily, or placebo. Subjects visited the study site at screening (within 2 weeks of the start of the single-blind placebo run-in period; Visit 1), at the end of the run-in period (Visit 2), and at the end of the double-blind treatment period (Week 4; Visit 3).

Number of Patients (planned, enrolled and analyzed):

Approximately 215 subjects were planned to be selected from urologists' or gynecologists' practices and enrolled, in order to obtain 172 subjects (43 subjects in each treatment group) evaluable for the primary efficacy analysis.

A total of 248 subjects were screened and entered the placebo run-in period. Of these 248 subjects, 189 subjects were included in the Safety Analysis Set (SAF) and 176 subjects were included in the Full Analysis Set (FAS).

Diagnosis and Main Criteria for Inclusion:

The study population consisted of men and women, aged ≥ 18 years but ≤ 65 years, with either spinal cord injury or multiple sclerosis, whose symptoms of the respective disease had been stable for at least 6 months. Subjects with multiple sclerosis had to have an Expanded Disability Status Scale (EDSS) grading of 8 or below. Subjects also had to have a diagnosis of neurogenic detrusor overactivity, and these symptoms should also have been stable for at least 6 months.

Test Product, Dose and Mode of Administration, Batch Numbers:

Solifenacin (Vesicare®) tablets for oral administration; 5 mg. Batch number: [redacted].

Duration of Treatment (or Duration of Study, if applicable):

A 2-week single-blind placebo run-in period followed by a 4-week double-blind treatment period.

Reference Products, Dose and Mode of Administration, Batch Numbers:

Oxybutynin overencapsulated tablets for oral administration; 5 mg. Batch numbers: [redacted].

Placebo solifenacin tablets. Batch number: [redacted].

Placebo oxybutynin capsules. Batch numbers: [redacted].

Criteria for Evaluation:

Efficacy was assessed from cystometry assessments (maximum cystometric capacity, bladder volume at first involuntary contraction, bladder volume at first leak, detrusor pressure at first leak, and maximum detrusor pressure), micturition diary (recordings of micturition, incontinence, and catheterization episodes), the Incontinence Quality of Life Questionnaire (I-QoL), the EuroQoL 5-Dimension Questionnaire (EQ-5D), a Visual Analogue Scale to rate the subject's satisfaction with the treatment (VAS-TS), and the validated Subject Perception of Bladder Condition (PBC) 6-point categorical scale.

Safety was assessed from the recording of treatment-emergent (serious) adverse events (AEs), and from changes from baseline in VAS dry mouth, constipation, blurred vision, fatigue, and memory and attention.

Statistical Methods:

The primary analysis was performed on the change from baseline to endpoint in maximum cystometric capacity. Only subjects receiving 1 of the 4 study drugs were included in the analyses. the primary efficacy analysis was performed on the FAS and also on the Per Protocol Set (PPS).

The primary analysis was based on a general linear model including the baseline value as a covariate, treatment and region as fixed factors. In addition, a supportive model adding indication (spinal cord injury, multiple sclerosis) and the interaction of treatment*indication was applied. Further, if a term other than treatment group was statistically significant, an interaction of this term with treatment group was added to the model .

Pairwise comparisons of all 3 active treatments and the pooled solifenacin vs. placebo and pairwise comparisons of solifenacin, pooled solifenacin and placebo groups vs. oxybutynin were performed using contrasts with the Estimate option of SAS®.

The primary analysis as described for endpoint was also performed for the micturition diary variables (i.e., the number of micturitions, catheterizations and/or incontinence episodes per 24 hours), I-QoL, EQ-5D VAS scores, VAS-TS, PBC and VAS scores of dry mouth, constipation, blurred vision, fatigue, and memory and attention. In addition, non-parametric Wilcoxon sum-rank tests were performed on the given primary and secondary variables.

Summary of Results/Conclusions:

Efficacy Results:

All values of efficacy variables are presented as mean (SD). All P-values based on an ANCOVA model with fixed effects for treatment group and geographic region and baseline of cystometric parameter as covariate.

Primary Efficacy Variable

The primary efficacy variable was the change from baseline to the end-of-study visit in the maximum cystometric capacity (in mL), calculated as the sum of the drained volume at the end of the cystometry and leakage. Table 1 presents a summary of the data for the FAS.

The mean maximum cystometric capacity at baseline was around 220 mL in all treatment groups, remained at a similar level in the placebo group (232 mL, Δ=5.4 mL) but increased to above 300 mL in the solifenacin and oxybutynin treatment groups, all changes statistically significantly greater than placebo.

The mean increase in the 10 mg solifenacin group was 134.2 mL ($P < 0.001$ vs placebo) and was not statistically significantly different from oxybutynin (165.4 mL; $P = 0.263$). The mean increase in the 5 mg solifenacin group was 77.8 mL and significantly larger than in the placebo group ($P = 0.007$) but significantly smaller than in the oxybutynin group ($P = 0.002$).

Secondary Efficacy Variables - Cystometry Assessments

The results for bladder volume at first involuntary contraction, bladder volume at first leak, detrusor pressure at first leak, and maximum detrusor pressure are summarized in Table 2 for the FAS. The table shows the mean (SD) values at baseline and at the end of the study, together with the mean (SD) changes from baseline and the corrsponsing P-values for the pairwise comparisons of solifenacin vs. placebo and vs. oxybutynin.

In comparison to placebo (-10.1 mL) there was a statistically significant increase in mean bladder volume at first involuntary contraction following treatment with 10 mg solifenacin (79.2 mL; $P < 0.001$), 5 mg solifenacin (60.0 mL; $P = 0.003$) and 15 mg oxybutynin (113.4 mL; $P < 0.001$). The increase in mean bladder volume at first involuntary contraction was not significantly different when 10 mg solifenacin and 15 mg oxybutynin were compared ($P = 0.147$) but the response to 15 mg oxybutynin was significantly greater ($P = 0.022$) than that to 5 mg solifenacin.

In comparison to placebo (-13.2 mL) there was an increase in the mean bladder volume at first leak following treatment with 10 mg solifenacin (83.3 mL), 5 mg solifenacin (59.8 mL) and 15 mg oxybutynin (142.5 mL); the increase was significantly greater than placebo for 10 mg solifenacin ($P = 0.020$) and 15 mg oxybutynin ($P = 0.004$) but not for 5 mg solifenacin ($P = 0.052$). There was however no statistically significant difference between 15 mg oxybutynin and either 5 mg ($P = 0.156$) or 10 mg solifenacin ($P = 0.339$).

In comparison to placebo (7.7 cm H_2O) there was a statistically significant decrease in the mean detrusor pressure at first leak following treatment with 10 mg solifenacin (-11.7 cm H_2O; $P = 0.010$), 5 mg solifenacin (-14.8 cm H2O; $P = 0.013$) and 15 mg oxybutynin (-27.6 cm H2O; $P = 0.002$). There was no significant difference between 10 mg solifenacin or 5 mg solifenacin and 15 mg oxybutynin ($P = 0.349$ and $P = 0.254$, respectively).

In comparison to placebo (7.5 cm H_2O) there was a statistically significant decrease in the mean maximum detrusor pressure in the 10 mg solifenacin (-10.5 cm H_2O; $P = 0.003$), 5 mg solifenacin (-16.6 cm H_2O; $P = 0.002$) and 15 mg oxybutynin (-24.3 cm H_2O; $P < 0.001$) treatment. There was no significant difference

between the effect of 10 mg solifenacin or 5 mg solifenacin and oxybutynin 15 mg (P = 0.168 and P = 0.222, respectively).

Secondary Efficacy Variables – Micturition Diary

The results for micturition episodes, catheterization episodes, incontinence episodes, the sum of micturition and catheterization episodes, and the sum of micturition, incontinence and catheterization episodes (all per 24 hours) are summarized in Table 3 for the FAS. The table shows the mean (SD) values at baseline and at the end of the study, together with the mean (SD) changes from baseline and the corrsponsing P-values for the pairwise comparisons of solifenacin vs. placebo and vs. oxybutynin.

The mean change in number of micturitions per 24 hours ranged from -0.46 (placebo) to -1.48 (5 mg solifenacin) but none of the changes were statistically significant.

The mean change in number of catheterizations per 24 hours ranged from -0.11 (placebo) to -0.26 (10 mg solifenacin) but none of the changes were statistically significant.

In comparison to placebo (-0.07) there was a statistically significant decrease in the mean number of incontinence episodes after 5 mg solifenacin (-0.91, P = 0.003) and 15 mg oxybutynin (-1.50; P < 0.001) but not after 10 mg solifenacin (-0.44; P = 0.246). The mean decrease in the oxybutynin group was statistically significantly larger than the effect in the placebo group (P < 0.001), but did not statistically significantly differ from the 5 mg solifenacin group (P = 0.440) or the pooled solifenacin group (P = 0.051).

The mean number of micturitions plus catheterizations per 24 hours decreased in all treatment groups, including placebo. None of the treatment comparisons were statistically significant.

In comparison to placebo (-0.64) the mean number of micturitions plus catheterizations plus incontinence episodes per 24 hours statistically significantly decreased following treatment with 5 mg solifenacin (-2.55; P = 0.011) and 15 mg oxybutynin (-2.89; P = 0.006) but not after 10 mg solifenacin (-1.46; P = 0.310). The mean decrease in the oxybutynin group was statistically significantly larger than the effect in the placebo group (P < 0.01), but was not statistically significantly different from solifenacin (all P > 0.05).

Findings from a responder analysis confirmed that the number of micturitions and number of catheterizations per 24 hours did not notably change after treatment with solifenacin or oxybutynin. A modest effect was observed on the number of incontinence episodes per 24 hours, i.e., between 41.0% and 46.7% of subjects in the solifenacin and oxybutynin treatment groups showing ≥ 50% response (a reduction in the number of events per 24 hours of at least 50%), with no relevant differences between groups, compared to 20.5% with placebo.

Secondary Efficacy Variables – Other

The results for I-QoL, EQ-5D VAS, VAS-TS and PBC are summarized in Table 4 for the FAS. The table shows the mean (SD) values at baseline and at the end of the study, together with the mean (SD) changes from baseline and the corrsponsing P-values for the pairwise comparisons of solifenacin vs. placebo and vs. oxybutynin.

Overall, the mean increase in the I-QoL total score and the I-QoL subscale scores was numerically larger in the solifenacin treatment groups compared to placebo, but only few comparisons reached statistically significance, i.e., 5 mg and 10 mg solifenacin and pooled solifenacin *vs* placebo for the avoidance and limiting behavior subscale (P = 0.014, P = 0.030 and P = 0.009, respectively), and pooled solifenacin *vs* placebo for the psychosocial impact subscale (P = 0.044). There was no statistically significant effect of treatment with oxybutynin *vs* placebo on the I-QoL scores, and none of the comparisons of solifenacin *vs* oxybutynin were statistically significant.

In comparison to placebo (-0.9) there was a statistically significant increase in the mean EQ-5D VAS score for the 15 mg oxybutynin group (8.6) and for the 10 mg (8.2) and the pooled solifenacin group (5.4; all P ≤ 0.05), but not for the 5 mg solifenacin group (2.4; P = 0.300). The mean increase in the 10 mg solifenacin group was not statistically significantly different from oxybutynin (P = 0.646). The mean increase in the 5 mg solifenacin group was also not statistically significantly different from oxybutynin (P = 0.073). The overall mean increase in the pooled solifenacin group was not statistically significant different from 15 mg oxybutynin (P = 0.197).

There was an increase in the mean VAS-TS scores in the solifenacin and oxybutynin treatment groups compared to placebo (all P ≤ 0.05). Mean scores in the placebo group were comparable at baseline and at the

end of the study (i.e., a change of +1.3). The mean increase in the 10 mg solifenacin group was 14.3, and this was not statistically significantly different from oxybutynin (11.7; P = 0.808). The mean increase in the 5 mg solifenacin group was 10.3, and was also not statistically significantly different from oxybutynin (P = 0.825). The overall mean increase in the pooled solifenacin group (12.4) was higher than the mean increase in the oxybutynin group, but the difference was not statistically significant (P = 0.792).

In comparison to placebo (-0.1) the only statistically significant improvement in PBC occurred following treatment with 10 mg solifenacin (-0.6; P = 0.041).

Safety Results:

There were no deaths. Two subjects had 1 or more serious adverse events (SAEs) during the double-blind treatment period: 1 subject in the placebo group had a wrist fracture of severe intensity and experienced impaired wound healing of severe intensity, and 1 subject in the solifenacin 10 mg group had a single episode of severe demyelination. None of the SAEs was considered related to treatment by the investigator.

Two subjects in the placebo group and 1 subject in the oxybutynin group discontinued prematurely from the double-blind treatment period due to the occurrence of adverse events (AEs).

Treatment-emergent adverse events (TEAEs) were reported for 6 subjects (12.5%) in the 5 mg solifenacin group, for 16 subjects (31.4%) in the 10 mg solifenacin group and for 16 subjects (34.0%) in the oxybutynin group. Ten (23.3%) placebo-treated subjects had 1 or more TEAEs.

The most common AEs (> 5% of pooled solifenacin subjects) were urinary tract infection (7.1%), dry mouth (6.1%), constipation (5.1%) and blurred vision (5.1%). The incidence of dry mouth, constipation and blurred vision was higher in the 10 mg group than in the 5 mg group, but there appeared to be no other clinically relevant differences between the 5 mg and 10 mg dose of solifenacin with respect to the incidence, nature, or severity of other AEs.

Dry mouth, constipation and blurred vision were also commonly reported during treatment with oxybutynin (17.0%, 4.3% and 6.4%, respectively). The incidence of dry mouth in the oxybutynin group was higher than in the solifenacin group, and this was confirmed by the statistically significantly larger increases in the VAS dry mouth compared to solifenacin or placebo (all P < 0.001). None of the other comparisons for the other VAS (i.e., constipation, blurred vision, fatigue, and memory and attention) were statistically significant.

CONCLUSIONS:

Treatment with 5 mg or 10 mg solifenacin for 4 weeks provided statistically significant improvements in cystometric parameters in patients with neurogenic detrusor overactivity (with the exception of the effect of 5 mg solifenacin on mean bladder volume at first leak); similar effects were seen 15 mg oxybutynin.

There were no statistically significant improvements in diary urinary variables of micturition and catheterization frequency but statistically significant improvements in incontinence frequency occurred after 4-week treatment with 5 mg solifenacin and 15 mg oxybutynin.

Treatment with 10 mg solifenacin for 4 weeks provided statistically significant improvements in the quality of life parameters EQ-5D VAS and PBC and on the Avoidance and Limiting Behavior subscale of the I-QoL but changes after 15 mg oxybutynin and 5 mg solifenacin (with the exception of I-QoL Avoidance and Limiting Behavior subscale) failed to achieve statistical significance.

Treatment was well tolerated, with a low incidence of SAEs and discontinuations. The most common AEs (dry mouth, constipation and blurred vision) were consistent with anti-muscarinic pharmacological effects; however, 15 mg oxybutynin, but not solifenacin (5 mg or 10 mg), was associated with statistically significant dry mouth severity as rated on the VAS.

Improvements in cystometric function in patients with neurogenic detrusor overactivity following treatment with solifenacin (5 mg and 10 mg) and oxybutynin (15 mg) were associated with statistically significant treatment satisfaction on the VAS-TS.

Date of Report: 23 January 2012 (final)

Table 1 Maximum Cystometric Capacity (FAS)

	Placebo	Solifenacin 5 mg	Solifenacin 10 mg	Oxybutynin 15 mg	Pooled Solifenacin
n [$]	40	46	51	39	97
Baseline	226.9 (108.10)	222.9 (115.41)	225.1 (107.54)	214.7 (102.66)	224.1 (110.76)
End-of-Study Visit	232.4 (101.93)	300.7 (149.72)	359.3 (152.34)	380.1 (169.29)	331.5 (153.16)
Change from baseline	5.4 (120.25)	77.8 (115.39)	134.2 (124.69)	165.4 (145.63)	107.5 (123.05)
P-value *vs* placebo	--	0.007	< 0.001	< 0.001	< 0.001
P-value *vs* oxybutynin	< 0.001	0.002	0.263	--	0.014

[$] Number of subjects with baseline and end-of-study cystometry data.
Values are are presented as mean (SD).

Table 2 Other Cystometry Assessments (FAS)

	Placebo	Solifenacin 5 mg	Solifenacin 10 mg	Oxybutynin 15 mg	Pooled Solifenacin
Bladder Volume at First Involuntary Contraction					
n [$]	38	42	45	36	87
Baseline	137.8 (85.47)	138.8 (84.82)	142.3 (87.38)	124.8 (88.28)	140.7 (85.74)
End-of-Study Visit	130.6 (62.83)	192.7 (112.33)	215.8 (142.11)	234.8 (105.64)	204.7 (128.39)
Change from baseline	-10.1 (83.10)	60.0 (109.16)	79.2 (122.27)	113.4 (101.40)	69.9 (115.86)
P-value *vs* placebo	--	0.003	< 0.001	< 0.001	< 0.001
P-value *vs* oxybutynin	< 0.001	0.022	0.147	--	0.034
Bladder Volume at First Leak					
n [#]	22	20	16	10	36
Baseline	155.0 (94.66)	157.0 (102.63)	137.4 (91.85)	165.7 (105.54)	147.8 (97.26)
End-of-Study Visit	141.2 (62.54)	202.2 (141.97)	230.3 (141.41)	215.3 (138.81)	216.3 (140.67)
Change from baseline	-13.2 (110.15)	59.8 (101.62)	83.3 (134.65)	142.5 (130.82)	70.2 (116.26)
P-value *vs* placebo	--	0.052	0.020	0.004	0.013
P-value *vs* oxybutynin	0.004	0.156	0.339	--	0.192
Detrusor Pressure at First Leak					
n [#]	21	18	15	9	33
Baseline	57.3 (27.33)	68.0 (38.28)	63.0 (35.76)	67.3 (42.74)	65.6 (36.80)
End-of-Study Visit	73.2 (39.51)	55.5 (28.66)	44.4 (16.24)	50.9 (33.02)	49.8 (23.48)
Change from baseline	7.7 (20.25)	-14.8 (24.43)	-11.7 (20.81)	-27.6 (43.66)	-13.4 (22.56)
P-value *vs* placebo	--	0.013	0.010	0.002	0.003
P-value *vs* oxybutynin	0.002	0.254	0.349	--	0.253
Maximum Detrusor Pressure					
n [$]	40	46	50	39	96
Baseline	74.0 (40.18)	74.0 (42.68)	60.6 (32.82)	68.9 (36.74)	66.9 (38.21)
End-of-Study Visit	81.5 (60.82)	57.4 (37.88)	49.8 (40.48)	44.6 (26.38)	53.4 (39.24)
Change from baseline	7.5 (50.96)	-16.6 (32.86)	-10.5 (37.22)	-24.3 (27.59)	-13.4 (35.15)
P-value *vs* placebo	--	0.002	0.003	< 0.001	< 0.001
P-value *vs* oxybutynin	< 0.001	0.222	0.168	--	0.139

[$] Number of subjects with baseline and end-of-study cystometry data.

[#] Number of subjects with baseline and end-of-study cystometry data, with leakage.
Values are are presented as mean (SD).

Table 3 Micturition Diary (FAS)

	Placebo	Solifenacin 5 mg	Solifenacin 10 mg	Oxybutynin 15 mg	Pooled Solifenacin
Number of Micturitions per 24 Hours					
n [$]	38	45	49	39	94
Baseline	6.15 (6.503)	7.31 (5.142)	7.81 (5.187)	7.21 (5.602)	7.56 (5.144)
End-of-Study Visit	5.72 (6.275)	6.00 (4.325)	6.81 (5.237)	5.97 (5.141)	6.43 (4.823)
Change from baseline	-0.46 (2.162)	-1.48 (2.935)	-0.75 (2.930)	-1.23 (2.582)	-1.10 (2.939)
P-value *vs* placebo	--	0.136	0.916	0.254	0.361
P-value *vs* oxybutynin	0.254	0.750	0.268	--	0.658
Number of Catheterizations per 24 Hours					
n [$]	38	45	49	39	94
Baseline	3.35 (3.694)	2.57 (3.368)	2.09 (3.513)	2.46 (3.286)	2.32 (3.434)
End-of-Study Visit	3.06 (3.466)	2.35 (2.931)	1.84 (2.857)	2.31 (2.834)	2.08 (2.888)
Change from baseline	-0.11 (0.672)	-0.15 (0.990)	-0.26 (1.262)	-0.15 (1.348)	-0.21 (1.135)
P-value *vs* placebo	--	0.494	0.137	0.498	0.219
P-value *vs* oxybutynin	0.498	0.986	0.429	--	0.663
Number of Incontinence Episodes per 24 Hours					
n [$]	38	45	49	39	94
Baseline	2.01 (2.690)	1.43 (1.836)	1.91 (2.901)	2.38 (3.913)	1.68 (2.443)
End-of-Study Visit	1.92 (2.635)	0.56 (1.087)	1.42 (3.122)	0.88 (2.328)	1.01 (2.422)
Change from baseline	-0.07 (1.327)	-0.91 (1.390)	-0.44 (2.028)	-1.50 (2.530)	-0.66 (1.758)
P-value *vs* placebo	--	0.003	0.246	< 0.001	0.019
P-value *vs* oxybutynin	< 0.001	0.430	0.008	--	0.051
Number of Micturitions and Catheterizations per 24 Hours					
n [$]	38	45	49	39	94
Baseline	9.50 (4.526)	9.88 (3.591)	9.89 (3.495)	9.67 (3.884)	9.89 (3.523)
End-of-Study Visit	8.77 (4.449)	8.35 (2.777)	8.65 (4.186)	8.28 (3.758)	8.51 (3.580)
Change from baseline	-0.57 (2.096)	-1.63 (2.861)	-1.01 (3.267)	-1.38 (2.683)	-1.31 (3.078)
P-value *vs* placebo	--	0.102	0.539	0.176	0.199
P-value *vs* oxybutynin	0.176	0.807	0.412	--	0.747
Number of Micturitions, Catheterizations and Incontinence Episodes per 24 Hours					
n [$]	38	45	49	39	94
Baseline	11.53 (5.573)	11.32 (3.881)	11.80 (4.883)	12.05 (4.328)	11.57 (4.409)
End-of-Study Visit	10.69 (5.401)	8.90 (2.885)	10.07 (6.427)	9.16 (3.966)	9.52 (5.093)
Change from baseline	-0.64 (2.552)	-2.55 (3.232)	-1.46 (4.386)	-2.89 (3.768)	-1.98 (3.894)
P-value *vs* placebo	--	0.011	0.310	0.006	0.042
P-value *vs* oxybutynin	0.006	0.759	0.055	--	0.208

[$] Number of subjects with baseline and end-of-study diary data.
Values are are presented as mean (SD).

Table 4 Other Secondary Efficacy Variables (FAS)

	Placebo	Solifenacin 5 mg	Solifenacin 10 mg	Oxybutynin 15 mg	Pooled Solifenacin
Incontinence Quality of Life Questionnaire (Total Score)					
n [$]	40	46	51	39	97
Baseline	44.63 (21.830)	51.04 (20.760)	44.73 (23.301)	52.33 (22.347)	47.72 (22.245)
End-of-Study Visit	48.49 (22.261)	59.17 (23.240)	54.21 (25.164)	57.96 (24.133)	56.56 (24.273)
Change from baseline	3.86 (13.260)	8.13 (15.053)	9.48 (17.693)	5.63 (17.344)	8.84 (16.423)
P-value *vs* placebo	--	0.099	0.079	0.327	0.053
P-value *vs* oxybutynin	0.327	0.527	0.483	--	0.449
Incontinence Quality of Life Questionnaire (Avoidance and Limiting Behavior)					
n [$]	40	46	51	39	97
Baseline	45.60 (20.690)	50.88 (18.675)	46.18 (21.715)	51.54 (20.800)	48.41 (20.362)
End-of-Study Visit	47.47 (22.895)	60.01 (21.741)	55.12 (23.490)	58.30 (21.552)	57.44 (22.693)
Change from baseline	1.87 (12.351)	9.14 (15.969)	8.96 (18.600)	6.76 (17.224)	9.04 (17.313)
P-value *vs* placebo	--	0.014	0.030	0.077	0.009
P-value *vs* oxybutynin	0.077	0.534	0.780	--	0.608
Incontinence Quality of Life Questionnaire (Psychosocial Impact)					
n [$]	40	46	51	39	97
Baseline	49.37 (25.203)	56.77 (25.132)	49.29 (26.481)	57.55 (24.804)	52.84 (25.988)
End-of-Study Visit	53.15 (23.751)	65.33 (25.382)	58.60 (26.714)	60.79 (27.237)	61.79 (26.175)
Change from baseline	3.77 (13.794)	8.54 (16.313)	9.30 (17.039)	3.24 (18.912)	8.94 (16.616)
P-value *vs* placebo	--	0.064	0.092	0.699	0.044
P-value *vs* oxybutynin	0.699	0.147	0.210	--	0.125
Incontinence Quality of Life Questionnaire (Social Embarrassment)					
n [$]	40	46	51	39	97
Baseline	38.96 (24.828)	45.46 (24.245)	38.73 (25.136)	47.95 (26.846)	41.92 (24.821)
End-of-Study Visit	44.88 (24.871)	52.17 (26.408)	48.92 (28.059)	54.83 (27.060)	50.46 (27.196)
Change from baseline	5.92 (19.497)	6.71 (17.603)	10.20 (20.856)	6.88 (20.588)	8.54 (19.361)
P-value *vs* placebo	--	0.534	0.267	0.414	0.326
P-value *vs* oxybutynin	0.414	0.818	0.818	--	0.999
EuroQoL 5-Dimension Visual Analogue Scale					
n [$]	39	45	50	39	95
Baseline	59.1 (24.13)	59.0 (22.90)	53.4 (20.44)	57.8 (21.76)	56.1 (21.72)
End-of-Study Visit	58.2 (24.91)	61.8 (22.72)	61.6 (20.03)	66.4 (23.17)	61.7 (21.23)
Change from baseline	-0.9 (12.63)	2.4 (14.84)	8.2 (16.23)	8.6 (18.39)	5.4 (15.77)
P-value *vs* placebo	--	0.300	0.016	0.007	0.050
P-value *vs* oxybutynin	0.007	0.073	0.646	--	0.197
Visual Analogue Scale - Treatment Satisfaction					
n [$]	38	46	51	39	97
Baseline	39.8 (34.13)	52.8 (38.06)	47.0 (38.62)	53.1 (35.97)	49.8 (38.27)
End-of-Study Visit	42.6 (33.09)	63.1 (33.81)	61.3 (33.67)	64.7 (31.43)	62.2 (33.57)
Change from baseline	1.3 (35.55)	10.3 (47.23)	14.3 (34.43)	11.7 (44.86)	12.4 (40.83)
P-value *vs* placebo	--	0.013	0.011	0.009	0.005
P-value *vs* oxybutynin	0.009	0.825	0.808	--	0.792
Subject Perception of Bladder Condition					
n [$]	40	46	51	39	97
Baseline	4.2 (1.19)	4.2 (0.98)	4.5 (1.05)	4.2 (1.16)	4.4 (1.02)
End-of-Study Visit	4.2 (1.17)	3.8 (1.22)	3.9 (1.28)	3.7 (1.31)	3.9 (1.25)
Change from baseline	-0.1 (0.92)	-0.4 (1.04)	-0.6 (1.04)	-0.5 (1.02)	-0.5 (1.04)
P-value *vs* placebo	--	0.118	0.041	0.056	0.041
P-value *vs* oxybutynin	0.056	0.668	0.986	--	0.814

[$] Number of subjects with baseline and end-of-study data for the respective questionnaire.
Values are are presented as mean (SD).