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ORIGINAL ARTICLE

Does BMI, gender or age affect efficacy/tolerability of solifenacin in the management of overactive bladder?

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Abstract
Introduction and Hypothesis Pooled data from seven randomized placebo-controlled trials were analysed to evaluate relationships between baseline body mass index (BMI), gender or age and the efficacy/tolerability of solifenacin (5 – 10 mg daily) in patients with overactive bladder (OAB).
Methods Changes in efficacy variables from baseline to 12 weeks were compared in patients with symptoms at baseline between solifenacin-treated and placebo-treated groups. Normalization rates were calculated (no more than eight micturitions in 24 h, no more than one episode of nocturia per night, zero values for other variables over 24 h). Treatment-emergent adverse events (TEAEs) were recorded.
Results The baseline incidence of incontinence and urgency incontinence increased with increasing BMI and age; relatively more women than men were incontinent. The baseline incidence of urgency was similar between genders and among age groups, but tended to increase with increasing BMI. The baseline frequencies of micturition and nocturia were similar in all BMI categories, between genders and in all age groups. The results from this meta-analysis of an integrated database of data from trials investigating solifenacin showed that solifenacin was more efficacious than placebo for all OAB symptoms across all BMI and age categories, and between genders. Normalization rates for micturition frequency, incontinence and urgency were greater in patients receiving solifenacin than in those receiving placebo across all categories. The overall incidence of TEAEs was higher in patients receiving solifenacin than in those receiving placebo; solifenacin was generally well tolerated in both groups. The overall frequency of TEAEs for solifenacin and placebo was slightly higher in women than in men and in older than in younger patients. The most commonly reported TEAEs were dry mouth and constipation.
Conclusions Regardless of BMI, gender or age, all patients with OAB can be considered candidates for solifenacin treatment.

Keywords Solifenacin · Integrated database · Body mass index · Gender · Age

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Introduction

Solifenacin is a competitive muscarinic receptor antagonist that attenuates bladder contraction. Its efficacy and safety in patients with overactive bladder (OAB) has been demonstrated in an extensive clinical trial programme [1]. Solifenacin can be administered using a flexible-dose regimen, starting at 5 mg once daily which may be increased to 10 mg once daily if sufficient benefit is not achieved at 5 mg and the 10-mg dose is well tolerated. This allows better individualized therapy, with the goal of optimizing efficacy and minimizing side effects. In addition to its established efficacy in women, solifenacin is a well-tolerated and efficacious treatment option for OAB in men without bladder outlet

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obstruction [2]. Flexibly dosed solifenacin has also been shown to be efficacious and well tolerated in patients of age 65 years and older, with comparable efficacy and safety results to those in younger populations [3, 4].

Subcategorizing patients with OAB according to their symptoms and comorbidities may potentially result in tailored therapies leading to more effective disease management. The predictive value of baseline characteristics in OAB patients has not previously been studied using a large database. The availability of patient-level data in over 5,000 patients with OAB from phase 3 and 4 clinical trials of solifenacin provided an opportunity to evaluate the relationships between solifenacin and patient body mass index (BMI), gender and age. Data were collated into a large integrated database (IDB) and analysed. Clinically important questions were formulated a priori by an expert panel of advisors. Questions included: 'Does being overweight or obese make a difference to efficacy and/or tolerability?', 'What is the impact of older age?', 'Do men and women react differently to solifenacin?', 'Does baseline symptomatology/syndrome severity correlate with magnitude of treatment response?' and 'Do any baseline characteristics predict who will or will not respond to solifenacin?'.

Materials and methods

Patient-level data from 11 randomized, placebo-controlled and/or active-controlled phase 3 and phase 4 clinical trials of solifenacin were consolidated into a large IDB. All studies took place between 2001 and 2008. Prior to integration, methodology developed by the Clinical Data Interchange Standards Consortium (CDISC) was used to map all individual datasets to a single format. The data structure was first harmonized using the CDISC Study Data Tabulation Model (SDTM) to ensure consistent categorization. Additional derived and categorical variables were included in the mapping according to standards defined as the Analysis Data Model (ADaM). Two independent programming teams each performed mapping to both SDTM and ADaM twice. Inconsistencies were compared, investigated and corrected in the final output where appropriate. Additional validation steps were completed by review of SAS® code and SAS log files.

Of the seven randomized, placebo-controlled solifenacin OAB clinical trials in the IDB, four were fixed-dose studies and three studies allowed the daily dose of solifenacin to be adjusted between 5 and 10 mg in each subject (Table 1). All studies were conducted in compliance with the International Conference of Harmonization—Good Clinical Practice Guidelines and the principles of the Declaration of Helsinki. Institutional Review Board/Independent Ethics Committee approval was obtained at all sites. All patients provided written, informed consent prior to enrolment. Data from all studies of longer duration were cut off at 12 weeks of treatment to make them comparable with the

Table 1 Clinical trials included in the analysis

Study	Region	Solifenacin dose (mg/day)		Duration (weeks)	Reference
		Analysis group 1	Analysis group 2		
905-CL-013	US	10	10	12	[5]
905-CL-014	US	10	10	12	[6]
905-CL-015	European Union	5, 10	5, 10	12	[7]
905-CL-018	European Union	5, 10	5, 10	12	[8]
905-EC-002 (SUNRISE)	European Union		5 – 10	16	[9]
905-UC-005 (VENUS)	US		5 – 10	12	[10]
905-UC-10 (VIBRANT)	US		5 – 10	12	[11]

Table 2 Baseline patient demographics and characteristics (full analysis set, analysis group 2)

Characteristic	Placebo (n = 2,077)	Solifenacin, any dose (n = 3,081)
BMI (kg/m^2), mean (SD)[a]	28.8 (6.7)	28.5 (6.4)
BMI, n (%)		
<25 kg/m^2 (normal)	452 (21.8)	641 (20.8)
25 to <30 kg/m^2 (overweight)	516 (24.8)	751 (24.4)
30 to <35 kg/m^2 (obese)	288 (13.9)	412 (13.4)
≥35 kg/m^2 (severely obese)	230 (11.1)	261 (8.5)
Missing	591 (28.5)	1016 (33.0)
Gender, n (%)		
Women	1708 (82.2)	2516 (81.7)
Men	369 (17.8)	565 (18.3)
Age (years)		
Mean (SD)	58.3 (13.2)	57.7 (13.5)
Range	18 – 88	18 – 89
Age group, n (%)		
18 to <40 years	189 (9.1)	299 (9.7)
40 to <65 years	1154 (55.6)	1721 (55.9)
65 to <75 years	513 (24.7)	748 (24.3)
≥75 years	221 (10.6)	313 (10.2)
OAB symptoms		
Micturitions per 24 h	11.84 (3.67)	11.78 (3.56)
Incontinence episodes per 24 h	1.98 (2.70)	1.83 (2.55)
Urgency episodes per 24 h	6.05 (4.02)	5.87 (4.06)
Urgency incontinence episodes per 24 h	1.38 (2.34)	1.34 (2.21)
Nocturia episodes per night[b]	1.78 (1.40)	1.81 (1.36)

[a] BMI was not determined in all patients

[b] Nocturia was not assessed in the 905-EC-002 (SUNRISE) study

12-week studies. To examine efficacy, an analysis group containing data from seven studies was examined (analysis 2). For safety, a subgroup comprising four placebo-controlled, monotherapy, fixed-dose studies was examined so that solifenacin doses could be compared (analysis 1).

The efficacy of solifenacin was assessed in terms of improvements in micturition frequency per 24 h, number of urgency episodes per 24 h, number of incontinence episodes per 24 h, number of urgency incontinence episodes per 24 h, number of nocturia episodes per night and volume voided per micturition. End-point values were based on the last observation carried forward. BMI categories were: <25 kg/m^2 (normal), 25 to <30 kg/m^2 (overweight), 30 to <35 kg/m^2 (obese), and ≥35 kg/m^2 (severely obese). Height and weight were not recorded in all studies; therefore BMI could not be determined in 1,601 patients (216 placebo-treated and 637 solifenacin-treated patients from study 905-EC-002, and 372 placebo-treated and 376 solifenacin-treated patients from study 905-UC-010). Because variables were recorded by different methods in the various studies, a remapping process was applied so that a common set

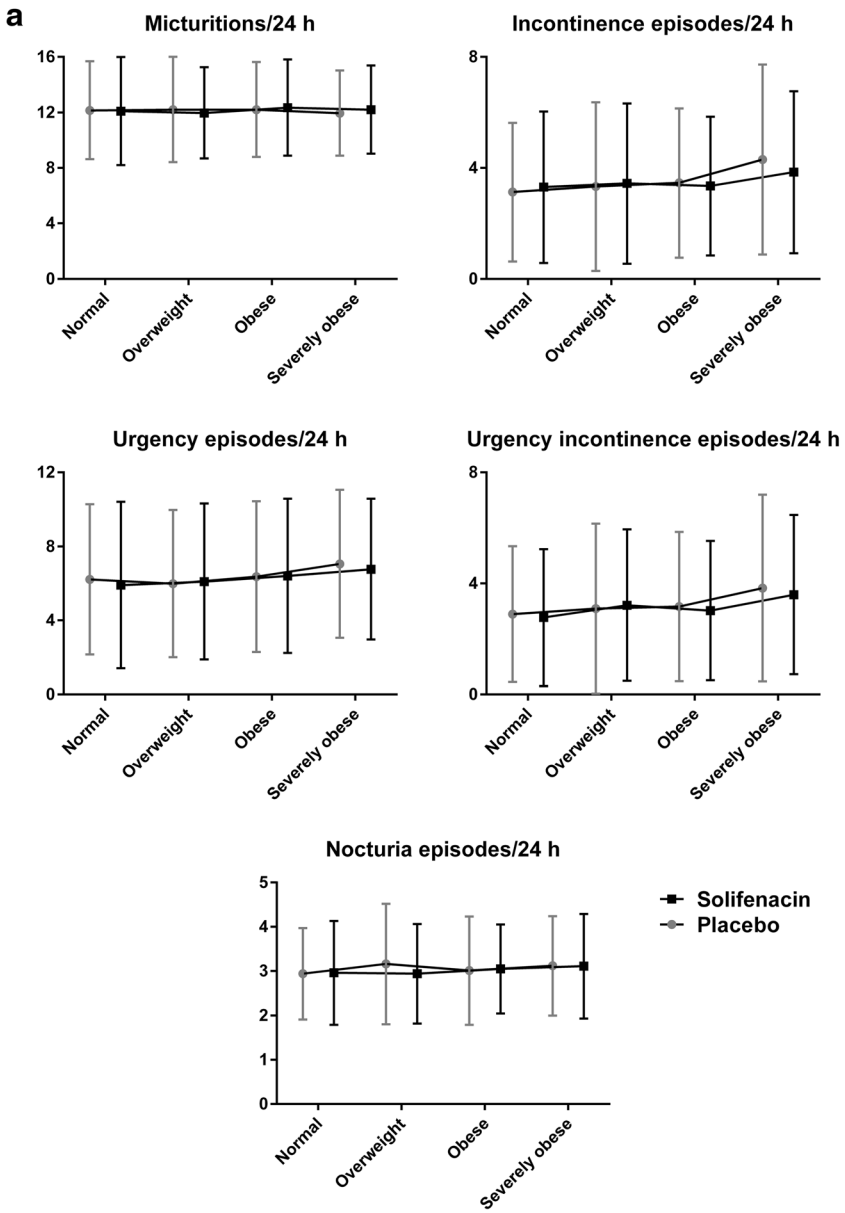


Fig. 1 Baseline incidence of OAB symptoms (**a**) by BMI group, (**b**) by gender, (**c**) by age group (analysis group 2). The data shown are means ± SD

of values was available for analysis. Age categories were 18 to <40 years, 40 to <65 years, 65 to <75 years, and ≥75 years.

Efficacy variables

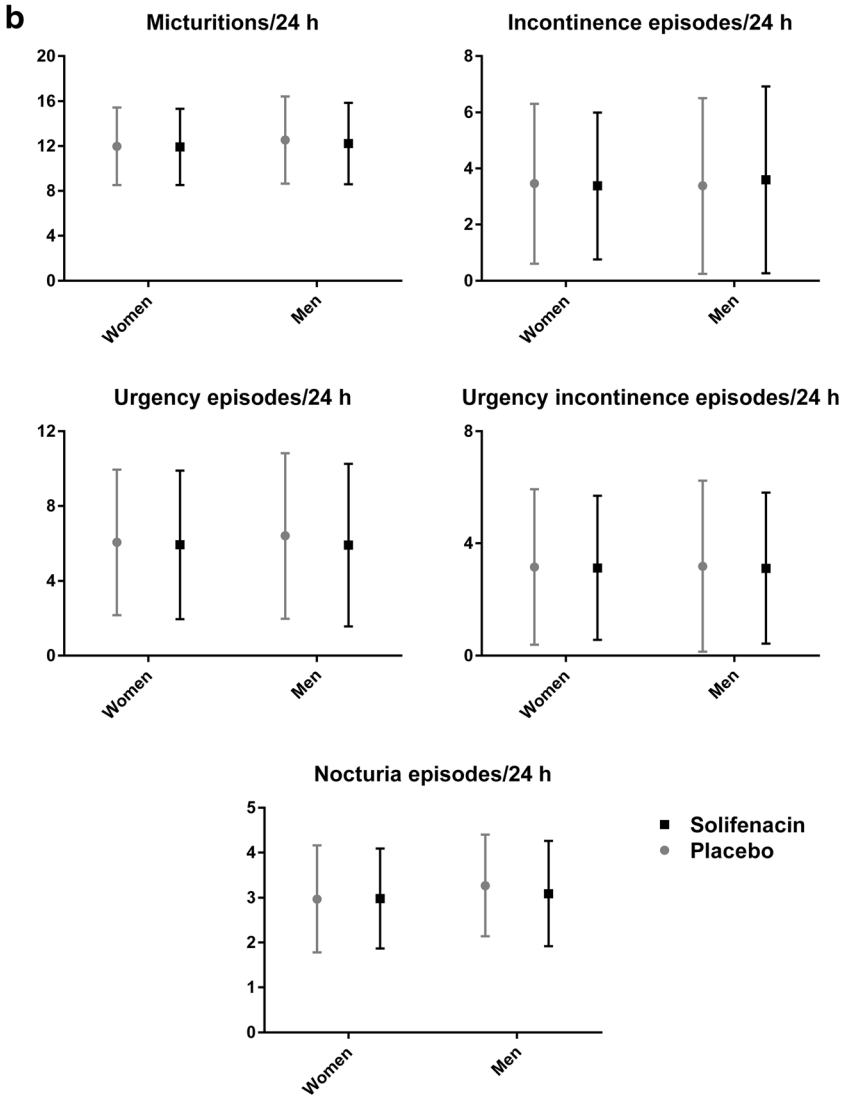
Changes in efficacy variables from baseline to 12 weeks were compared in patients with symptoms at baseline in each BMI, gender and age category between those receiving solifenacin and those receiving placebo. Normalization (remission) rates were also calculated; these were reduction to no more than eight micturitions in 24 h on average (in subjects with eight or more micturitions in 24 h at baseline), reduction to zero episodes of incontinence, urgency and urgency incontinence (in subjects with at least one episode at baseline); and reduction to no more than one episode of nocturia.

Safety variables

The safety of solifenacin in the various subpopulations was assessed by evaluation of treatment-emergent adverse events (TEAEs), summarized according to MedDRA system organ class and preferred term (MedDRA version 11.1). The incidence and severity of TEAEs were recorded, including those of special interest (dry mouth, constipation, blurred vision, urinary retention and acute urinary retention). For Study 905-EC-002 (16-week study), TEAEs collected beyond week 12 were not included in the meta-analysis.

Statistical methods

Prognostic factors associated with changes in efficacy variables at the end-point (gender and age) were evaluated



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using odds ratios and 95 % confidence intervals and analysis of covariance (ANCOVA) of the pooled placebo arms of all placebo-controlled studies. For placebo-controlled monotherapy studies, predictive factors associated with changes in efficacy variables at the end-point (gender and age) were examined using ANCOVA. The Cochran-Mantel-Haenszel test was used to calculate odds ratios for normalization and for TEAEs of interest.

Results

Baseline patient demographics

A total of 5,158 patients were included in the full analysis set for analysis group 2. Almost 70 % of the patients (2,458) had a BMI ≥25 kg/m^2 and 82 % of the patients (4,224) were women (Table 2). The mean age of the patients was 58 years.

The baseline incidence of incontinence and urgency incontinence increased with increasing BMI and age. Relatively more women than men were incontinent; however, for those with incontinence at baseline, the frequency of incontinence was similar in men and women. The baseline incidence of urgency was similar in men and women and among age groups, but tended to increase with increasing BMI. Baseline micturitions and nocturia frequency were similar across BMI categories and age groups, and in men and women (Fig. 1).

Efficacy outcomes

Solifenacin was more efficacious than placebo for all OAB symptoms across all BMI and age categories, and in both men

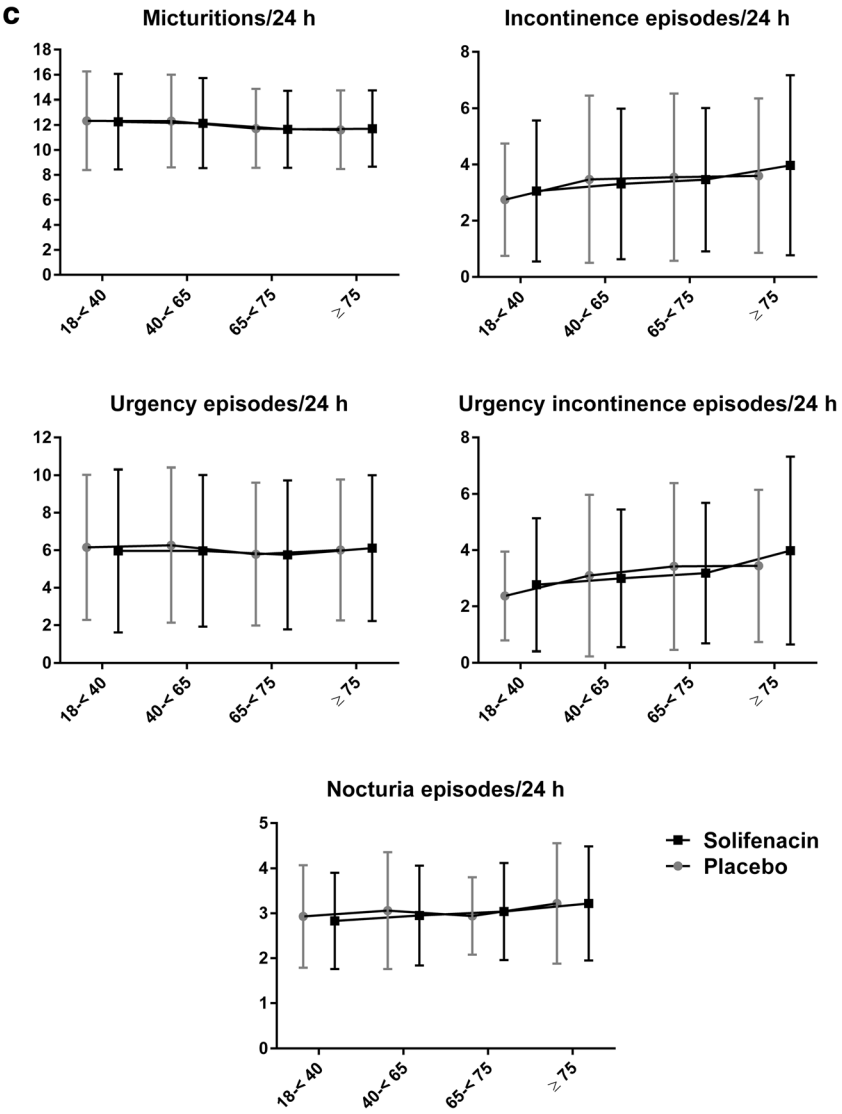

Fig. 1 (continued)

and women (Fig. 2). Normalization rates for micturition frequency, incontinence and urgency were greater in patients treated with solifenacin than in those treated with placebo across all categories. Solifenacin was not consistently better than placebo across categories in reduction of nocturia episodes, although there was some evidence that nocturia im-

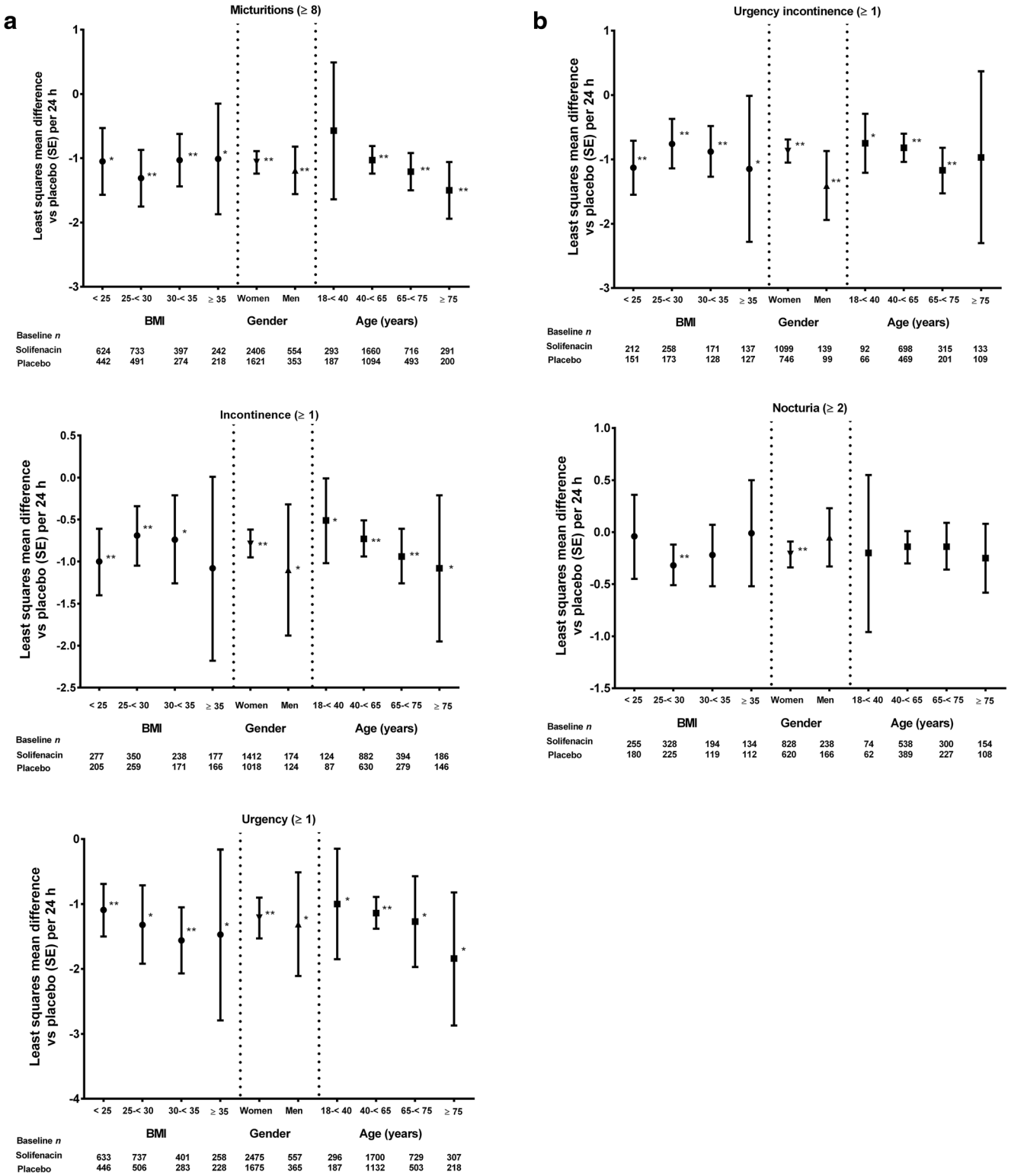

Fig. 2 Changes in efficacy variables from baseline to endpoint in patients with symptoms at baseline expressed as mean differences (*error bars* standard errors) between patients treated with solifenacin 5 – 10 mg per day and patients treated with placebo (analysis group 2; $*p \leq 0.05$, $**p \leq 0.001$)

Table 3 Significance of normalization rates in OAB symptoms at 12 weeks (analysis group 2) in relation to BMI

OAB symptom	BMI group (kg/m^2)							
	<25 (normal)		25 to <30 (overweight)		30 to <35 (obese)		≥35 (severely obese)	
	Placebo	Solifenacin	Placebo	Solifenacin	Placebo	Solifenacin	Placebo	Solifenacin
Micturition								
Episodes/24 h at baseline	442	624	491	733	274	397	218	242
Normalization to <8 episodes/24 h (%)	20	34	22	36	23	32	26	40
Odds ratio	2.16		2.04		1.64		1.97	
p value vs. placebo	<0.001		<0.001		0.007		0.001	
Incontinence								
Episodes/24 h at baseline	269	381	334	451	215	286	196	208
Normalization to 0 episodes/24 h (%)	36	54	36	53	39	50	31	51
Odds ratio	2.04		2.07		1.65		2.29	
p value vs. placebo	<0.001		<0.001		0.008		<0.001	
Urgency								
Episodes/24 h at baseline	446	636	511	748	283	405	228	259
Normalization to 0 episodes/24 h (%)	17	27	17	27	17	24	12	25
Odds ratio	1.71		1.59		1.34		2.31	
p value vs. placebo	<0.001		0.001		0.156		<0.001	
Urgency incontinence								
Episodes/24 h at baseline	231	311	272	381	172	236	163	182
Normalization to 0 episodes/24 h (%)	43	61	45	63	49	61	36	60
Odds ratio	2.03		1.98		1.62		2.65	
p value vs. placebo	<0.001		<0.001		0.021		<0.001	
Nocturia								
Episodes per night at baseline	410	576	461	683	264	377	214	241
Remission to 0 episodes/24 h (%)	16	22	14	18	14	16	13	15
Odds ratio	1.38		1.52		1.25		1.17	
p value vs. placebo	0.061		0.014		0.346		0.566	

Table 4 Significance of normalization rates in OAB symptoms at 12 weeks (analysis group 2) in relation to gender

OAB symptom	Women		Men	
	Placebo	Solifenacin	Placebo	Solifenacin
Micturition				
Episodes/24 h at baseline	1,627	2,412	355	556
Normalization to <8 episodes/24 h (%)	23	37	16	28
Odds ratio	1.95		2.16	
p value vs. placebo	<0.001		<0.001	
Incontinence				
Episodes/24 h at baseline	1,269	1,772	175	252
Normalization to 0 episodes/24 h (%)	34	50	40	60
Odds ratio	1.87		2.21	
p value vs. placebo	<0.001		<0.001	
Urgency				
Episodes/24 h at baseline	1,690	2,499	367	562
Normalization to 0 episodes/24 h (%)	15	25	20	28
Odds ratio	1.72		1.41	
p value vs. placebo	<0.001		0.036	
Urgency incontinence				
Episodes/24 h at baseline	1,058	1,509	149	220
Normalization to 0 episodes/24 h (%)	42	58	45	67
Odds ratio	1.88		2.46	
p value vs. placebo	<0.001		<0.001	
Nocturia				
Episodes per night at baseline	1,354	1,755	311	440
Remission to 0 episodes/24 h (%)	17	20	11	14
Odds ratio	1.30		1.34	
p value vs. placebo	0.006		0.202	

proved more in patients treated with solifenacin across all age groups. Analyses of the normalization rates in OAB symptoms in relation to BMI, gender and age are shown in Tables 3, 4 and 5, respectively.

Safety outcomes

A total of 1,802 solifenacin-treated and 1,209 placebo-treated patients were included in the safety analysis set for analysis 1. The overall incidence of TEAEs was higher in patients treated with solifenacin than in those treated with placebo, but solifenacin was generally well tolerated across all categories. The overall frequency of TEAEs was slightly higher in women than in men and in older than in younger patients in both the solifenacin and placebo groups. Subgroup analyses revealed that the frequency of TEAEs following treatment with solifenacin was dose-related across BMI categories. The frequencies of TEAEs in relation to BMI, gender and age are shown in Tables 6, 7 and 8, respectively. Discontinuations due to TEAEs increased with increasing age. The most commonly reported TEAEs were dry mouth and constipation. Incidence of urinary retention was low, and there were no cases of acute urinary retention. The percentage of patients discontinuing treatment was consistently lower for solifenacin patients than for placebo patients. Reasons for discontinuation are depicted in Fig. 3.

Discussion

Analysis of this large solifenacin IDB, the biggest cohort studied to date for the evaluation of risk factors in OAB, revealed that irrespective of BMI, gender or age, solifenacin is effective for the treatment of OAB symptoms. It is notable that in this IDB analysis of a large population, incontinence normalization rates in men treated with solifenacin were significantly different from the rates in men receiving placebo. This is in contrast to the results of individual OAB studies, which, because of their smaller sample sizes and the fact that men are seldom incontinent, have failed to show such a difference.

Baseline data showed that women were more likely to be incontinent than men and that the incidence of incontinence and urgency incontinence increased with increasing age; this is consistent with previously reported findings [12–15]. In addition, patients with a higher BMI were more likely to be incontinent at baseline.

Table 5 Significance of normalization rates in OAB symptoms at 12 weeks (analysis group 2) in relation to age

OAB symptom	Age group (years)							
	18 to <40		40 to <65		65 to <75		≥75	
	Placebo	Solifenacin	Placebo	Solifenacin	Placebo	Solifenacin	Placebo	Solifenacin
Micturition								
Episodes/24 h at baseline	187	293	1,098	1,665	496	719	201	291
Normalization to <8 episodes/24 h (%)	28	37	22	35	18	34	23	35
Odds ratio	1.66		1.90		2.46		1.76	
p value vs. placebo	0.013		<0.001		<0.001		0.006	
Incontinence								
Episodes/24 h at baseline	108	160	797	1,127	365	505	174	232
Normalization to 0 episodes/24 h (%)	45	58	36	53	33	47	29	45
Odds ratio	1.67		2.03		1.75		1.84	
p value vs. placebo	0.043		<0.001		<0.001		0.004	
Urgency								
Episodes/24 h at baseline	187	299	1,142	1,711	508	741	220	310
Normalization to 0 episodes/24 h (%)	13	24	16	25	17	27	17	23
Odds ratio	1.95		1.68		1.62		1.35	
p value vs. placebo	0.011		<0.001		0.001		0.199	
Urgency incontinence								
Episodes/24 h at baseline	85	131	675	977	292	433	155	188
Normalization to 0 episodes/24 h (%)	47	68	43	60	42	56	41	55
Odds ratio	2.46		2.06		1.73		1.61	
p value vs. placebo	0.002		<0.001		<0.001		0.032	
Nocturia								
Episodes per night at baseline	147	198	908	1,214	417	544	193	239
Remission to 0 episodes/24 h (%)	28	35	17	21	10	12	12	13
Odds ratio	1.53		1.31		1.29		1.12	
p value vs. placebo	0.080		0.020		0.234		0.711	

Table 6 Frequencies of TEAEs of special interest (safety analysis set, analysis group 1) in relation to BMI

TEAE (%)	BMI group (kg/m^2)														
	<25 (normal)				25 to <30 (overweight)				30 to <35 (obese)				≥35 (severely obese)		
	Placebo ($n = 380$)	Solifenacin			Placebo ($n = 440$)	Solifenacin			Placebo ($n = 220$)	Solifenacin			Placebo ($n = 176$)	Solifenacin		
		5 mg/day ($n = 214$)	10 mg/day ($n = 380$)	All doses ($n = 594$)		5 mg/day ($n = 219$)	10 mg/day ($n = 458$)	All doses ($n = 677$)		5 mg/day ($n = 109$)	10 mg/day ($n = 242$)	All doses ($n = 351$)		5 mg/day ($n = 35$)	10 mg/day ($n = 153$)	All doses ($n = 188$)
Dry mouth	3.9	11.2	28.9	22.6	4.8	11.0	27.7	22.3	5.5	11.0	26.0	21.4	1.7	8.6	26.8	23.4
Constipation	4.5	6.1	13.7	10.9	2.0	5.9	12.7	10.5	2.3	3.7	14.0	10.8	2.3	2.9	15.0	12.8
Blurred vision	1.3	5.1	3.7	4.2	1.8	4.1	4.6	4.4	1.8	0.9	5.8	4.3	2.8	2.9	6.5	5.9
Urinary retention	0.3	0	0.3	0.2	0.2	0	0.4	0.3	0.5	0	1.7	1.1	0	0	0.7	0.5
Overall	48.2	45.3	57.6	53.2	52.0	46.6	63.3	57.9	51.4	44.0	66.9	59.8	63.1	51.4	68.0	64.9

Increasing incontinence frequency with increasing BMI is also consistent with previously reported findings [14, 16–18]. In a survey of 3,114 women, increased BMI was directly associated with urinary incontinence of all types, independent of other risk factors [19]. In addition, a post hoc analysis of integrated data from two randomized, placebo-controlled phase 2 trials showed that the mean number of daily micturitions and urge urinary incontinence episodes at baseline were significantly greater in subjects with higher BMI (≥35 kg/m^2) than in those with a lower BMI (<30 kg/m^2; $p \leq 0.01$) [20]. In a study of 368 women, obesity was significantly more common among patients with stress urinary incontinence and detrusor overactivity [21]. It has been hypothesized that excess body weight increases intraabdominal pressure [22], which in turn leads to increased bladder pressure and intravesical pressure [17]. Since elevated BMI has been shown to be a risk factor for OAB [23], recommended first-line therapy for treatment of OAB symptoms includes behavioural interventions, such as life-style changes, with or without pharmacotherapy. Weight loss in overweight and obese women with urinary incontinence results in a significant reduction in the frequency and severity of incontinence episodes [24, 25].

Other drugs used for the treatment of OAB have also shown efficacy irrespective of BMI. The β_3-adrenoceptor agonist, mirabegron, at a dose of 50 mg/day for 3 months demonstrated good efficacy in terms of both subjective and objective parameters in 169 women at study end, regardless of whether they had a normal BMI, or were overweight or obese [26]. In a post hoc analysis of integrated data from two randomized, placebo-controlled phase 2 trials, 60 mg trospium chloride extended release once daily in patients with a BMI <30 kg/m^2 and ≥35 kg/m^2 was associated with a significantly greater mean reduction in the mean number of daily toilet voids and urge urinary incontinence episodes at week 12 than treatment with placebo ($p \leq 0.05$) in both BMI groups [20]. In addition, in a postmarketing surveillance study of 3,766 OAB patients, age, gender and BMI had no clinically relevant impact on the efficacy or tolerability of darifenacin [27].

In contrast, a large observational study in 2,250 patients treated with tolterodine for 12 weeks demonstrated a slight but statistically significant adverse effect of age on treatment [28], with a slight decrease in efficacy in older patients, although there was no decrease in tolerability. This small negative effect was compensated by increasing severity of baseline symptoms with age and greater treatment-associated improvement in patients with more severe symptoms. A very small but statistically significant negative effect of age on treatment-associated improvement in OAB symptoms and global efficacy was

Table 7 Frequencies of TEAEs of special interest (safety analysis set, analysis group 1) in relation to gender

TEAE (%)	Women				Men			
	Placebo ($n = 983$)	Solifenacin			Placebo ($n = 233$)	Solifenacin		
		5 mg/day ($n = 452$)	10 mg/day ($n = 977$)	All doses ($n = 1,429$)		5 mg/day ($n = 125$)	10 mg/day ($n = 256$)	All doses ($n = 381$)
Dry mouth	4.0	12.2	28.9	23.6	5.2	6.4	23.0	17.6
Constipation	3.1	5.3	13.9	11.2	2.1	5.6	12.1	10.0
Blurred vision	1.8	3.8	5.2	4.8	1.7	4.0	3.1	3.4
Urinary retention	0.2	0	0.6	0.4	0	0	0.4	0.3
Overall	53.6	47.8	64.2	59.0	46.8	39.2	57.8	51.7

Table 8 Frequencies of treatment-emergent adverse events (TEAE) of special interest (safety analysis set, analysis group 1) in relation to age

TEAE (%)	Age group (years)															
	18 to <40				40 to <65 years				65 to <75				≥75			
	Placebo ($n = 112$)	Solifenacin			Placebo ($n = 680$)	Solifenacin			Placebo ($n = 295$)	Solifenacin			Placebo ($n = 129$)	Solifenacin		
		5 mg/day ($n = 60$)	10 mg/day ($n = 126$)	All doses ($n = 186$)		5 mg/day ($n = 325$)	10 mg/day ($n = 675$)	All doses ($n = 1,000$)		5 mg/day ($n = 136$)	10 mg/day ($n = 295$)	All doses ($n = 431$)		5 mg/day ($n = 56$)	10 mg/day ($n = 137$)	All doses ($n = 193$)
Dry mouth	1.8	5.0	20.6	15.6	4.3	10.5	26.4	21.2	5.1	11.0	31.2	24.8	3.9	19.6	32.8	29.0
Constipation	1.8	0	6.3	4.3	2.2	4.0	11.7	9.2	4.7	8.1	18.3	15.1	3.1	12.5	19.0	17.1
Blurred vision	0	3.3	4.0	3.8	1.8	3.4	5.8	5.0	2.4	4.4	3.4	3.7	2.3	5.4	3.6	4.1
Urinary retention	0	0	0	0	0.1	0	0.6	0.4	0.3	0	1.0	0.7	0	0	0	0
Overall	40.2	36.7	55.6	49.5	54.0	44.3	61.9	56.2	52.9	47.8	65.4	59.9	52.7	60.7	68.6	66.3

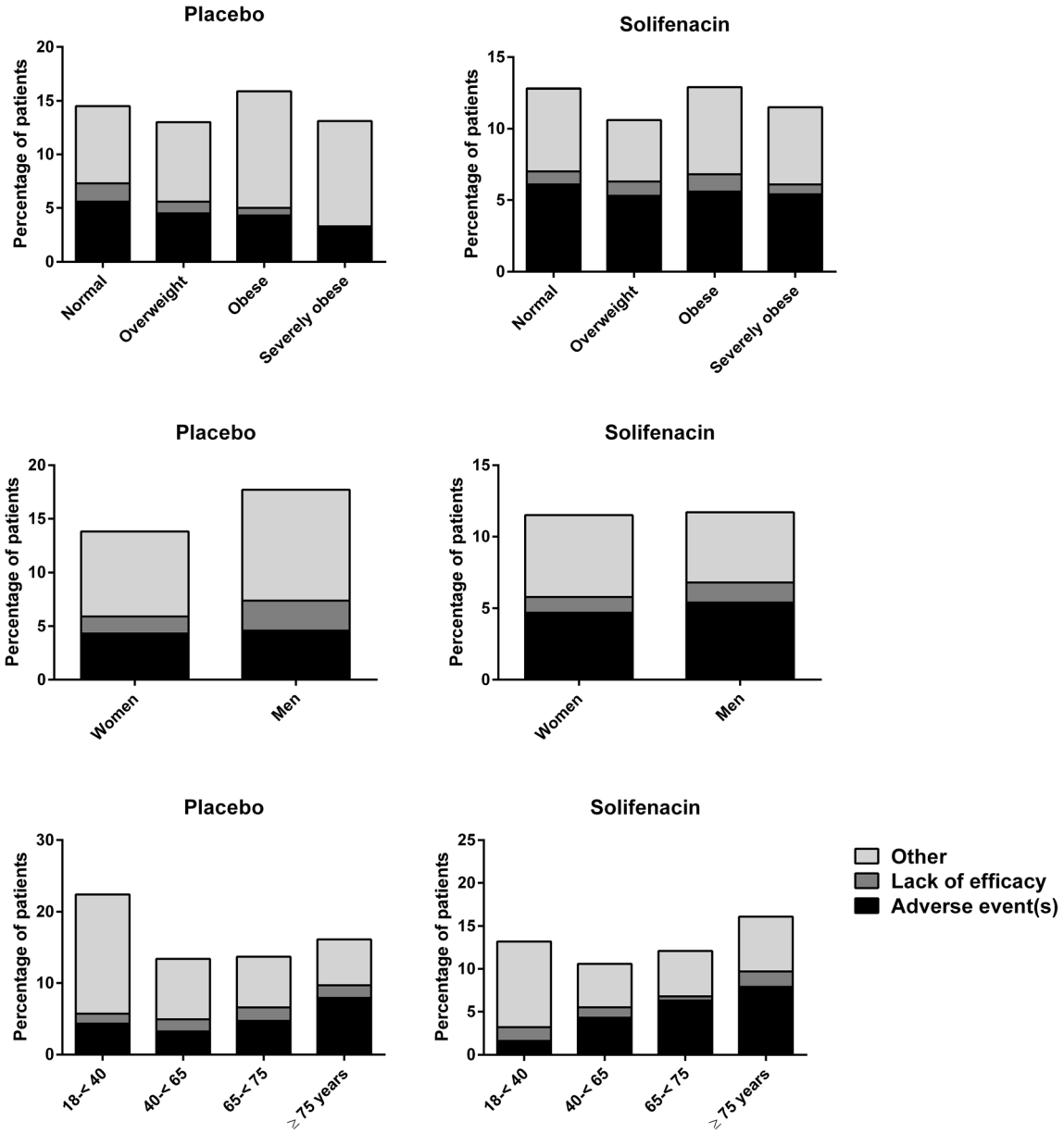

Fig. 3 Reasons for discontinuation due to treatment-emergent adverse events in the BMI, gender and age groups

also found in patients treated with darifenacin for 12 weeks in an observational, open-label study. However, the authors concluded that this was unlikely to be clinically relevant [27].

In the current study of solifenacin, no consistent significant reduction in nocturia episodes was seen with solifenacin compared with placebo across categories. This may be partially explained by the multifactorial nature of nocturia and the fact that nocturia was not an inclusion criterion in the source studies. In addition, patients with nocturnal polyuria, which is unlikely to be managed with antimuscarinic treatment, were not excluded from these trials. Less than 20 % of the population with OAB were men. Although this proportion seems to be higher in more recent studies of OAB, patients included in clinical trials of OAB are predominantly women. Another limitation was that changes in patient weight during the study were not accounted for.

The safety results were in line with those reported previously for solifenacin [29, 30], with a higher overall incidence of TEAEs with the 10 mg per day dose of solifenacin than with the 5 mg per day dose, and with dry mouth and constipation the most commonly reported TEAEs.

In conclusion, the current literature shows a link between some OAB symptoms and BMI, gender and age. Results from this meta-analysis of a solifenacin IDB confirm this link.

However, irrespective of BMI, gender or age, solifenacin is effective for the treatment of OAB symptoms. These data suggest that regardless of BMI, gender or age, all patients with OAB should be considered candidates for solifenacin treatment.

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Compliance with ethical standards

Conflicts of Interest Linda Cardozo is a consultant and speaker for Astellas and Allergan, a consultant for BMR, and a consultant and researcher for Pfizer. Sender Herschorn receives grants and personal fees from Astellas and Allergan, and personal fees from Pfizer and Merus. Robert Snijder and Emad Siddiqui are employees of Astellas. Christopher R. Chapple is a consultant, researcher and speaker for Astellas, Allergan, Medtronic and Recordati, a consultant and speaker for Lilly, a researcher and speaker for Ono and Pfizer, and a speaker for Ranbaxy.

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