CLINICAL ARTICLE

What are the chances of improvement or cure from overactive bladder? A pooled responder analysis of efficacy and treatment emergent adverse events following treatment with fesoterodine

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Abstract

Aim: This study describes patients with different degrees and combinations of symptom resolution in response to fesoterodine exposure to aid physicians in counselling patients with overactive bladder (OAB) on the likelihood of treatment success.

Methods: Data came from 12-week fixed-dose studies of fesoterodine. The proportions of patients experiencing symptom resolution and change in patient-reported outcome measures (PROM) at 4, 8, and 12 weeks were calculated. Treatment-emergent adverse events (TEAE) were reported according to response in urinary urgency episodes (UUE). The relationship between PROM and response was examined.

Results: Out of 6689 patients, 81.6% female, urgency urinary incontinence (UUI) episodes/24 h were more responsive to fesoterodine than UUE; with roughly 50% of patients reporting a 50% reduction and fewer than 10% reporting absence of UUE at 12 weeks compared to approximately 40%–50% reporting absence of UUI. TEAE was numerically lower in patients with greater response. There was a statistically significant relationship between improvement in urinary urgency and associated change in OAB-q symptom bother scores, $r = 0.54$, $p < 0.001$. At Week 4, 64.0%–76.7% of patients who had achieved a significant change in Patient Perception of Bladder Condition (PPBC) had a 50% reduction in UUI. At Week 12 this proportion was between 80% and 87.9%, with those being exposed to fesoterodine treatment reporting response in PPBC at numerically higher rates.

Conclusion: These data provide clinicians with information from which they may usefully communicate the likelihood of symptom resolution in response to pharmacotherapy for OAB and answer a key clinical question posed by

many care providers. Roughly ⅓ of fesoterodine treated patients reported a 50% reduction urgency and ¾ reported 50% resolution of incontinence at 12 weeks. Total resolution of all symptoms was seldom achieved.

KEYWORDS

older adult, overactive bladder, quality of life, treatment efficacy

1 | INTRODUCTION

Overactive bladder (OAB) is a clinical symptom syndrome defined as urinary urgency, usually accompanied by increased daytime frequency and/or nocturia, with urinary incontinence (OAB-wet) or without (OAB-dry), in the absence of urinary tract infection or other detectable diseases.[1,2] OAB affects approximately 13%–36% of women and 11%–22% of men.[3] The likelihood of experiencing urgency urinary incontinence (UUI) increases with age.[4] OAB severity also progresses over time; individuals who initially present with OAB-dry may subsequently develop UUI.[5] Both OAB and UUI are associated with considerable burden including falls and fractures, skin infections, functional impairment, and depression.[6,7] In those of working age, OAB-wet is associated with considerable economic burden in terms of lost employment.[8]

Recommended initial therapy includes behavioral and conservative interventions.[9] Should these fail to achieve improvement, then pharmacological therapy is recommended. The majority of national and international guidelines recommend antimuscarinic agents as first-line pharmacological therapy following lifestyle and behavioral measures.[10] The effect of antimuscarinic drugs for OAB is often dismissed as being clinically insignificant, something belied by the significant improvements in patient-reported outcome measures (PROMs) in these trials, but often cited.[11] In terms of predicting response to therapy, data are limited in that they only describe the mean shift of any variable across the entire patient sample; responder analyses, of considerable utility to prescribers, enabling them to describe to patients their likelihood of improvement in symptoms are mostly limited to dry rates, usually reported as the absence of incontinence during a bladder diary observation period before a research trial visit.[12–15] A single study, which has not been repeated, examined symptom response in various combinations of symptoms.[16] This study therefore aimed to describe the proportion of patients experiencing different degrees and combinations of symptom resolution in response to fesoterodine exposure to aid physicians in describing to patients with OAB the likelihood of treatment success. Secondary aims were to describe responders according to age or sex, explore the relationship between treatment-emergent adverse events (TEAEs) and clinical response, and document the association between urinary urgency and PROM.

1.1 | Patients and methods

1.1.1 | Data sources

Data came from all available 12-week, randomized, controlled, parallel-arm, fixed-dose studies of fesoterodine in OAB (A0221094: NCT01302054, A0221095: NCT01302067, A0221008: NCT00444925, A0221046: NCT00611026, A0221012: NCT00220363, and A0221013: NCT00138723). Each study has been individually reported.[17–22] Efficacy analyses were based on the Full Analysis Set; all randomized patients who took at least one dose of the study drug, where incontinence was a variable, had OAB-wet, and had a baseline efficacy assessment. The safety analysis set included all randomized patients who received at least one dose of double-blind study medication. Missing data were imputed using the last observation carried forward method.

Descriptive data analyses were carried out using SAS software (SAS Version 9.4, SAS Institute). Correlations were performed using Spearman's correlation analyses. A $p < 0.05$ was considered significant.

1.1.2 | Efficacy analysis

At 4, 8, and 12 weeks, the proportion of subjects achieving a 100% or 50% reduction in

- urinary urgency episodes (UUE)/24 h (calculated as a proportional change from the number of episodes at baseline).
- urinary urgency incontinence (UUI) episodes/24 h, where baseline UUI episodes > 0 (calculated as a proportional change from the number of episodes at baseline).
- daytime micturition frequency (DMF)/24 h (100% resolution was defined as DMF < 8/24 h).
- nocturnal micturition frequency (NMF)/24 h (where 100% resolution was defined as NMF < 1).

- three symptoms, reduction in all of the urgency episodes/24 h, DMF/24 h, and UUI episodes/24 h based upon bladder diary data at the relevant time point were calculated. Only 100% resolution (to normalization, as defined above) was calculated for DMF and NMF.

Additional analyses were conducted stratified by age <65, 65–75, >75 years and sex.

1.1.3 | Patient-reported outcome measure

Change in the validated patient perception of bladder condition (PPBC),[23] rated on a 6-point scale with a response defined as a negative score change of 1 or more points versus baseline, was calculated at 4, 8, and 12 weeks.

The total OAB questionnaire (OAB-q) symptom bother score and health-related quality of life scores (not collected in A0221012 and A0221013) were calculated.[24] An improvement in either score was defined as a 10 point change, in accordance with the accepted minimal important difference (MID).[25]

1.1.4 | Association between bladder diary variables and PROMs

The association of patients reporting a clinically relevant improvement in UUE/24 h (defined as a reduction by 50% or 100%) and those reporting a clinically important response in PROMs (PPCB and OAB-q) was visually explored using heat maps, Spearman's correlation coefficients between UUE and PPBC, OAB-q HRQL total score or OAB-q symptom bother score were also calculated. Likewise, the proportion of patients reporting an improvement in PROM who also reported an improvement in UUE/24 h was explored (the reverse association).

1.1.5 | Treatment-emergent adverse events

The percentage of patients experiencing any adverse event, whether related to treatment or not, was calculated according to the proportion of patients reporting either a 50% or 100% reduction in UUE/24 h by fesoterodine dose, timepoint and according to age (<65, 65–75, >75 years) and sex. The reporting of CNS adverse events[26] focused on adverse events of cognitive nature and included Medical Dictionary for Regulatory Activities (MedDRA) terms from the index of nervous systems disorders (e.g., dementia,

disturbance in attention, and memory impairment) and psychiatric disorders (e.g., confusional state, disorientation, and mental status change) were selected for the analysis. TEAE were captured up to 7 days post-exposure at all time points.

All data were descriptively analyzed due to the exploratory nature of the study, and the high risk of generating false-positive signals (Type I error) in an analysis with a large number of variables collected for multiple treatment groups and time points. Bladder diary and PROM variables were analyzed as responder rates and MIDs rather than as continuous variables, producing objective clinical meaningful measures.

2 | RESULTS

Data from 6689 patients (1233 men and 5456 women) were analyzed. In total, 81.6% of the study participants were women. The sample at each time point comprised 6234 at Week 4, 1603 at Week 8, and 6317 at Week 12. The age of the included patients ranged between 18 and 95 years. Body mass index ranged between 16.5 and 56.1 kg/m^2 for the 1233 men and 13.7 and 65.8 kg/m^2 for the 5456 women; other demographic and baseline data are shown in Table 1.

The proportions of patients experiencing a 50% or 100% reduction in symptoms at Weeks 4, 8, and 12 for UUE, UUI, DMF, NMF, and the combination of all symptoms according to treatment exposure are shown in Figure 1. Daily UUI episodes were generally more responsive to fesoterodine treatment than the number of UUE; with roughly ⅓ of patients reporting a 50% reduction and fewer than 10% reporting complete resolution of daily UUE at 12 weeks compared to approximately ¾ of patients reporting 50% resolution and ~40%–50% reporting complete resolution of UUI . Generally, drug treatment at any dose resulted in a numerically greater response than placebo treatment, except for the combination of symptoms. A total absence of UUE, UUI, and normalization of DMF and NMF occurred in only 5.2% of patients treated with fesoterodine 8 mg at 12 weeks versus 2.9% on placebo.

2.1 | Age stratification

The sample consisted of 4340 patients <65 years of age, 1760 patients between 65 and 75 and 589 patients >75 years old. For all three groups of treatment combined, at Week 4, a 50% response in UUE was reported by 19.9% <65 years, 19.0% 65–75 years, and 16.6% >75 years. At Week 8, this response was reported by 9.0% <65 years olds; 8.3% of

TABLE 1 Demographics and baseline characteristics

	Placebo			Fesoterodine 4 mg			Fesoterodine 8 mg		
	Male	Female	Total	Male	Female	Total	Male	Female	Total
Total sample, N	384	1669	2053	273	1100	1373	576	2687	3263
Mean age (years) (SD)	60.8 (13.9)	58.1 (13.1)	58.6 (13.3)	62.1 (12.7)	57.6 (13.2)	58.5 (13.2)	60.0 (14.3)	57.8 (13.0)	58.2 (13.3)
Race (% white)	78.4	83.4	82.5	81.0	85.6	84.7	75.3	82.8	81.5
Mean BMI (m/kg^2) (SD)	28.4 (5.6)	29.5 (7.1)	29.3 (6.8)	28.4 (5.5)	30.0 (7.4)	29.7 (7.1)	28.0 (5.5)	29.5 (6.7)	29.2 (6.5)
Mean DMF/24 h (SD) N*	10.1 (2.9) 264	9.8 (2.9) 1260	9.9 (3.0) 1524	9.8 (2.4) 91	10.2 (3.0) 382	10.1 (3.0) 473	9.6 (2.8) 384	9.7 (2.9) 1968	9.7 (2.9) 2352
Mean NMF/24 h (SD) N*	2.3 (1.4) 264	2.1 (1.4) 1260	2.1 (1.4) 1524	2.5 (2.0) 91	2.0 (1.4) 382	2.1 (1.6) 473	2.4 (1.4) 384	2.1 (1.4) 1968	2.1 (1.4) 2352
Mean UUE/24 h (SD) N*	10.9 (4.4) 334	10.5 (4.1) 1576	10.6 (4.1) 1910	11.7 (4.0) 234	11.2 (4.0) 1029	11.3 (4.0) 1263	10.7 (4.1) 534	10.4 (4.0) 2591	10.4 (4.0) 3125
Mean UUI/24 h (SD) N*	3.0 (2.4) 334	3.4 (2.6) 1576	3.3 (2.6) 1910	3.5 (2.4) 234	3.9 (2.7) 1029	3.9 (2.7) 1263	2.9 (2.2) 534	3.3 (2.5) 2591	3.2 (2.5) 3125

Note: N* – all patients with UUI > 1 at baseline.

Abbreviations: BMI, body mass index; DMF, daytime micturition frequency; NMF, nocturnal micturition frequency; SD, standard deviation; UUE, urinary urgency episode; UUI, urgency incontinence episode.

65–75 years olds and 7.1% >75 years olds and at Week 12, 30.9%, 28.7%, and 25.4%, respectively. For a 50% response in UUI, the proportions at Week 4 were 63.3%, 62.9%, and 57.6%; at Week 8, 59.4%, 62.4%, and 43.2%. By Week 12, a 50% response in UUI was reported in 74.1% <65 years olds, 73.8% of 65–75 years olds, and 67.7% of >75 years olds. The proportions of patients experiencing a 100% response to each variable are shown in Table 2.

2.2 | Sex

For all three groups of treatment combined, at Week 4, 20.4% of 5080 women and 15.0% of 1154 men reported a 50% response in UUE h. At Week 8, these proportions were 8.5% of 1265 women and 9.2% of 338 men. By Week 12, 30.9% of women and 25.4% of men reported a 50% response. For 50% response in UUI/24 h, these proportions were at Week 4, 62.5% of 4841 women and 63.6% of 1037 men; at Week 8, 56.6% of 1048 women and 67.6% of 225 men and at Week 12, 72.7% of 4906 women and 77.3% of 1049 men. The proportions experiencing a 100% response to each variable are shown in Table 3.

2.3 | Patient-reported outcome measure

The proportions of responders at 12 weeks by treatment exposure are shown in Figure 2. The proportions of patients achieving either a 50% or 100% response in OAB symptoms who were responders to PPBC, OAB-q symptom bother, and total health-related quality of life score are shown in Table S1. Of responders to PPBC at Week 12, 81.6% of fesoterodine 4 mg and 87.9% of fesoterodine 8 mg exposed patients achieved a 50% reduction in UUI; 47.6% and 62.7%, respectively, achieved a 100% reduction. Of patients reporting a response in OAB-q symptom bother score, 58.7% of fesoterodine 4 mg and 66.0% of fesoterodine 8 mg achieved a 100% reduction in UUI at Week 12. The proportions of patients reporting a 100% reduction in UUE who reported a response in this scale were much lower at 6.2% and 9.4%, respectively. These proportions were larger than those reported by placebo-treated patients but the differences were small. This pattern was reflected in the proportions of patients achieving symptom reduction who reported a response in OAB-q total HRQL scores. Table S2 shows the reverse association, the proportions of patients

FIGURE 1 Proportions of 50% or 100% responders in OAB symptoms at Weeks 4–12 by treatment status. (A) 50% responders in urinary urgency episodes (UUEs)/24 h or urinary urgency incontinence (UUI)/24 h. (B) 100% responders in UUEs/24 h or UUI/24 h. (C) 100% responders in daytime micturition frequency (DMF)/24 h, nocturnal micturition frequency (NMF)/ 24 h, and all symptoms combined. OAB, overactive bladder
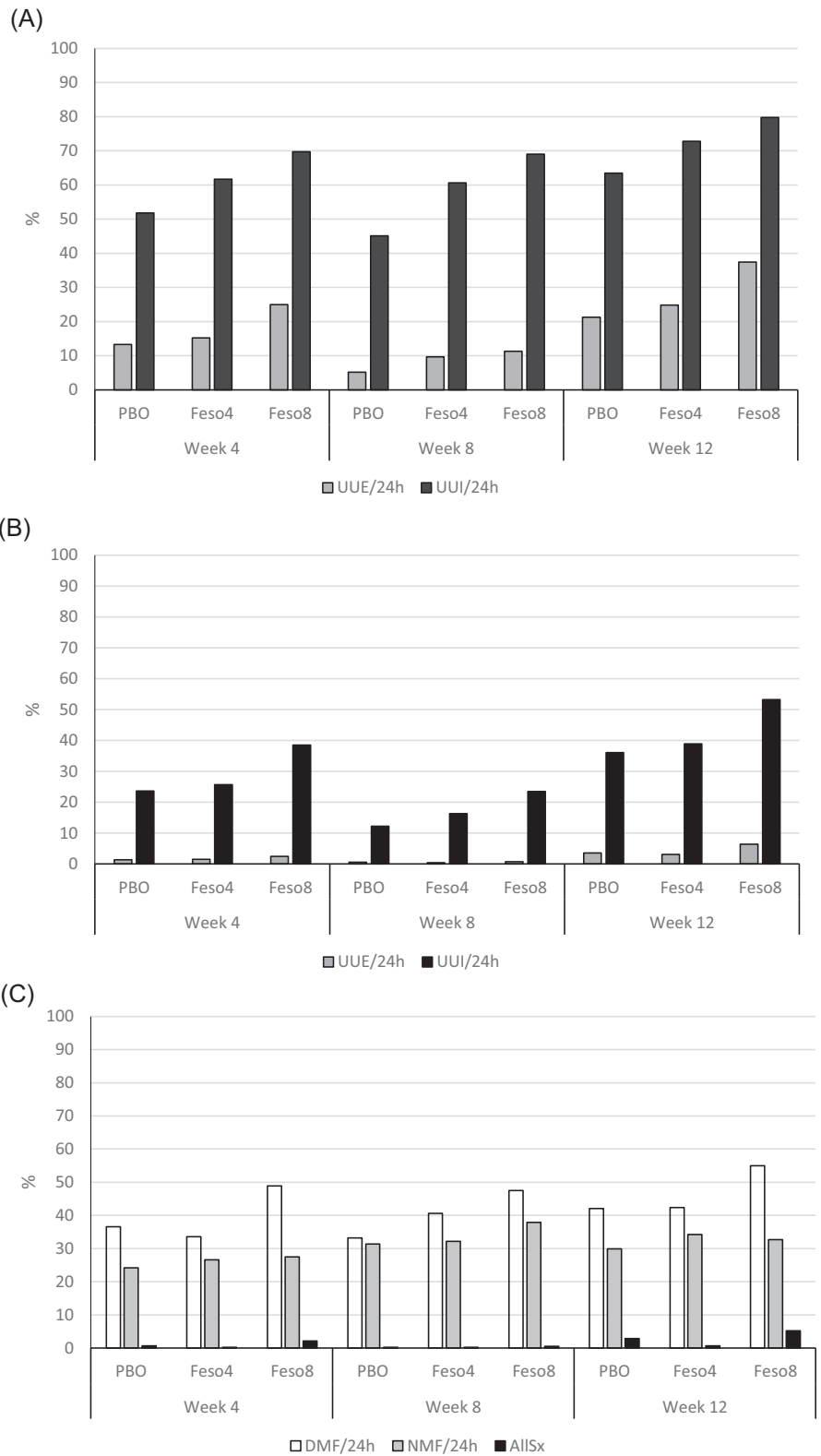
TABLE 2 100% responders by time point and age group (all treatment groups combined)

	<65 years		65 – 75 years		>75 years	
		100% responders		100% responders		100% responders
	N	*n* (%)	*N*	*n* (%)	*N*	*n* (%)
Week 4						
UUE/24 h	4063	79 (1.9)	1630	34 (2.1)	541	8 (1.5)
UUI/24 h	3801	1240 (32.6)	1553	466 (30.0)	524	142 (27.1)
DMF/24 h	2958	1179 (39.9)	1123	527 (46.9)	374	196 (52.4)
NMF/24 h	2958	945 (31.9)	1123	181 (16.1)	374	43 (11.5)
All OAB Sx	2693	39 (1.5)	1045	15 (1.4)	357	4 (1.1)
Week 8						
UUE/24 h	1074	6 (0.6)	388	3 (0.8)	141	0 (0.0)
UUI/24 h	829	150 (18.1)	319	62 (19.4)	125	10 (8.0)
DMF/24 h	1074	401 (37.3)	388	181 (46.7)	141	66 (46.8)
NMF/24 h	1074	435 (40.1)	388	84 (21.7)	141	23 (16.3)
All OAB Sx	829	3 (0.4)	319	1 (0.3)	125	0 (0.0)
Week 12						
UUE/24 h	4123	198 (4.8)	1647	89 (5.4)	547	22 (4.0)
UUI/24 h	3857	1795 (46.5)	1568	676 (43.1)	530	217 (40.9)
DMF/24 h	2991	1395 (46.6)	1133	598 (52.8)	378	209 (55.3)
NMF/24 h	2991	1148 (38.4)	1133	228 (20.1)	378	59 (15.6)
All OAB Sx	2723	105 (3.9)	1053	45 (4.3)	361	12 (3.3)

Abbreviations: DMF, daytime micturition frequency; NMF, nocturnal micturition frequency; Sx, symptoms; UUE, urinary urgency episode; UUI, urgency incontinence episode.

with symptom improvement who also reported an improvement in OABq-total HRQL, OAB-SS, or PPBC. Generally, for UUI a greater proportion of patients reported PROM response with 100% resolution.

2.4 | PROM and symptom response

There was a statistically significant relationship between raw change (baseline to 12 weeks) in percent improvement in urinary urgency and associated change in OAB-q symptom bother scores, $r = 0.54$, $p < 0.001$ (Figure S1). Likewise, there was a statistically significant association between percent change in UUE and PPBC score between baseline and 12 weeks, $r = 0.49$, $p < 0.001$. Table S3 shows the correlation coefficients between percent change from baseline to Week 12 for different bladder diary variables and PROM. Changes in PPBC and OAB-q symptom bother scores were positively associated with reductions in bladder diary variables, whereas changes in OAB-q total HRQL scores were negatively associated with bladder diary variables, that is, the higher change values on OAB-q total HRQL scores the better

reduction in OAB symptoms. All of the correlations were of moderate nature in according to Cohen's benchmarks ($|r|$ 0.1, 0.3, 0.5 as small, medium, and large, respectively), except between PPBC and NMF ($r = 0.54$) and OAB-q symptom bother scores and UUE ($r = 0.54$) where large correlations were found.

2.5 | Treatment-emergent adverse events

The number of TEAE according to either 50% or 100% response in UUE/24 h at 12 weeks compared to baseline by treatment is shown in Table S4. Of the 1223 evaluable men, 476 (38.6%) reported at least one TEAE of which 33 (2.7%) was serious and 54 (4.4%) severe. Sixty-one patients (4.9%) discontinued and 8 (0.6%) temporarily stopped their medication during the trial. Of the 5456 women, 2475 (45.4%) reported at least one TEAE of which 102 (1.9%) were classified as serious and 201 (3.7%) as severe. Two hundred twenty-nine women (4.2%) women discontinued treatment and 74 (1.4%) temporarily stopped treatment during the trial.

TABLE 3 100% response rates by time point and sex (all treatment groups combined)

	Women		Men	
	N	100% responders, *n* (%)	*N*	100% responders, *n* (%)
Week 4				
UUE/24 h	5080	106 (2.1)	1154	15 (1.3)
UUI/24 h	4841	1490 (30.8)	1037	358 (34.5)
DMF/24 h	3632	1562 (43.0)	823	340 (41.3)
NMF/24 h	3632	1015 (27.9)	823	154 (18.7)
All OAB Sx	3389	50 (1.5)	706	8 (1.1)
Week 8				
UUE/24 h	1265	5 (0.4)	338	4 (1.2)
UUI/24 h	1048	170 (16.2)	225	52 (23.1)
DMF/24 h	1265	506 (40.0)	338	142 (42.0)
NMF/24 h	1265	439 (34.7)	338	103 (30.5)
All OAB Sx	1048	3 (0.3)	225	1 (0.4)
Week 12				
UUE/24 h	5147	265 (5.2)	1170	44 (3.8)
UUI/24 h	4906	2169 (44.2)	1049	519 (49.5)
DMF/24 h	3669	1809 (49.3)	833	393 (47.2)
NMF/24 h	3669	1236 (33.7)	833	199 (23.9)
All OAB Sx	3425	134 (3.9)	712	28 (3.9)

Abbreviations: DMF, daytime micturition frequency; NMF, nocturnal micturition frequency; Sx, symptoms; UUE, urinary urgency episode; UUI, urgency incontinence episode.

FIGURE 2 Proportion of patient-reported outcome measures (PROM) responders by exposure at Week 12 (all with urgency urinary incontinence > 0 at baseline)
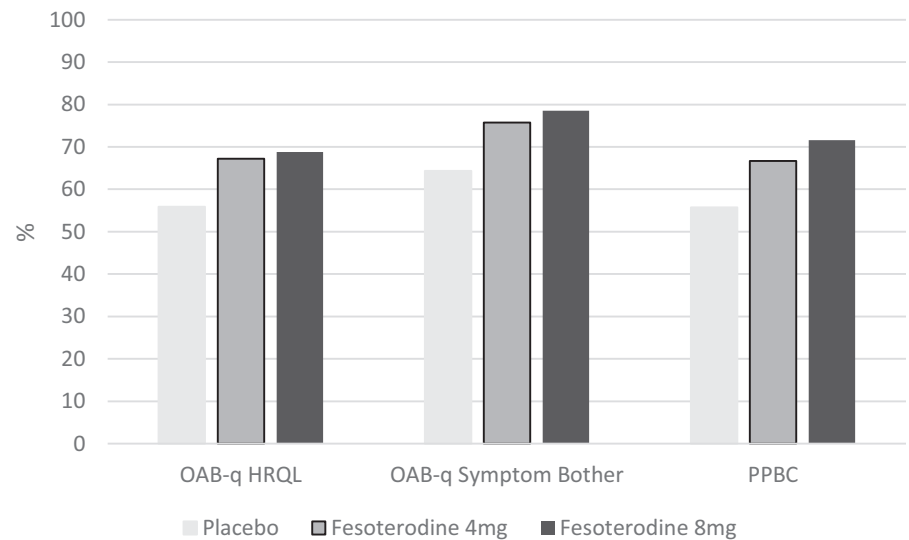
In terms of age, 42.6% (1847) of <65 years old patients, 46.4% (816) 65 to 75 years old patients, and 48.9% (288) >75 years old patients reported at least one TEAE. The distribution of AE according to the nervous system and psychiatric terms of MedDRA is shown in Table S5.

3 | DISCUSSION

Giving patients a realistic expectation of treatment outcomes improves treatment adherence and reduces the likelihood of treatment failure in a disease area where

adherence with pharmacological therapy is poor, with marked drop-off early after prescription.[27–29] This study has described the likelihood of response to OAB treatment for the cardinal symptoms of OAB at time points out to twelve weeks. The proportion of patients with a response in UUI/24 h was greater than those with a response in UUE/24 h at all time points, regardless of treatment exposure. The resolution of UUI appears to be the most important outcome for patients.[30,31] Resolution of UUE appears to be more difficult to achieve, urgency as a subjective phenomenon may be much more difficult to wholly eradicate, even when assessed over the time period where the patient in a trial completes a bladder diary. An alternative approach might have been to only describe the change in severe UUE, but this too would be subjective and perhaps will more difficult to explain to patients during clinical counseling.

As in the pivotal trials, nocturia proved difficult to normalize, with approximately 20% of patients reporting a response which improved numerically in association with time, active treatment, and dose. The clinical value of this is debatable but, in OAB treatment trials, apart from global polyuria (defined in trial protocols as ≥ 3 L/24 h), other causes of nocturia were not evaluated.

The response to treatment generally increased over the 12 weeks of the studies. Although the differences observed in Week 8 results may represent true differences, the results may reflect sampling variability due to the smaller number of patients available at Week 8; only two studies collected these data.

Complete resolution of all OAB symptoms was reported by few patients, regardless of treatment and time. This finding is, in of itself, of utility in giving realistic expectations of treatment and may not be as important as we think given that the absence of incontinence episodes appears to be the most important outcome to patients.[30,32] Normalization was also defined according to an accepted or idealized norm. However, in the non-OAB age-matched population this norm may not be "normal;" this may be why the PROMs confirm a benefit despite the continued presence of symptoms.

The results by age suggest an attenuated response to the majority of OAB symptoms in the >75 years old patients, apart from normalization of DMF. However, approximately 40% of older adults experienced 100% resolution of UUI at Week 12, compared to 43% of younger patients. This is similar to the results of an observational, open-label surveillance flexible-dosing study of OAB treatment with the antimuscarinic darifenacin, where age had a small negative impact on treatment efficacy.[33] In the trials of flexibly dosed fesoterodine, which prospectively recruited older people, the majority of patients escalated their dose to 8 mg to achieve the greatest

efficacy, and factors associated with dose escalation have been reported.[34–36] The observation of a slightly reduced effect with age may well be due to increased severity of disease, not adjusted for in this analysis. This explanation certainly fits with the greater propensity for older adults to up-titrate to achieve optimal efficacy.

The relationship between outcomes, measured by degree of resolution in symptoms and PROM, has not been well-described in the literature. When the degree of symptom resolution in patients reporting a PROM response is examined, there is an inconsistent relationship between the proportion of patients reporting resolution of certain symptoms (e.g., UUI showing numerically higher association with PROM responder status than UUE), across treatments. These proportions are generally lower across all degrees of symptom resolution. When examined from the perspective of the number of patients with either 50% or 100% symptom resolution reporting a positive change in PROM we see, as perhaps might be expected, an increase in the (mostly much greater) proportions of patients reporting a positive change in PROM in association with active treatment, compared with placebo, but numerically small changes between the 4 and 8 mg dose of fesoterodine. This may well be a result of using an enriched study population, with exclusion of non-symptom responders which leads to reporting positive change in PROM, regardless of treatment dose. Likewise, the larger proportions of patients reporting a positive response to PROM increases as the degree of resolution of symptoms increases.

Here, we also report the proportion of patients reporting TEAE in association with the degree of resolution of either 50% or 100% response in UUE/24 h at 12 weeks. We observe a numerically smaller proportion of patients reporting a TEAE in association with an increase in the degree of resolution. Although the difference is numerically small, this warrants comment; does this reflect a true decrease in the incidence of TEAE or are patients who experience a greater resolution in symptoms just less likely to report them as they internally balance the benefits versus harms of their treatment? Clearly, this cannot be answered from these data, but this finding does perhaps bear further investigation. The data provided here may also be of value when comparing the relative values of symptom resolution and adverse events when considering treatment benefits and weighting. A recently reported multi-criterion decision analysis for OAB using specialist clinician-derived weighting has recently been reported.[37]

Despite the novel perspectives on data presented here, using trial data clearly has its limitations. Data came from study participants, who have met strict inclusion criteria and may not reflect "real life" practice in terms of comorbid diseases and co-existent medications;

likewise, baseline disease variable severity may differ from the typical patient started on drug therapy in routine clinical practice. OAB is also a symptom complex and anchoring this analysis to a single symptom may not have captured the complex interplay between them, this may well account for the loose association between symptom improvement and PROM results. We also did not take into account the prior treatment experience of patients; it is well-recognized that treatment-experienced patients are less likely to report TEAE but may not achieve similar levels of treatment benefit.[38] Finally, data here were generated from trials with a single agent, and the results may not be generalizable across all antimuscarinic therapy. However, fesoterodine is the only antimuscarinic agent which has a consistent dose–response across disease variables demonstrated in clinical trials.[21,22]

In conclusion, in this novel analysis, we can provide clinicians with information from which they may usefully communicate the likelihood of symptom resolution in response to pharmacotherapy for OAB, and answer a key clinical question posed by many clinicians.

CONFLICT OF INTERESTS
Adrian Wagg reports personal fees from Astellas Pharma, grants from Essity Health & Hygiene AB, grants and personal fees from Pfizer Corp, personal fees from Pierre Fabre Medicaments, personal fees from Sanofi, outside the submitted work; his spouse is an employee of Pfizer. Sender Herschorn reports personal fees from Pfizer, grants and personal fees from Astellas, grants from Urovant, outside the submitted work. Martin Carlsson and Mireille Fernet are employees of Pfizer and may own stock or stock options; Matthias Oelke reports nonfinancial support and others from Apogepha Arzneimittel, personal fees, nonfinancial support and other from Astellas, personal fees, nonfinancial support and other from Pfizer, personal fees, nonfinancial support and other from Pierre Fabre, outside the submitted work.

AUTHOR CONTRIBUTIONS
Concept & design: Adrian S. Wagg, Martin Carlsson, and Mireille Fernet. *Data analysis*: Martin Carlsson, *Interpretation*: Adrian S. Wagg, Sender Herschorn, and Matthias Oelke. *Writing*: Adrian S. Wagg, Matthias Oelke, Sender Herschorn, and Martin Carlsson. *Critical analysis, review and revision*: Adrian S. Wagg, Sender Herschorn, Martin Carlsson, Mireille Fernet, and Matthias Oelke.

DATA AVAILABILITY STATEMENT
Data subject to third-party restrictions. The data that support the findings of this study are available from Pfizer. Restrictions apply to the availability of these data, which were used under license for this study but are available with permission.

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SUPPORTING INFORMATION

Additional Supporting Information may be found online in the supporting information tab for this article.