HOW COMMON ARE ADVERSE EVENTS IN PATIENTS WITH EITHER A 50% OR 100% RESOLUTION OF URINARY URGENCY EPISODES DURING TREATMENT WITH FESOTERODINE.

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INTRODUCTION & AIMS

Overactive bladder (OAB) is a common condition affecting the quality of life of many people. Antimuscarinics, the current first-line treatments for OAB are associated with adverse events which are more likely to occur in patients with either multimorbidity or polypharmacy [1], however, clinicians could benefit from a clearer understanding of the benefit/risk ratio of antimuscarinics in order to manage patient expectations and, where possible, improve adherence to medication. This study examined the efficacy and safety information from patients in fesoterodine trials to explore the relationship between Treatment Emergent Adverse Events (TEAE) and clinical response defined according to resolution of OAB symptoms.

METHODS

This study used pooled data from 6 fixed dose studies of fesoterodine, each a parallel, 12 week, double blind RCT to describe the degree of symptom improvement by end of treatment weeks 4, 8 and 12, after exposure to either placebo, 4mg or 8mg of fesoterodine. Analysis was based on all subjects who took at least one dose of assigned study drug and contributed data to at least one baseline and post-baseline efficacy assessment with the baseline value of the outcome variable > 0. The following measures were used: the proportion of patients achieving a 100% and 50% reduction in urinary urgency episodes/24h (UUE)

AE occurring up to 7 days post exposure to study drug were included. CNS and cognitive AE were specifically included according to MEDRA accepted terms.

RESULTS

Data from 6689 patients, (fesoterodine 4mg =1373, fesoterodine 8mg = 3263, placebo =2053, mean age 58.4y) were included. The most frequent TEAE (all causality) in the fesoterodine groups were dry mouth and constipation. Responders tended to have similar or numerically lower rates of TEAEs compared to the whole study population (Table 1). CNS and cognitive adverse events were few across all treatment arms and categories of response to urgency symptoms.

	Placebo n=2053	Placebo n = 417	Placebo n = 71	Fesoterodine 4mg n = 1373	Fesoterodine 4mg n = 319	Fesoterodine 4mg n = 40	Fesoterodine 8mg n = 3263	Fesoterodine 8mg n = 1150	Fesoterodine 8mg n = 198
	All patients	50% response	100% response	All patients	50% response	100% response	All patients	50% response	100% response
No. of Subjects with: (n(%))									
Any TEAE	707 (34.4)	142 (34.1)	18 (25.4)	612 (44.6)	123 (38.6)	12 (30.0)	1632 (50.0)	559 (48.6)	88 (44.4)
Any serious TEAE*	47 (2.3)	11 (2.6)	2 (2.8)	30 (2.2)	1 (0.3)	0 (0)	58 (1.8)	17 (1.5)	4 (2.0)
Discontinuation due to TEAE	58 (2.8)	3 (0.7)	1 (1.4)	59 (4.3)	4 (1.3)	1 (2.5)	173 (5.3)	21 (1.8)	3 (1.5)
Dose reduction or temporary d/c	25 (1.2)	3 (0.7)	0 (0)	13 (0.9)	1 (0.3)	0 (0)	44 (1.3)	13 (1.1)	1 (0.5)
Adverse event of interest									
Cognitive effects	4 (0.2)	1 (0.2)	0 (0)	4 (0.3)	0 (0)	0 (0)	3 (0.1)	1 (0.1)	0 (0)
Constipation	38 (1.9)	9 (2.2)	1 (1.4)	37 (2.7)	6 (1.9)	1 (2.5)	158 (4.8)	49 (4.3)	7 (3.5)
CNS	53 (2.6)	11 (2.6)	1 (1.4)	41 (3.0)	5 (1.6)	0 (0)	77 (2.4)	19 (1.7)	2 (1.0)
Dizziness	21 (1.0)	4 (1.0)	0 (0)	18 (1.3)	3 (0.9)	0 (0)	27 (0.8)	8 (0.7)	0 (0)
Dry mouth	111 (5.4)	28 (6.7)	7 (9.9)	209 (15.2)	53 (16.6)	5 (12.5)	916 (28.1)	336 (29.2)	51 (25.8)
Headache	43 (2.1)	6 (1.4)	1 (1.4)	32 (2.3)	6 (1.9)	1 (2.5)	94 (2.9)	31 (2.7)	2 (1.0)
TEAEs ≥ 2% (n (%))									
Asthma	-	-	0 (0)	-	-	1 (2.5)	-	-	0 (0)
Atrial fibrillation	-	-	0 (0)	-	-	1 (2.5)	-	-	1 (0.5)
Bronchitis	22 (1.1)	5 (1.2)	1 (2.5)	10 (0.7)	-	0 (0)	17 (0.5)	-	1 (1.4)
Depression	-	-	0 (0)	-	-	1 (2.5)	0 (0)	-	0 (0)
Dry eye	14 (0.7)	3 (0.7)	0 (0)	16 (1.2)	2 (0.6)	1 (2.5)	49 (1.5)	16 (1.4)	4 (2.0)
Dry throat	0 (0)	-	1 (1.4)	-	-	1 (2.5)	-	-	2 (1.0)
Diarrhoea	27 (1.3)	4 (1.0)	-	25 (1.8)	3 (0.9)	-	39 (1.2)	17 (1.5)	-
Dyspepsia	6 (0.3)	2 (0.5)	0 (0)	17 (1.2)	6 (1.9)	1 (2.5)	63 (1.9)	20 (1.7)	2 (1.0)
Fatigue	0 (0)	3 (0.7)	0 (0)	0 (0)	6 (1.9)	1 (2.5)	0 (0)	8 (0.7)	0 (0)
GERD	0 (0)	-	0 (0)	0 (0)	-	1 (2.5)	0 (0)	-	1 (0.5)
Hypertension	16 (0.8)	-	0 (0)	15 (1.1)	-	1 (2.5)	24 (0.7)	-	1 (0.5)
BP increased	-	-	0 (0)	-	-	1 (2.5)	-	-	2 (1.0)
Muscle twitching	-	-	0 (0)	-	-	1 (2.5)	-	-	0 (0)
Nausea	22 (1.1)	7 (1.7)	2 (2.8)	15 (1.1)	10 (3.1)	1 (2.5)	46 (1.4)	15 (1.3)	0 (0)
Nasopharyngitis	50 (2.4)	5 (1.2)	-	41 (3.0)	9 (2.8)	-	50 (1.5)	21 (1.8)	-
Rash	-	-	2 (2.8)	-	-	0 (0)	-	-	1 (0.5)
Urinary tract infection	32 (1.6)	4 (1.0)	0 (0)	34 (2.5)	6 (1.9)	0 (0)	74 (2.3)	21 (1.8)	3 (1.5)

Table 1 Treatment-emergent Adverse Events (all causality) according to response rates

* **Serious TEAE** were defined as any TEAE that resulted in death, was life-threatening, required inpatient hospitalization or prolongation of existing hospitalization, resulted in a persistent or significant disability/incapacity or resulted in congenital anomaly/birth defect.

-- : Specific number of patients, not reported as rate within treatment response group was <1%.

CONCLUSIONS

The most frequent TEAE (all causalities) were dry mouth and constipation. Fewer than 3% of TEAEs were serious or led to treatment discontinuation. With the exception of dry mouth, resolution in urgency symptoms appeared to be associated with a lower likelihood of adverse events compared to TEAE in all patients. Whether this reflected a "tolerance" on behalf of individual patients who balanced benefit against adverse effects or a true drug effect remains speculative. An association between cognitive TEAE and fesoterodine dose or the resolution of urgency symptoms was not observed. However, the incidence of these AE was low across all treatment groups.

Compared to all treated patients, resolution of urinary urgency by either 50% or 100% at week 12 appears to be associated with a reduction in the number of TEAE. The incidence of CNS and cognitive AE was low regardless of fesoterodine dose

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https://congress-download.pfizer.com/ics_2018_philadelphia_ics_2018_453_toviaz_wagg_1.html

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