WITH WHAT DEGREE OF IMPROVEMENT IN PROMS IS RESOLUTION OF OAB SYMPTOMS ASSOCIATED? DATA FROM A POOLED ANALYSIS OF OAB TREATMENT WITH FESOTERODINE.

WAGG, A.[1], LABOSSIERE, J. R.[2], HERSHORN, S.[2], , FERNET, M.[3], CARLSSON, M.[4], OELKE, M.[5]

[1]University of Alberta, Edmonton, AB Canada, [2]University of Toronto, ON, Canada [3]Pfizer Canada, Montreal, QC, Canada, [4] Pfizer Inc. New York, USA, [5] St. Antonius Hospital, Gronau, Germany

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INTRODUCTION & AIMS

Overactive bladder (OAB) is a common, debilitating disorder with a negative impact upon health and quality of life outcomes. Treatment with antimuscarinic agents remains the first line therapeutic option for symptom control, supported by clinical trials. This study aimed to examine the relationship between disease variable resolution at end of 4, 8 or 12 weeks treatment with fesoterodine and the proportion of patients achieving a significant improvement in Patient Reported Outcome Measures (PROM). The study also sought to describe the proportion of patients which make a significant improvement in PROM who also achieve either total or 50% resolution in their OAB symptoms

METHODS

This study used pooled data from 6 fixed dose studies of fesoterodine to describe the degree of symptom improvement by end of treatment weeks 4,8 and 12, after exposure to either 4mg, 8mg fesoterodine or placebo. Analysis was based on the full analysis set which included 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)
- Urinary urgency incontinence (UUI) episodes /24h (where baseline UUI episodes>0)

The proportion of patients achieving a normalization in

- Daytime micturition frequency (DMF) /24 h (100% resolution defined as DMF<8/24h)
- Nocturnal Micturition Frequency/24h (NMF) (where 100% resolution is defined as N<1)
- All 3 symptoms, reduction in all of urgency, DMF and UUI

PROMs included the Patient Perception of Bladder Condition, Overactive Bladder Questionnaire (OAB-q) and symptom bother score. A significant change in PPBC was defined as a shift of -1 category from baseline. Change in score was calculated at each time point relative to baseline. The proportion of patients achieving the MID on OAB-q (10 points) was calculated according to the degree of symptom resolution at 4 and 12 weeks relative to baseline.

RESULTS I

6689 patients (fesoterodine 4mg, 1373, fesoterodine 8mg 3263, placebo 2053, mean age 58.4y) were included, Table 1 shows the proportion of 3982 patients who had achieved a response in PPBC who also achieved a 50% or 100% response in OAB symptoms at each of 4, 8 and 12 weeks. Table 2 shows the proportion of patients who had achieve a significant response in OAB-q who also achieved a 50% or 100% response in OAB symptoms at 4 and 12 weeks.

REFERENCES

1. Eur Urol. 2006 Dec;50(6):1306-14

https://congress-download.pfizer.com/ics_2018_philadelphia_ics_2018_453_toviaz_wagg_3.html

RESULTS II

Table 1 OAB-symptom responder rates in patients categorized as PPBC responders

PPBC responders				
Week 4				
		Placebo %, (N/total sample)	Fesoterodine 4mg %, (N/total sample)	Fesoterodine 8mg %, (N/total sample)
50% response	UUE	**19.4** (201/1038)	**19.9** (156/783)	**30.3** (643/2121)
	UUI	**64.0** (620 /969)	**66.7** (487/730)	**76.7** (1576/2054)
100% response	UUE	**2.0** (21/1038)	**1.8** (14/783)	**3.0** (63/2121)
	UUI	**31.2** (302/969)	**30.4** (222/730)	**43.9** (902 (2054)
	DMF	**40.2** (339/843)	**35.8** (110/307)	**52.9** (863/1632)
	NMF	**27.8** (234/843)	**28.7** (88/307)	**30.6** (499 (1632)
	Combined OAB Sx	**1.0** (8/771)	**0.4** (1/254)	**2.7.2** (42/1566)
Week 8				
50% response	UUE	**7.8** (21/269)	**13.3** (40/301)	**13.9** (46/331)
	UUI	**58.4** (118/202)	**67.7** (168/248)	**77.4** (212/274)
100% response	UUE	**1.1** (3/269)	**0.3** (1/301)	**1.2** (4/331)
	UUI	**18.3** (37/202)	**20.6** (51/248)	**27.7** (76/274)
	DMF	**34.6** (93/269)	**45.2** (136/301)	**50.8** (68/331)
	NMF	**34.9** (94/269)	**35.9** (108/301)	**42.3** (140/331)
	Combined OAB Sx	**0.5** (1/202)	**0.4** (1/248)	**0.7** (2/274)
Week 12				
50% response	UUE	**34.0** (357/1049)	**33.1** (264/798)	**47.0** (1004/2135)
	UUI	**80.0** (784/980)	**81.6** (607/744)	**87.9** (1818/2068)
100% response	UUE	**6.2** (65/1049)	**4.4** (35/798)	**8.5** (181/2135)
	UUI	**50.2** (492/980)	**47.6** (354/744)	**62.7** (1297/2068)
	DMF	**49.1** (418/851)	**49.0** (152/310)	**60.9** (998/1640)
	NMF	**34.9** (297/851)	**38.4** (119/310)	**36.7** (692/1640)
	Combined OAB Sx	**5.0** (39/780)	**1.2** (3/256)	**6.8** (107/1574)

Table 2 OAB-symptom responder rates in patients categorized as OAB-q symptom score and OAB-q HQRL Total score responders.

OAB-q symptom bother score responders				
Week 4				
		Placebo %, (N/total sample)	Fesoterodine 4mg %, (N/total sample)	Fesoterodine 8mg %, (N/total sample)
50% response	UUE	**23.9** (202/845)	**27.0** (140/518)	**33.3** (620/1863)
	UUI	**68.7** (580/844)	**76.8**, (398/518)	**76.9** (1427/1856)
100% response	UUE	**2.5** (21/845)	**2.7** (14/518)	**3.4** (63/1863)
	UUI	**36.3** (306/844)	**41.5** (215/518)	**46.7** (867/1856)
	DMF	**44.6** (282/632)	**0.0** (0)	**55.1** (737/1338)
	NMF	**27.4** (173/632)	**0.0** (0)	**29.5** (394/1338)
	Combined OAB Sx	**1.3** (8/630)	**0.0** (0)	**3.0** (40/1332)
Week 12				
50% response	UUE	**39.7** (340/857)	**45.5** (242/532)	**51.3** (965/1880)
	UUI	**84.5** (723/856)	**86.8** (462/532)	**87.8** (1645/1873)
100% response	UUE	**6.8** (58/857)	**6.2** (33/532)	**9.4** (177/1880)
	UUI	**55.0** (471/856)	**58.7** (312/532)	**66.0** (1237/1873)
	DMF	**54.1** (346/640)	**100.0** (1/1)	**61.5** (828/1346)
	NMF	**32.5** (208/640)	**0.0** (0)	**34.8** (468/1346)
	Combined OAB Sx	**5.6** (36/638)	**0.0** (0)	**7.8** (104/1340)
OAB-q HQRLTotal score responders				
Week 4				
50% response	UUE	**24.3** (178/733)	**26.9** (124/461)	**34.2** (557/1629)
	UUI	**68.4** (501/732)	**76.8** (354/461)	**77.3** (12541623)
100% response	UUE	**2.3** (17/733)	**2.4** (11/461)	**3.5** (57/1629)
	UUI	**35.8** (262/732)	**41.0** (189/461)	**47.9** (778/1623)
	DMF	**44.3** (239/540)	**100.0** (1/1)	**55.6** (637/1145)
	NMF	**26.7** (144/540)	**0.0** (0)	**30.7** (352/1145)
	Combined OAB Sx	**0.9** (5/537)	**0.0** (0)	**3.3** (37/1140)
Week 12				
50% response	UUE	**40.7** (302/742)	**48.2** (228/473)	**54.3** (893/1646)
	UUI	**83.1** (621/741)	**86.3** (408/473)	**88.8** (1457/1640)
100% response	UUE	**6.6** (49/742)	**6.6** (31/473)	**9.5** (156/1646)
	UUI	**56.6** (419/741)	**58.4** (276/473)	**67.9** (1113/1640)
	DMF	**54.0** (294/541)	**100.0** (2/2)	**63.1** (728/1154)
	NMF	**33.3** (181/544)	**0.0** (0)	**36.2** (418/1154)
	Combined OAB Sx	**5.2** (28/542)	**0.0** (0)	**8.2** (94/1149)

CONCLUSIONS

At week 4, 64.0 – 76.7% of patients who had achieved a significant change in PPBC had a 50% reduction in UUI. At week 12 this proportion had increased to between 80 – 87.9%, with those being exposed to fesoterodine treatment experiencing a significant reduction in PPBC at numerically higher rates. Generally, for each category of treatment response, the proportion of people who reached either 50% or 100% symptom relief the minimal important difference in OAB-q symptom bother score or health related quality of life score increased over the 12 weeks of the study. PROM responses appear to occur earlier, highlighting the need to give time for drug therapy to reach its maximum benefit. OAB treated patients reporting a significant response to patient reported outcome measures report varying degrees of symptom relief at different time points. Maximum relief appears to take at least 12 weeks to be achieved.

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