Final study report

Title: A 12 week, multi centre, open label study to evaluate the effect of fesoterodine flexible dosing regimen on the sexual function of women with overactive bladder.

Study acronym: Fesoterodine in OAB

EudraCT: 2010-023851-27

REC number: 12/EE/0029

IRAS: 48710

Co-Sponsors: King's College Hospital

IMP: Fesoterodine Fumarate 4mg and 8 mg

Indication studied: Impact of the sexual function of women with overactive bladder

Study design: This was a multi-centre open label study which aimed to enter 132 female subjects with OAB symptoms. Sexual function and efficacy assessments was evaluated via 3-day bladder diaries, questionnaires (KHQ, PISQ-12, SQoL, PAC-QoL, SAGA, PPBC) and urodynamics. Tolerability and safety was evaluated at every visit with recording of adverse events.

Primary Outcome

PISQ-12

Paired T-Test PISQ-12 Total Score

Of the 20 subjects tested, the average PISQ-12 score decreased between week 0 ($\bar{x}$ =15.85, SE =1.74) and week 12 ($\bar{x}$ = 11.5, SE = 1.52). This difference of 4.35 points, BCa 95% CIs [7.35, 1.572], was statistically significant $t_{(19)} = 3.159$, $p = 0.005$, and reflects a moderate effect size, $h = 0.542$.

Overall there was mean reduction in PISQ-12 score of 4.35 which was significant (p=0.005). When considering specific questions related to desire, there was very little change in the frequency of sexual desire, the number of orgasms experienced or whether women feel "turned on". However, by week 12 there was a significant improvement in satisfaction with the variety of sexual activities in the women's sex life.

SQOL-F

Paired T-Test SQOL-F Total Score

Of the 20 subjects tested, the average SQOL score increased between week 0 ($\bar{x}$ = 66.1, SE = 3.62) and week 12 ($\bar{x}$ = 73.45, SE = 2.42). This difference of -7.35 points, BCa 95% CIs [-2.55, -13],

was statistically significant $t_{(19)}$ = -2.673, p = 0.015, and reflects a moderate effect size, h = -0.486.

Secondary Outcomes

Bladder diary variables

Complete bladder diaries were available for 17 subjects. Paired T-Tests were performed to establish differences in bladder diary variables from week 0 to week 12.

Number of episodes of micturition per 24hrs

The average number of episodes of micturition per 24 hrs decreased between week 0 ($\bar{x}$ = 10.05, SE = 0.63) and week 12 ($\bar{x}$ = 6.95, SE = 0.72). This difference of 3.11 episodes, BCa 95% CIs [1.98, 4.26], was statistically significant $t_{(16)}$ = 4.839, p < 0.001, and reflects a large effect size, h = 0.993.

Number of Episodes of nocturia per 24hrs

The average number of episodes of nocturia per 24hrs decreased between week 0 ($\bar{x}$ = 0.82, SE = 0.12) and week 12 ($\bar{x}$ = 0.32, SE = 0.10). This difference of 0.51 points, BCa 95% CIs [0.26, 0.75], was statistically significant $t_{(16)}$ = 4.441, p < 0.001, and reflects a large effect size, h = 0.973.

Number of Episodes of UUI per 24hrs

The average number of episodes of UUI per 24hrs decreased between week 0 ($\bar{x}$ = 1.68, SE = 0.43) and week 12 ($\bar{x}$ = 0.65, SE = 0.45). This difference of 1.02 points, BCa 95% CIs [0.49, 1.59], was statistically significant $t_{(16)}$ = 3.096, p = 0.007, and reflects a moderate effect size, h = 0.502. This represents a 61.3% reduction in UUI episodes per week.

Number of Episodes of U per 24hrs

The average number of episodes of U per day decreased between week 0 ($\bar{x}$ = 4.65, SE = 0.55) and week 12 ($\bar{x}$ = 1.31, SE = 0.38). This difference of 3.34 points, BCa 95% CIs [2.38, 4.39], was statistically significant $t_{(16)}$ = -5.95, p = 0.00, and reflects a large effect size, h = 1.524.

Number of Episodes of U per 3 day diary

The average number of episodes of U per week decreased between week 0 ($\bar{x}$ = 13, SE = 1.4) and week 12 ($\bar{x}$ = 4.12, SE = 1.13). This difference of 8.88 episodes, BCa 95% CIs [6.14, 11.5], was statistically significant $t_{(16)}$ = 6.862, p < 0.001, and reflects a large effect size, h = 1.51. This represents a 68.3% reduction in urgency episodes per week.

KHQ

Paired T-Test King's Health Questionnaire (KHQ) Total Score

Of the 20 subjects tested, the average KHQ score decreased between week 0 ($\bar{x}$ = 520.18, SE = 40.2) and week 12 ($\bar{x}$ = 288.21, SE = 43.48). This difference of 231.97 points, BCa 95% CIs [302.41, 164.64], was statistically significant $t_{(19)} = 6.892$, p <0.001, and reflects a large effect size, $h = 1.126$.
There were significant changes in every domain of the KHQ with the greatest changes observed in role limitations, emotions and incontinence impact domains (mean difference of 35.01, 32.8, 30.84 respectively). The least change was seen in the general health perception and present problems domains (mean difference 5.0 and 5.15 respectively).

PAC-QOL

Paired T-Test PACQOL Total Score

Of the 20 subjects, the average PACQOL score decreased between week 0 ($\bar{x}$ = 28.25, SE = 5.57) and week 12 ($\bar{x}$ = 25.6, SE = 4.5). This difference of 2.65 points, BCa 95% CIs [8.97, -3.65], was not statistically significant $t_{(19)} = 0.716$, $p = 0.483$, it reflects a small effect size, $h = 0.106$.
There were no significant differences noted in any domain of the PAC-QOL questionnaire.

PPBC

Paired T-Test Patient Perception of Bladder Condition (PPBC)

Of the 20 subjects, the average PPBC score decreased between week 0 ($\bar{x}$ = 4.55, SE = .24) and week 12 ($\bar{x}$ = 3.2, SE = .24). This difference of 1.35 points, BCa 95% CIs [1.8, 0.9], was statistically significant $t_{(19)} = 5.81$, $p < 0.001$, and reflects a large effect size, $h = 1.165$.

SAGA

When considering overall goal achievement in the study only one subject did not achieve her goals with a further 35% somewhat achieving their goals. 60% of subjects achieved their goals with 40% of those exceeding or greatly exceeding their expectations.

Although this study did not proceed as planned, the results of the secondary outcomes are in keeping with most other clinical trials using fesoterodine. Given these similarities, it could be suggested that as there were trends towards improvement in the primary outcome measures, that as a proof of concept study, this does confirm that this is an appropriate area for investigation and that there is potential for a positive benefit of fesoterodine for the treatment of OAB on women's SF. However, further investigation into the sample population is necessary to determine the scope of the problem and understand how to identify these women in practice so that appropriate and reliable sampling methods can be developed for future studies.