Comparison of the Efficacy, Tolerability and Safety of Propiverine for the Treatment of OAB in Younger vs Older Patients (</≥ 65 Years): A Post-hoc Analysis of a Randomized, Double-Blind Study

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Hypothesis / Aims of study

The prevalence of the overactive bladder (OAB) increases with aging. A randomized study in adult OAB patients (pts) of any age showed superiority of PROP extended release 30 mg once-daily (PROP ER) or PROP immediate release 15 mg twice-daily (PROP IR) over placebo [1]. However, no data have yet become available on the effects of PROP in elderly patients. Therefore, the aim of this analysis was to compare the efficacy, tolerability and safety of PROP in younger vs older OAB pts.

Study design, materials and methods

A post-hoc analysis of data from a randomized, double-blind, placebo-controlled, 4-week phase III/IV study was performed in a cohort of 723 OAB pts who represent the *PP* population without the placebo group of the original study [1]. The efficacy of PROP in pts aged <65 years vs ≥65 years was investigated. The primary efficacy parameter of the original study was change of incontinence episodes/24 h. Primary objectives were, besides others, parameters from bladder diaries (number of micturitions/24 h, number of urgency episodes/24 h, and change of volume per single micturition) and patient-reported adverse drug reactions (ADR). The safety population of the original study was evaluated for determination of tolerability and safety of PROP.

Results

360 pts treated with PROP IR and 363 pts with PROP ER were included in this post-hoc efficacy analysis. Demographic data of the *PP* study population are shown in **table 1**.

Table 1: Demographic data

	PROP IR 15 mg		PROP ER 30 mg	
	<65 years	≥65 years	<65 years	≥65 years
No. pts [n]	240	120	254	109
Mean Age [years]	48.4	71.0	47.8	71.5
Mean BMI [kg/m²]	26.8	27.2	26.8	27.3
Men [n] Women [n]	17 223	21 99	28 226	10 99

Tolerability and safety analysis were conducted with the safety population which included 531 younger pts with PROP IR (mean age: 48.7 y) or PROP ER (mean age: 48.3 y) vs 255 older pts with PROP IR (mean age: 71.0 y) or PROP ER (mean age: 71.3 y).

Figures 1a and 1b show mean changes from baseline to end of treatment with regard to incontinence episodes per 24 h for PROP IR and PROP ER which reduced incontinence in pts <65 years by 2.2 and 2.45 episodes/24 h, respectively, whereas PROP IR and ER reduced incontinence in pts ≥65 years by 2.45 and 2.58 episodes/24 h, respectively. The difference between younger and older pts for the two PROP groups was not significant. Compared with younger individuals, pts aged ≥65 years showed similar results in voiding diary parameters from baseline to end of treatment with regard to mean changes of no. of voids/24 hours, no. of urgency episodes/24 hours, and voided volume/ micturition (table 2). No significant differences of the analysed parameters were seen between younger and older pts in the PROP IR or PROP ER groups.

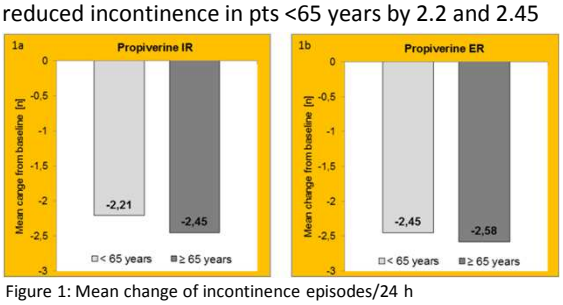

Figure 1: Mean change of incontinence episodes/24 h

Table 2: Mean change of voiding diary parameters

	PROP IR 15 mg		PROP ER 30 mg	
	<65 y	≥65 y	<65 y	≥65 y
Number of voids [n]	-3.93	-3.20	-3.80	-3.28
Number of urgency episodes/24 h [n]	-2.75	-2.16	-2.99	-2.70
Increase of voided volume/micturition [ml]	+48.3	+42.0	+39.1	+42.9

During treatment, 175/531 younger pts (33.0%) experienced ADRs vs 89/255 older pts (29.0%). Dry mouth was the most frequent adverse event in both age groups (21.8% of pts <65 years vs 23.1% of pts ≥65 years). Trial participation was prematurely terminated due to adverse events by 14 younger pts (2.6%) and 11 older pts (4.3%). The median differences from baseline pulse rate (PR) treated with PROP IR and PROP ER in younger vs older patients were 0 beats/min. Bazett-corrected QT intervals [msec] showed no differences between the age and treatment groups (**table 3)**.

Table 3: Mean change of QTc interval [msec]

	PROP IR		PROP ER		Placebo	
	<65 y	≥65 y	<65 y	≥65 y	<65 y	≥65 y
Baseline	407.6	413.7	407.3	412.9	403.6	416.0
End of Treatment	407.7	413.8	406.3	411.9	405.4	414.1
Mean change	0.5	-0.3	-1.1	0.0	0.6	-0.9

Interpretation of results

Treatment effects of PROP IR or PROP ER for all efficacy parameters were very similar in younger and older patients during the 4-week study period. Additionally, tolerability and safety were also comparable between the age and treatment groups. These findings confirm earlier results in elderly patients who showed a favourable benefit-risk-ratio, without the appearance of cardiac arrhythmia [2]. The current analysis further demonstrates that QTc intervals and the pulse rate were not altered in younger or older patients.

Concluding message

The results of this post-hoc analysis confirm that PROP IR and PROP ER are effective and safe for the treatment of OAB, also in older patients. Age did not have any effects on the efficacy, tolerability or safety of PROP IR and PROP ER. Therefore, propiverine is suitable for the therapy of OAB patients of any age.

[1] Juenemann et al. Urol Int 2006; 77:334-339; [2] Dorschner et al. EurUrol 2000; 37:702-708