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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

Hypothesis / aims of study

The prevalence of the overactive bladder (OAB) increases with aging. Regardless the proven efficacy and acceptable adverse event profile in younger patients, specific data are necessary to ascertain the efficacy, tolerability and safety of muscarinic receptor antagonists in the elderly population. Propiverine is a unique muscarinic receptor antagonist with calcium channel blocking capabilities for OAB treatment. A randomized study in adult OAB patients of any age showed superiority of propiverine extended release 30 mg once-daily (Prop ER) or propiverine immediate release 15 mg twice-daily (Prop IR) over placebo [1]. However, no data have yet become available on the effects of propiverine in elderly patients. Therefore, the aim of this analysis was to compare the efficacy, tolerability and safety of propiverine in younger vs older OAB patients.

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 patients who represent the *PP* population without the placebo group of the original study [1]. The efficacy of propiverine in patients 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 propiverine.

Results

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

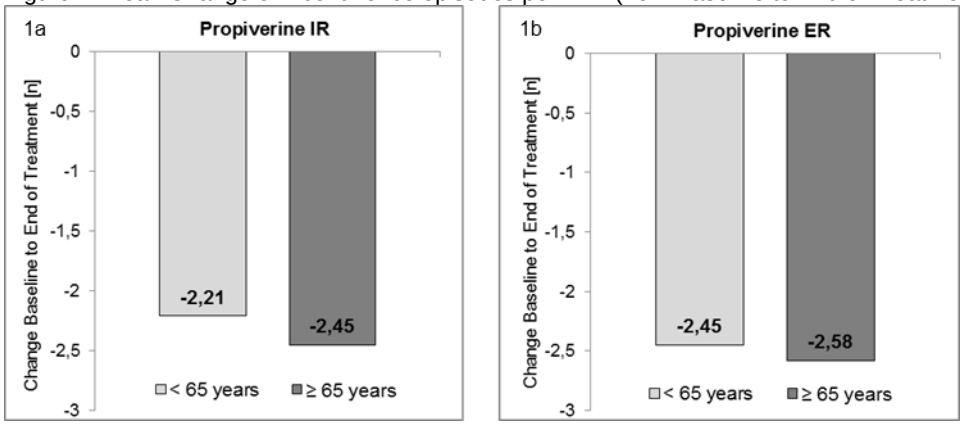
Table 1	Prop IR 15 mg		Prop ER 30 mg	
	< 65 y	≥ 65 y	< 65 y	≥ 65 y
Number of patients [N]	240	120	254	109
Mean Age [years]	48.4	71.0	47.8	71.5
Mean BMI [kg/m²]	26.8	27.2	26.8	27.3
Sex: Men [n] Women [n]	 17 (7.1 %) 223 (92.9 %)	 21 (17.5 %) 99 (82.5 %)	 28 (11.0 %) 226 (89.0 %)	 10 (9.2 %) 99 (90.8 %)

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

Efficacy

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 patients <65 years by 2.2 and 2.45 episodes/24 h, respectively, whereas Prop IR and ER reduced incontinence in patients ≥65 years by 2.45 and 2.58 episodes/24 h, respectively. The difference between younger and older patients for the two propiverine groups was insignificant.

Figure 1: Mean Change of incontinence episodes per 24 h (from Baseline to End of Treatment)



Compared with younger individuals, patients aged ≥65 years showed similar results in voiding diary parameters from baseline to end of treatment with regard to mean changes of number of voids/24 hours, number of urgency episodes/24 hours, and voided

volume/micturition (**table 2**). No significant differences of the analyzed parameters were seen between younger and older patients in the Prop IR or Prop ER groups.

Table 2:	Prop IR 15 mg		Prop ER 30 mg	
	< 65 y	≥ 65 y	< 65 y	≥ 65 y
Number of voids/24 h [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

Tolerability and safety

During treatment, 175/531 younger patients (33.0%) experienced ADRs vs 89/255 older patients (29.0%). Dry mouth was the most frequent adverse event in both age groups (21.8% of patients <65 years vs 23.1% of patients ≥65 years). Trial participation was prematurely terminated due to adverse events by 14 younger patients (2.6%) and 11 older patients (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 showed no differences between the age and treatment groups (**table 3)**.

Table 3: QTc interval (Bazett´s formula)

QTc interval [msec]	Prop IR 15 mg		Prop ER 30 mg		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 favorable 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.

References

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

Disclosures

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