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AGE-RELATED EFFICACY OF THE SELECTIVE B3-ADRENOCEPTOR AGONIST MIRABEGRON FOR THE TREATMENT OF OVERACTIVE BLADDER (OAB): POOLED ANALYSIS OF THREE PROSPECTIVE, RANDOMISED PHASE III STUDIES IN PATIENTS AGED ≥ 65 YEARS

Hypothesis / aims of study

The prevalence of overactive bladder (OAB) increases with age affecting approximately 15% of people aged ≥ 65 years [1]. Consequently OAB represents a growing problem in aging societies. Oral antimuscarinic agents are currently the mainstay of pharmacotherapy for the treatment of OAB in the elderly. However, in certain cases clinicians need to be conscious about the anticholinergic burden to which an elderly patient is exposed. Furthermore, some older patients have a suboptimal response to treatment or find it difficult to tolerate the common adverse events associated with antimuscarinics, such as dry mouth and constipation [2]. Mirabegron is a potent and selective β_3-adrenoceptor agonist that has been developed for the treatment of OAB and may provide a new therapeutic option in these older patients. The aim of this pooled analysis of data from 3 phase III trials (NCT00689104, NCT00662909 and NCT00912964) was to investigate the efficacy of mirabegron, in OAB patients ≥65 years.

Study design, materials and methods

In a prospective pooled analysis of three randomised, double-blind, placebo-controlled, 12-week studies (one of the studies included an active-controlled arm with tolterodine whose data are not reported here) in patients with OAB, mirabegron (50 or 100 mg) demonstrated statistically significant benefit over placebo for the co-primary endpoints: reduction in incontinence episodes/24 h and micturition frequency/24 h. To investigate the benefit of mirabegron in elderly OAB patients the pooled data from the three randomised studies was analysed in the OAB population aged ≥ 65 years for the same co-primary endpoints (change from Baseline to Final Visit [End of Treatment] in mean number of incontinence episodes/24 hours and mean number of micturitions/24 hours). Efficacy analysis was based on the Full Analysis Set (FAS; all randomised patients who had at least one dose of study drug and who had a micturition measurement in the baseline diary and at least one post-Baseline visit diary with a micturition measurement) for the mean number of micturitions/24 hours, and the Full Analysis Set-Incontinence (FAS-I; FAS patients with ≥1 incontinence episode recorded in the Baseline 3-day micturition diary) for the mean number of incontinence episodes/24 hours. Subgroup analysis for age (< 65 years and ≥ 65 years) on the co-primary efficacy endpoints were assessed using an analysis of covariance (ANCOVA) model with treatment group, gender, study, age subgroup, and treatment by age subgroup interaction as fixed factors and baseline as a covariate. Assuming that at least 85% of the randomised patients were evaluable, approximately 430 patients were to be randomised to each treatment group in each study, assuming a dropout rate of approximately 20% during the placebo run-in period.

Results

Overall, 3542 patients with OAB were included in the pooled FAS (placebo, n=1328; mirabegron 50 mg, n= 1324; mirabegron 100 mg, n=890) and 2317 patients in the pooled FAS-I (placebo n=878; mirabegron 50 mg n=862; mirabegron 100 mg n=577). Patient demographics and Baseline characteristics were comparable across the mirabegron groups and placebo in the FAS population. Approximately 38% of patients were ≥ 65 years of age (placebo n=504; mirabegron 50 mg n=499; mirabegron 100 mg n=340). The mean age of patients in the FAS-I population and the distribution of patients in the age group ≥ 65 years across dose groups in the FAS-I was relatively consistent with the FAS population. Mirabegron 50 mg and 100 mg were effective in reducing the mean number of incontinence episodes/24 hours from Baseline to Final Visit (end of treatment) for patients ≥65 years of age with an adjusted mean difference versus placebo of -0.66 and -0.68, respectively. A similar benefit was observed for the reduction in the mean number of micturitions/24 hours for patients aged ≥65 years with an adjusted mean difference versus placebo of -0.62 and -0.75, respectively, for the mirabegron 50 and 100 mg groups (Table).

Interpretation of results

In patients aged < and ≥65 years of age with OAB, mirabegron 50 mg and 100 mg were effective in reducing mean number of incontinence episodes/24 hours and micturitions/24 hours from Baseline to Final Visit.

Concluding message

Given the increasing prevalence of OAB in aging populations these findings confirm the benefit of mirabegron in elderly OAB patients.

Table: Effect of mirabegron (50 mg and 100 mg) and placebo on the adjusted change from Baseline to Final Visit in the mean number of incontinence episodes/24 h (FAS-I) and micturitions/24 hours (FAS) in OAB patients aged ≥ 65 years			
	mirabegron		**Placebo**
	50 mg	**100 mg**	
Number of incontinence episodes/24 h			
FAS-I population	*N=355*	*N=235*	*N=345*
Adjusted Mean (SE)† (SE), 95% CI	–1.61 (0.105) (–1.82, –1.41)	–1.63 (0.131) (–1.89, –1.38)	–0.96 (0.106) (–1.16, –0.75)
Adjusted difference vs placebo†, mean (SE), 95% CI	–0.66 (0.149) (–0.95, –0.37)	–0.68 (0.169) (–1.01, –0.35)	---
Number of micturitions/24 h			
FAS population	*N=499*	*N=340*	*N=504*
Adjusted Mean† (SE), 95% CI	–1.68 (0.115) (–1.90, –1.45)	–1.81 (0.141) (–2.08, –1.53)	–1.05 (0.114) (-1.28, -0.83)
Adjusted difference vs placebo†, mean (SE), 95% CI	–0.62 (0.161) (–0.94, –0.30)	–0.75 (0.182) (–1.11, –0.40)	---
† Least squares mean adjusted for treatment group, gender, study, age subgroup, and treatment by age subgroup interaction as fixed factors and baseline as a covariate. FAS: All randomised patients who took at least one dose of double-blind study drug and who had a micturition measurement in the baseline diary and at least one post-baseline visit diary with a micturition measurement. FAS-I: All patients in the FAS who had least one incontinence episode in the baseline diary.			

References

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Disclosures

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