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POST-VOID RESIDUAL (PVR) VOLUME AND URINARY RETENTION ASSESSMENTS IN A RANDOMIZED, DOUBLE-BLIND, PHASE IIIB TRIAL OF MIRABEGRON ADD-ON TREATMENT IN INCONTINENT OVERACTIVE BLADDER (OAB) PATIENTS WITH AN INADEQUATE RESPONSE TO 4-WEEK SOLIFENACIN MONOTHERAPY (BESIDE)

Hypothesis / aims of study

Combination therapy with mirabegron and solifenacin 5 mg has been shown to provide greater improvements in OAB symptoms than solifenacin 5 or 10 mg monotherapy. In the Phase IIIb BESIDE study (NCT01908829), adult patients with OAB who remained incontinent after 4-weeks single-blind daily solifenacin 5 mg were randomized (1:1:1) to receive daily, double-blind treatment with combination (solifenacin 5 mg + mirabegron 25 mg; titrating up to mirabegron 50 mg after 4 weeks), solifenacin 5 mg, or solifenacin 10 mg for 12 weeks. At end of treatment (EoT), significant benefits were seen for combination therapy versus solifenacin 5 mg and 10 mg monotherapy in terms of improving most OAB symptoms. Since both mirabegron (a β3-adrenoceptor agonist) and solifenacin (an antimuscarinic agent) act on the bladder, lower urinary tract related adverse events (AEs) could theoretically increase in frequency when combination therapy is administered. This abstract assesses PVR volume and treatment-emergent adverse events (TEAEs) related to urinary retention.

Study design, materials and methods

Patients with a baseline PVR >150 mL were to be excluded from enrolment into the study. PVR volume was assessed by bladder scan at screening, baseline, weeks 4, 8, and 12, EoT and follow up. Changes from baseline values were summarized by treatment group and visit for continuous variables, as well as for the following categories: ≥0 to <150 mL, ≥150 to <300 mL, ≥300 mL. Shifts from baseline to each post-baseline visit for PVR volume based on the 3 categories were summarized for each treatment group. TEAEs for urinary retention were summarized by System Organ Class, Preferred Term (PT), Lower Level Term and treatment group, based on a pre-defined list of PTs.

Results

Overall, 2174 patients were randomized to combination (n=727), solifenacin 5 mg (n=728) or solifenacin 10 mg (n=719). In each group, 83% of patients were female and 17% were male. Mean change in PVR volume from baseline to EoT was comparable across treatment groups (5.5 mL, 3.0 mL and 7.4 mL, respectively; Table). Over 97% of patients in each treatment group had no shift from baseline to a higher category. Shifts from baseline <150 mL to between 150 mL and 300 mL at EoT were noted in 13 (1.9%), 6 (0.8%) and 14 (2.0%) patients, respectively. Fewer patients had shifts from baseline to ≥300 mL: 6 (0.8%), 5 (0.7%) and 5 (0.7%) of patients, respectively. Six patients had reported AEs of residual urine volume increased; 1 female and 1 male patient in the combination group, 1 female and 1 male patient in the solifenacin 5 mg group, and 2 female patients in the solifenacin 10 mg group.

Two patients (0.3%) in the combination group and 1 patient (0.1%) in the solifenacin 5 mg group reported a PT of urinary retention as a TEAE. In the solifenacin 10 mg group, urinary retention was reported by 5 (0.7%) patients. In the solifenacin 10 mg group, 2 female patients discontinued due to urinary retention, but there were no discontinuations due to urinary retention in other groups. There were no cases of acute urinary retention and no patients required catheterization.

Change from baseline to EoT in PVR volume (SAF)			
	Combination (n=725)	**Solifenacin 5 mg (n=728)**	**Solifenacin 10 mg (n=719)**
Mean (SD) baseline [n] (mL)	26.2 (37.0) [720]	23.1 (36.2) [727]	24.1 (38.5) [718]
Median (range) baseline (mL)	12.00 (0 to 259)	10.00 (0 to 291)	10.0 (0 to 383)
Change from baseline to EoT, mean (SD) [n] (mL)	5.5 (51.6) [706]	3.0 (43.5) [713]	7.4 (54.1) [707]
Change from baseline to EoT, median (range) (mL)	0 (–175 to 479)	0 (–203 to 454)	0 (–144 to 602)
No shift from baseline at EoT, n (%)	683 (96.7%)	700 (98.2%)	685 (96.9%)
Shift from baseline to 150–300 mL at EoT, n (%)	14 (2.0%)	8 (1.1%)	16 (2.3%)
Shift from baseline to ≥300 mL at EoT, n (%)	6 (0.8%)	5 (0.7%)	5 (0.7%)
EoT=end of treatment, PVR=post void residual, SD=standard deviation.			

Interpretation of results

Combination treatment demonstrated satisfactory lower urinary tract safety and showed no synergistic effects on PVR volume beyond those known from either monotherapy. There were no cases of acute urinary retention and there were similar low incidences of urinary retention AEs across treatment groups.

Concluding message

Mean change in PVR volume from baseline to EoT was comparable across treatment groups (5.5 mL, 3.0 mL and 7.4 mL, in the combination, solifenacin 5 mg, and solifenacin 10 mg groups, respectively). Over 97% of patients in each treatment group had no shift from baseline PVR volume to a higher category. A similar proportion of patients in each group reported an event indicative of urinary retention as a TEAE (4 patients [0.6%], 3 patients [0.4%], and 7 patients [1.0%], respectively); there were no cases of acute urinary retention. This analysis demonstrates that there was no increased risk for urinary retention or significant increase in PVR volume in combination therapy versus monotherapy, despite a significant increased benefit in OAB symptoms.

Disclosures

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