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RESULTS OF A RANDOMIZED PHASE 3 STUDY COMPARING SOLIFENACIN SUCCINATE WITH TOLTERODINE AND PLACEBO IN PATIENTS WITH SYMPTOMATIC OVERACTIVE BLADDER

Aims of Study

The full therapeutic potential of antimuscarinic agents, the mainstay treatment for overactive bladder (OAB), is limited by side effects such as dry mouth. Solifenacin succinate (Vesicare®; YM905) is a new, bladder-selective antimuscarinic agent suitable for once-daily administration. In this phase 3 study, the primary objective was to assess the efficacy of solifenacin 5 mg and 10 mg once daily in patients with OAB. Secondary objectives were to evaluate the safety and tolerability of solifenacin and to compare the efficacy and safety of solifenacin with tolterodine 2 mg twice daily.

Methods

Male and female patients aged ≥18 years with symptoms of OAB for 3 months or more first entered a 2-week, single-blind placebo run-in period. Patients were subsequently randomized to 12-week double-blind treatment with solifenacin 5 mg (n = 279) or 10 mg (n = 268), tolterodine (n = 263), or placebo (n = 267). The primary efficacy variable was mean change in mean number of micturitions/24 h from baseline to endpoint. Secondary efficacy variables included mean change in number of episodes of urgency and incontinence and mean change from baseline in volume voided per micturition.

Results

The efficacy evaluation included 1033 patients (253 placebo, 266 and 264, solifenacin 5 mg and 10 mg, respectively, and 250 tolterodine). Solifenacin, at both 5-mg and 10-mg doses, was significantly more effective than placebo in improving all OAB symptoms (Table). Compared with placebo, tolterodine produced lesser, nonsignificant reductions in episodes of urgency and incontinence than did solifenacin. Over 50% of solifenacin-treated patients incontinent at baseline became continent by study end. Incidences of dry mouth, the most bothersome side effect, were 4.9% (placebo), 14.0% (solifenacin 5 mg), 21.3% (solifenacin 10 mg), and 18.6% (tolterodine). Treatment with solifenacin was well tolerated, with a low discontinuation rate.

Variable	Placebo	Solifenacin		Tolterodine
		5 mg	10 mg	
Mean change from baseline to endpoint: episodes/24 h*				
Micturitions	–1.20	–2.19[a]	–2.61[b]	–1.88[c]
Urgency	–1.41	–2.85[b]	–3.07[b]	–2.05
Urge incontinence	–0.62	–1.41[d]	–1.36[e]	–0.91
Volume voided/micturition	7.4	32.9[b]	39.2[b]	24.4[b]

*Full analysis set.
Difference vs placebo: [a]*P* = 0.0003; [b]*P* = 0.0001; [c]*P* = 0.0145; [d]*P* = 0.0020; [e]*P* = 0.0028.

Conclusions

Solifenacin succinate 5 mg or 10 mg once daily produces a significant improvement in the symptoms of OAB. Solifenacin is a highly active new agent with a favorable therapeutic index for treatment of OAB.