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SOLIFENACIN USE IN ELDERLY PATIENTS WITH OVERACTIVE BLADDER: VOLT AND VERSUS DATA

Hypothesis / aims of study

At least 25% of people 65 years or older are affected by overactive bladder (OAB) [1]. Reports on the effects of antimuscarinic agents to treat OAB have focused mainly on diary-based efficacy data and safety; data on patient-reported outcomes (PRO) in elderly patients are limited**. To** assess the efficacy and tolerability of solifenacin in patients older than 65 years we conducted post-hoc analyses of data from the **V**ESIcare **O**pen-**L**abel **T**rial (VOLT) and the **V**ESIcare **E**fficacy and **R**esearch **S**tudy **US** (VERSUS).

Study design, materials and methods

Both 12-week studies were open-label, flexible-dosing protocols involving patients with OAB for a minimum of 3 months. In both studies, solifenacin could be increased to 10 mg/day at Week 4, and maintained or decreased to 5 mg or increased to 10 mg at Week 8. For VOLT, patients taking OAB medication underwent a 7-day washout before receiving solifenacin. For VERSUS inclusion, patients were recruited who had received tolterodine ER 4 mg for at least 4 weeks and who wished to switch to solifenacin due to lack of sufficient improvement in urgency episodes. VERSUS patients had to continue having at least 3 urgency episodes/day at Pre-Washout for inclusion. Baseline values recorded after cessation of tolterodine during the washout period (on no drug) are used here. VOLT and VERSUS common endpoints included validated PRO measures: the Patient Perception of Bladder Condition (PPBC) scale, which assessed overall symptom bother, and the Overactive Bladder Questionnaire (OAB-q), which measured symptom bother and health-related quality of life (HRQoL). In addition, a horizontal visual analog scale (VAS) was used in VOLT to assess the extent to which patients were bothered by individual OAB symptoms. Diary-recorded symptom data were captured in VERSUS but not in VOLT.

Results

A total of 880/2205 patients (39.9%) in the full analysis set in VOLT and 194/440 patients (44.1%) in VERSUS were 65 years or older. In VERSUS, older patients who transitioned from tolterodine ER 4 mg showed significant improvements in urgency episodes/day and all other diary variables from baseline to study end (see Table), reflecting significant improvements in the full study population [2]. PPBC scores improved significantly in 69.1% of older patients in VOLT (–1.3; 95% CI:–1.41, –1.23) and in 65.2% of older patients in VERSUS (–1.0; 95% CI: –1.3, –0.8). In addition, for VOLT patients, improvements were seen across all domains on the VAS. For patients 65 years or older in both studies, improvements were seen across all OAB-q domains as well (see Table). These improvements were consistent with the significant improvements observed in the full study populations [2,3].

Treatment-related adverse events (AEs) were reported by 43.7% (390/892) of those over the age of 65 years in the safety population of VOLT and 37.1% (72/194) in this age group for VERSUS. Most of these AEs were anticholinergic and of mild-to-moderate severity. In total, 23.0% of VOLT patients and 19.1% of VERSUS patients older than 65 years reported dry mouth; 15.7% and 12.4% of VOLT and VERSUS patients, respectively, reported constipation; 3.1% and 1.0%, respectively, reported headache; 2.7% and 2.1%, respectively, reported blurred vision; and 1.7% and 3.6%, respectively, reported dry eyes. In total, only 12.9% of VOLT patients and 5.2% of VERSUS patients older than 65 years discontinued treatment due to AEs.

	VOLT			**VERSUS**		
Parameter (mean)	**Patients ≥65 (n=880)**			**Patients ≥65 (n=194)**		
	Baseline	**Change from baseline**	**95% CI**	**Baseline‡**	**Change from baseline**	**95% CI**
Urgency episodes/day†	–	–	–	6.55	–3.61**	–4.30, –2.93
Micturitions/day†	–	–	–	11.17	–1.87**	–2.31, –1.43
Incontinence episodes/day†	–	–	–	4.19	–2.76**	–3.28, –2.25
Nocturia episodes/day†	–	–	–	1.98	–0.61**	–0.76, –0.45
Nocturnal voids/day†	–	–	–	2.39	–0.58**	–0.78, –0.39
PPBC score†	4.3	–1.3*	–1.41, –1.23	4.2	–1.0**	–1.3, –0.8
VAS score						
Urgency†	66.5	–35.2*	–37.5, –32.8	–	–	–
Urge incontinence†	63.3	–36.8*	–39.4, –34.2	–	–	–
Frequency†	67.4	–37.2*	–39.7, –34.7	–	–	–
Nocturia†	65.2	–32.0*	–34.5, –29.6	–	–	–
OAB-q domain score						
Bother†	55.5	–25.0*	–26.7, –23.3	57.5	–25.9**	–29.5, –22.3
Coping	56.0	23.2*	21.4, 24.9	52.5	24.8**	21.3, 28.2
Concern	55.6	23.7*	21.8, 25.5	52.6	27.6**	24.0, 31.1
Sleep	50.7	22.9*	21.1, 24.8	49.1	22.0**	18.5, 25.4

Social interaction	78.9	11.3*	9.8, 12.8	78.0	13.5**	10.7, 16.4
Overall HRQoL	59.4	20.9*	19.3, 22.5	56.9	22.8**	19.9, 25.7

[†]Negative score change indicates improvement (improvements in all other domains are indicated by positive score changes); [‡]On no drug; **P<0.0001; *P<0.001.

Interpretation of results

After 12 weeks of treatment with solifenacin, patients 65 years or older experienced decreases in OAB symptoms (recorded by 3-day diaries) and improvements from baseline in bother and HRQoL, as measured by the PPBC, VAS, and OAB-q. These results were consistent with the full study populations.

Concluding message

In this large group of patients 65 years or older, flexibly-dosed solifenacin was associated with reductions in OAB symptoms and improvements in patients' perception of bladder condition and HRQoL, reflecting the significant treatment effect observed in the full study populations. Despite the potential for older patients to be more sensitive to anticholinergic medication side effects, solifenacin was generally well tolerated in patients 65 years or older.

References

1. World J Urol (2003); 20: 327-36.
2. Int Urogyn J (2006); 17(suppl 9): 361-488.
3. Clin Ther (2006); 28: 1935-46.

Specify source of funding or grant	**This study was sponsorred by Astellas Pharma US, Inc. and GlaxoSmithKline**
Is this a clinical trial?	**Yes**
Is this study registered in a public clinical trials registry?	**Yes**
Specify Name of Public Registry, Registration Number	**The trial registry number for the VOLT trial is NCT00463541, and the number for the VERSUS trial is NCT00454740**
What were the subjects in the study?	**HUMAN**
Was this study approved by an ethics committee?	**Yes**
Specify Name of Ethics Committee	**Both studies were conducted in accordance with Good Clinical Practice and in accordance with the ethical principles that have their origin in the Declaration of Helsinki and FDA regulations**
Was the Declaration of Helsinki followed?	**Yes**
Was informed consent obtained from the patients?	**Yes**