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Title: LONG-TERM HEALTH-RELATED QUALITY OF LIFE OF PATIENTS WITH OVERACTIVE BLADDER RECEIVING TOLTERODINE

Aims of Study:

To evaluate long-term health-related quality of life (HRQOL) as measured by the King's Health Questionnaire (KHQ) in overactive bladder (OAB) patients receiving treatment with tolterodine for 15 months (TT group) or placebo for 3 months followed by tolterodine for 12 months (PT group).

Methods:

This two-part, randomized, parallel groups, multinational study evaluated efficacy and safety of tolterodine. In the double-blind study, OAB patients (n=1,529) with an average of ≥8 micturations/day over a seven-day period and >5 urge incontinence episodes/wk were randomized to receive tolterodine 4mg prolonged release (PR), tolterodine 2mg (IR), or placebo. In the open-label study, 1,077 patients who completed the double-blind study continued on tolterodine PR.

The KHQ is a 32-item, disease-specific questionnaire designed to evaluate the impact of OAB on HRQOL, including areas of physical and emotional function shown to be important to patients [1,2,3]. The KHQ was self administered at baseline (Visit 2), end of blinded treatment (12 weeks) and rollover to open-label study (Visit 4), 3 months of open-label treatment (Visit 7) and 12 months of open-label treatment (Visit 10) for those countries with available translations (n=1,312). KHQ domains are scored on a 0 (best) to 100 (worst) scale.

Analyses used a split plot ANCOVA with repeated measures with visits and treatment group as factors with age, gender and country as covariates. The primary analysis used the intent-to-treat (ITTb) including all KHQ responses at rollover (n=838), and a secondary analysis used the ITTa (n=1,312), including all KHQ responses at baseline. Last observation carried forward (LOCF) was used for missing responses, except for the Personal Relationships domain where not applicable responses make this inappropriate. Hypothesis-wise error due to multiple comparisons was controlled for using the Hochberg procedure [4].

Results:

The PT group experienced significant improvements in 7 of the 10 KHQ domains after 3 months and 9 of 10 domains after 12 months of tolterodine treatment. The TT group continued to experience significant improvement during the first 3 months of open-label study on 9 of 10 domains. At 12 months of open-label study (15 months of tolterodine treatment), the TT group continued to experience significant improvements in Incontinence Impact and Role Limitations from the beginning of the open-label study, and with the exception of General Health Perception, maintained HRQOL levels on all other domains. The PT group experienced significantly more improvement on the Incontinence Impact, Role Limitations, Physical Limitations, and Sleep and Energy domains at 12 months and Symptom Severity at both time points.

Difference in LS Mean KHQ Change from Rollover (Visit 4) Scores Using ITTb Population

	PT		TT	
Domain	**Change from V4 to V7**	**Change from V4 to V10**	**Change from V4 to V7**	**Change from V4 to V10**
Incontinence Impact [a,b]	-13.0 [c]	-12.7 [c,d]	-7.4 [c]	-5.9 [c]
Role Limitations [a,b]	-10.3 [c]	-11.6 [c,d]	-5.0 [c]	-4.1 [c]
Physical Limitations [a,b]	-7.3 [c]	-10.1 [c,d]	-3.9 [c]	-2.9
Social Limitations	-3.1	-4.1 [c]	-2.1 [c]	-0.5
Personal Relationships	-3.8	-5.2 [c]	-3.1 [c]	-0.6
Emotions [b]	-6.8 [c]	-5.6 [c]	-3.6 [c]	-2.5
Sleep and Energy [a,b]	-5.4 [c]	-6.2 [c,d]	-2.4 [c]	-0.5
Severity (coping) Measures [a,b]	-4.2 [c]	-5.1 [c]	-2.9 [c]	-2.1
General Health Perception	0.3	-0.2	1.1	2.1 [c]
Symptom Severity [a,b]	-6.6 [c,d]	-6.6 [c,d]	-2.1 [c]	-0.8

[a] tolterodine 4mg PR group and [b] tolterodine 2mg IR group were significantly different from placebo in double-blind study

[c] within group comparison was significantly different from rollover using Hochberg procedure

[d] PT group significantly different from TT group

ITTa analyses yielded similar results. All domains except General Health Perception showed statistically significant within group improvement from baseline at both time points. The TT group had better improvement compared with the PT group in the Incontinence Impact and Symptom Severity domains at 3 months only and in the Severity (coping) Measures at both time points.

Conclusions:

HRQOL, measured by the KHQ, improved with tolterodine treatment and these improvements were sustained over a 12 to 15 month time period. After a three-month placebo run-in, patients experienced statistically significant improvement on 7 of 10 domains after 3 months and 9 of 10 domains after 12 months of treatment with tolterodine. Patients receiving tolterodine during the three-month blinded study continued to improve with three additional months of treatment on 9 of 10 domains and the HRQOL levels at the beginning of the open-label study were sustained through the 12 months of open-label treatment. These improvements are generally consistent when all patients who entered the double-blind study are included in the analyses. These results support the long-term use of tolterodine in the treatment of OAB in patients experiencing urinary incontinence.

References:

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