**210**

Rudy D[1], Hanno P[2], Caramelli K[3], Thomas H[3], Hoel G[3]
***1.*** *Urology Associates of North Texas, Arlington, TX,* ***2.*** *University of Pennsylvania, Philadelphia, PA,* ***3.*** *Watson Laboratories, Salt Lake City, UT*

# QUALITY OF LIFE IN A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY OF OXYBUTYNIN CHLORIDE TOPICAL GEL TREATMENT OF PATIENTS WITH OVERACTIVE BLADDER

Hypothesis/aims of study

Oxybutynin chloride topical gel (OTG) is a 10% by weight ethanolic gel formulation that is applied to the skin once daily [1,2]. The efficacy of OTG in improving urinary symptoms associated with overactive bladder (OAB) was demonstrated in a 12-week, multicenter, randomized, double-blind, placebo-controlled phase 3 study [3]. OTG significantly reduced the number of incontinence episodes per day, decreased urinary frequency, and increased voided volumes versus placebo [3]. The effects of OTG on health-related quality of life (HRQoL), a planned secondary end point in the study, were evaluated in order to measure patients' perceptions of improvement in their OAB symptoms.

Study design, materials and methods

Women and men aged ≥18 years with urge urinary incontinence were enrolled at 76 US centers in this phase 3 study (NCT00350636 at clinicaltrials.gov). Patients were randomized in a 1:1 ratio to receive 1 g OTG once daily or matching placebo gel for up to 12 weeks. The treatment allocation schedule implemented a computer-generated randomized design that sequentially assigned each patient to 1 of 2 treatments according to the randomization number. Double-blind treatment status was maintained throughout the study by use of identical appearing gels and packaging. Approximately 700 patients were targeted for enrollment in the study, based on estimates that 350 patients in each treatment group would provide 85% power to detect a significant difference between active and placebo treatments with the use of a 2-tailed *t* test. To assess HRQoL, investigators asked patients to complete 2 disease-specific questionnaires (Incontinence Impact Questionnaire [IIQ]; King's Health Questionnaire [KHQ]) at baseline and weeks 1, 4, 8, and 12. IIQ scale scores and KHQ domain scores could range from 0 (least impairment) to 100 (greatest impairment); a total score for the IIQ (possible range, 0 to 400) was calculated by summing the 4 individual IIQ scale scores. Effects on HRQoL were assessed by computing mean change in questionnaire scores from baseline to week 12 or last observation. Differences between active and placebo treatments were compared through analysis of covariance and considered significant if $P<.05$.

Results

In this study, completed May 2007, 704 women and 85 men were enrolled; 389 patients received OTG and 400 received placebo. IIQ total score improved significantly more in patients treated with OTG (mean change, −72.1 points; $P=.0005$) than in those receiving placebo (mean change, −49.5 points) (Figure 1). HRQoL also improved significantly more with OTG ($P\leq.0078$) than with placebo in all 4 IIQ subscales (Travel, Physical Activity, Social Relationships, and Emotional Health) (Figure 1). Mean KHQ scores improved significantly more ($P\leq.0489$) with OTG than with placebo in 6 of 10 domains, many directly associated with OAB symptoms (Incontinence Impact, Symptom Severity, Role Limitations, Personal Relationships, Sleep/Energy, and Severity [Coping] Measures) (Figure 2). Dry mouth was the most common treatment-related adverse event in patients given OTG (27/389; 6.9%) (Table) but was not a primary reason for any patient to stop treatment.

**Figure 1. Mean changes in IIQ total score and subscale scores from baseline to study end.** Error bars indicate standard errors of the mean; ***P*<.05, analysis of covariance.

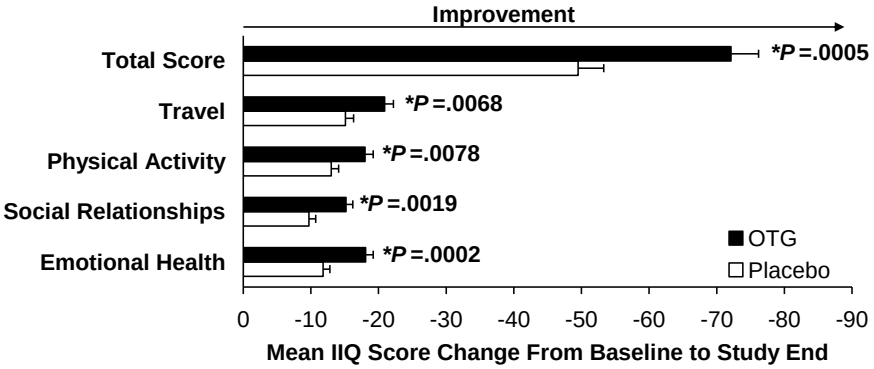


**Figure 2. Mean changes in KHQ domain scores from baseline to study end.** Error bars indicate standard errors of the mean; ***P*<.05, analysis of covariance.

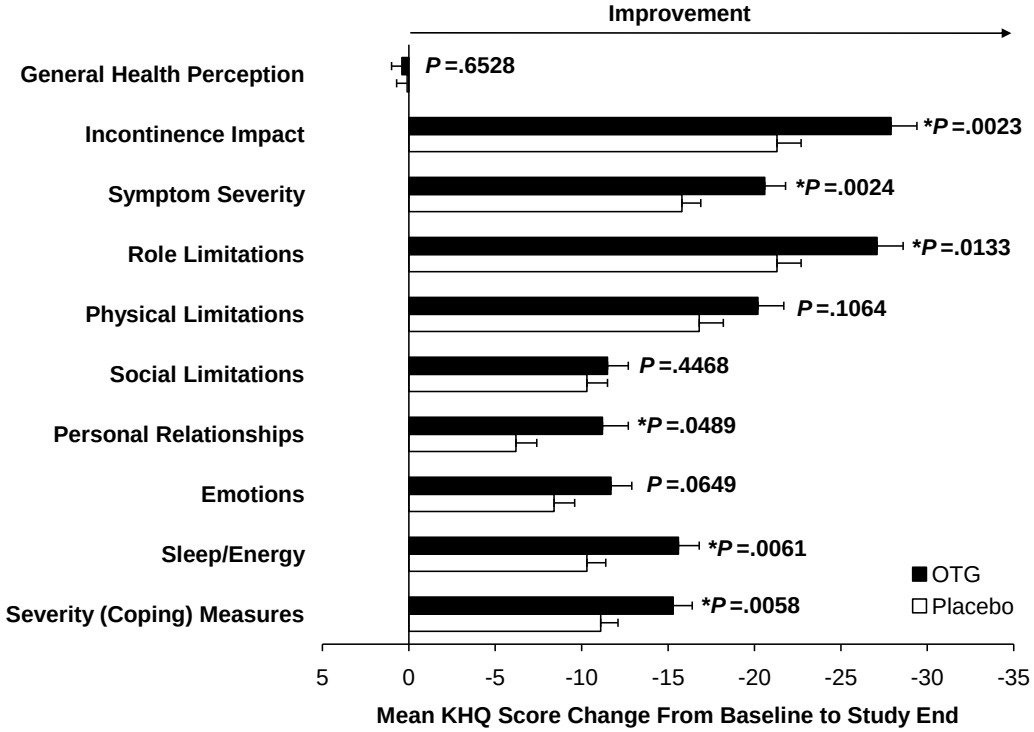


**Table. Treatment-Related Adverse Events in ≥1% of Patients Given OTG**

| Adverse Events, n (%) | OTG (n = 389) | Placebo (n = 400) | *P* Value |
|---|---|---|---|
| Dry mouth | 27 (6.9) | 11 (2.8) | .0060[a] |
| Application site pruritus | 8 (2.1) | 3 (0.8) | .1176[a] |
| Application site dermatitis | 7 (1.8) | 1 (0.3) | .0358[b] |
| Headache | 6 (1.5) | 11 (2.8) | .2428[a] |
| Constipation | 5 (1.3) | 4 (1.0) | .7494[b] |
| Dizziness | 6 (1.5) | 2 (0.5) | .1719[b] |
| Pruritus | 5 (1.3) | 5 (1.3) | 1.0000[b] |

[a]Chi-square test; [b]Fisher's exact test.

Interpretation of results

OTG treatment had a significant positive effect on most HRQoL measures compared with placebo. OTG-related improvements in objective outcomes now have been corroborated by patient-reported improvements in symptoms and other negative aspects of OAB.

Concluding message

The positive effects of OTG on patient-reported outcomes, combined with its demonstrated efficacy and excellent safety profile, are expected to make it an attractive treatment option for adults with OAB.

References

1. Caramelli KE, Staskin DR, Volinn W. Steady-state pharmacokinetics of an investigational oxybutynin topical gel in comparison with oxybutynin transdermal system. Poster presented at: Annual Meeting of the American Urological Association; May 17-22, 2008; Orlando, FL. Abstract #1508
2. Newman DK, Caramelli KE, Stanworth S, Volinn W, Hoel G. Oxybutynin chloride topical gel for overactive bladder: effects of showering, sunscreen, and person-to-person transference. Poster presented at: Annual Conference of the Society of Urologic Nurses and Associates; October 3-6, 2008; Philadelphia, PA
3. Staskin DR, Dmochowski RR, Sand PK, MacDiarmid SA, Caramelli KE, Thomas H, Hoel G. Efficacy and safety of oxybutynin chloride topical gel for treatment of adults with overactive bladder: a randomized, double-blind, placebo-controlled, multicenter study. J Urol. 2009;181(4):1764-1772


| | |
|---|---|
| ***Specify source of funding or grant*** | **This work was funded by Watson Pharma, Inc.**<br>**The study protocol was approved by local institutional review boards, and each patient granted fully informed, written consent before enrollment.** |
| ***Is this a clinical trial?*** | **Yes** |
| ***Is this study registered in a public clinical trials registry?*** | **Yes** |
| ***Specify Name of Public Registry, Registration Number*** | **Clinicaltrials.gov, number NCT00350636** |
| ***What were the subjects in the study?*** | **HUMAN** |
| ***Was this study approved by an ethics committee?*** | **Yes** |
| ***Specify Name of Ethics Committee*** | **The study protocol was approved by local institutional review boards, and each patient granted fully informed, written consent before enrollment.** |
| ***Was the Declaration of Helsinki followed?*** | **Yes** |
| ***Was informed consent obtained from the patients?*** | **Yes** |