

IMPROVEMENT IN HEALTH-RELATED QUALITY OF LIFE FOLLOWING TREATMENT WITH ONABOTULINUMTOXINA IN PATIENTS WITH URINARY INCONTINENCE DUE TO NEUROGENIC DETRUSOR OVERACTIVITY

Hypothesis / aims of study

To evaluate the impact of onabotulinumtoxinA on health-related quality of life (HRQoL) in patients with urinary incontinence (UI) due to neurogenic detrusor overactivity (NDO).

Study design, materials and methods

Here we present the results of a pooled analysis of two pivotal, multicenter, double-blind, randomized, placebo-controlled Phase 3 studies that were identical in study design (ClinicalTrials.gov identifiers NCT00311376 and NCT00461292), except for the UI retreatment threshold. Eligible patients had NDO due to multiple sclerosis (MS) or spinal cord injury (SCI) with ≥ 14 UI episodes/week and were not adequately managed by anticholinergics, though the continued use of anticholinergics was permitted throughout the study. Patients received 30 intradetrusor injections of placebo, onabotulinumtoxinA 200U, or onabotulinumtoxinA 300U, administered cystoscopically, avoiding the trigone. Patients could request a second treatment from 12 weeks post first treatment onward. Retreatment required the patient to have a $< 50\%$ (study 1) or $< 30\%$ (study 2) reduction from baseline in weekly UI episodes. The results presented here from this placebo-controlled comparison focus on the first 12 weeks post treatment 1, prior to possible retreatment. The primary efficacy endpoint in both studies was the same: change from baseline in number of UI episodes at week 6 following the first treatment. Secondary endpoints included mean change from baseline in the 22-item Incontinence Quality of Life (I-QOL; comprised of a total score and 3 domain scores [avoidance/limiting behavior, psychosocial impact, and social embarrassment]) and the 16-item modified Overactive Bladder Patient Satisfaction with Treatment Questionnaire (OAB-PSTQ; comprised of the total score from the original 12-items of the OAB-PSTQ plus 4 additional items that were added to assess satisfaction with treatment, goal attainment, treatment expectations, and side effects. Study 1 was designed to provide 90% power to detect a 7.5 episode difference in the primary endpoint (frequency of UI episodes) between the onabotulinumtoxinA group and placebo, with a two-sided type I error of 0.025. The common standard deviation was assumed to be 15 episodes. Study 2 was powered for 80% under the same assumptions as in study 1.

Results

The pooled analysis population consisted of a total of 691 patients (416 patients in study 1, and 275 patients in study 2). Overall baseline and disease characteristics of the ITT population were similar across treatment groups (mean age 45.9 years, 57.9% female, 85.8% Caucasian, 58.9% on anticholinergic therapy, mean duration of NDO of 7.7 years). At baseline, I-QOL total scores were 35.3, 35.4, and 33.9 in the placebo, onabotulinumtoxinA 200U, and 300U groups, respectively, and 24.3%, 17.2%, and 30.5% of patients, respectively, were very satisfied with their treatment. At week 6, significant improvements in mean I-QOL total scores were observed with both doses of onabotulinumtoxinA (25.9 and 29.2 for the 200U and 300U doses, respectively) versus placebo (11.2) ($P < 0.001$ for both comparisons vs placebo). Results at week 12 were similar. OAB-PSTQ total scores at weeks 6 and 12 were also improved for both the 200U and 300U onabotulinumtoxinA groups versus placebo. In this pooled analysis, 20.6%, 58.4%, and 56.6% of patients in the placebo, onabotulinumtoxinA 200U, and 300U groups, respectively, reported they were very satisfied with treatment at week 6 ($P < 0.001$ vs placebo). Approximately 60% of patients in the onabotulinumtoxinA 200U and 300U treatment groups reported attaining or significantly progressing towards their primary treatment goal and reported that they met or significantly exceeded their treatment expectations compared to placebo (11.9% and 15.3%, respectively). There were no clinically meaningful differences in effects on QoL and satisfaction between onabotulinumtoxinA dosage groups.

Interpretation of results

Both doses of onabotulinumtoxinA provided significant and clinically relevant improvements in the HRQoL of patients with UI due to NDO. In addition, higher proportions of patients in the onabotulinumtoxinA treatment groups were satisfied, attained their treatment goals, and reported their expectations were met versus placebo.

Concluding message

NDO patients treated with onabotulinumtoxinA 200U or 300U had significantly improved QoL and greater satisfaction with treatment compared with placebo-treated patients, with no clinically relevant differences in between onabotulinumtoxinA doses.

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Is this study registered in a public clinical trials registry?	Yes
Specify Name of Public Registry, Registration Number	clinicaltrials.gov (NCT00461292 and NCT00311376)
Is this a Randomised Controlled Trial (RCT)?	Yes
What were the subjects in the study?	HUMAN
Was this study approved by an ethics committee?	Yes
Specify Name of Ethics Committee	The institutional review boards or ethics committees at each participating center approved the study.
Was the Declaration of Helsinki followed?	Yes
Was informed consent obtained from the patients?	Yes

