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SUSTAINED IMPROVEMENTS IN HEALTH-RELATED QUALITY OF LIFE FOLLOWING REPEAT ONABOTULINUMTOXINA DETRUSOR INJECTIONS IN PATIENTS WITH NEUROGENIC DETRUSOR OVERACTIVITY: RESULTS FROM TWO PHASE 3 STUDIES

Hypothesis / aims of study
Urinary incontinence (UI) due to neurogenic detrusor overactivity (NDO) has been shown to negatively impact patients' health-related quality of life (HRQOL). A single intradetrusor injection of onabotulinumtoxinA 200U or 300U has been shown to significantly improve HRQOL in patients with UI due to NDO. However, additional data on the effects of repeat onabotulinumtoxinA treatment on HRQOL in NDO patients are needed. In addition, patient-reported goals for the treatment of NDO are not well documented. The objective of the present analysis was thus to evaluate the effects of repeat onabotulinumtoxinA treatment on HRQOL, and to assess changes in HRQOL by patients' baseline treatment goals. We assessed HRQOL improvements over two treatments as a first step in assessing treatment benefit over time.

Study design, materials and methods
Data from two phase 3, double-blind, placebo-controlled, randomized studies with identical entry criteria and treatments were pooled for assessment of HRQOL after two cycles of treatment with onabotulinumtoxinA 200U over a 52-week period. Eligible patients had NDO (≥14 UI episodes/week at baseline) due to multiple sclerosis (MS) or spinal cord injury (SCI) and were not adequately treated with at least one anticholinergic. Patients received 30 intradetrusor injections of placebo, onabotulinumtoxinA 200U or 300U, administered cystoscopically, avoiding the trigone. Patients could request a second treatment from 12 weeks post-first treatment onward. The analysis presented here focuses on patients who received at least one treatment cycle of onabotulinumtoxinA 200U. At study entry, patients were asked to list their top 2 primary goals for treatment of their overactive bladder. Patient qualitative responses were then grouped into 9 categories based on the domains from the King's Health Questionnaire (KHQ). Qualitative responses were categorized by 2 independent raters. Categories included: role limitations, social limitations, physical limitations, personal relationships, emotions, sleep/energy, severity measurements, general health perception/QOL, and incontinence impact. A number of the responses did not fit into these initial 9 categories. These responses were aggregated into other categories: dry, reduce other OAB therapies, improve bladder control, reduce frequency of urination, reduce urgency, and reduce other bladder symptoms. KHQ categories that had <2% of responses were included in the 'other' category (role limitations, social limitations, personal relationships, and severity measurements). This resulted in a total of 12 categories (Table). We analyzed the frequency distribution of treatment goals at study entry in each of the 12 categories. The mean change from baseline in the total scaled score of the Incontinence-Quality of Life (I-QOL) questionnaire was used to evaluate HRQOL 6 weeks after onabotulinumtoxinA 200U treatment. The scaled total I-QOL score ranges from 0 to 100 with a higher score indicating improvement in HRQOL. A clinically-meaningful improvement in total I-QOL Score is defined as a ≥11-point increase from baseline. Mean changes from baseline in total I-QOL Score for each treatment goal category and by neurological disease (MS or SCI) were also analyzed.

Results
A total of 215 and 176 patients received 1 and 2 treatment cycles of onabotulinumtoxinA 200U, respectively, over the 52-week period. The most common patient-reported treatment goals at baseline were 'to be dry' (36.3% of patients), 'to reduce OAB therapies' (19.5% of patients) and 'to improve bladder control' (15.3% of patients). Clinically meaningful improvements in mean overall total I-QOL scores from baseline were observed after both onabotulinumtoxinA 200U treatments; increases from baseline were 26.2 and 29.9 for cycles 1 and 2, respectively. Improvements in total I-QOL scores were observed in all treatment goal categories. Reduced activity limitations and reduced urgency were the treatment goals with the highest mean improvement in total I-QOL scores after treatment cycles 1 and 2, respectively (Table). Clinically meaningful improvements in mean overall total I-QOL scores were observed in both the MS and SCI subpopulations.

Interpretation of results
This pooled analysis of data from two large phase III studies demonstrated significant and clinically meaningful improvements from baseline in HRQOL following treatment with onabotulinumtoxinA 200U in patients with UI due to NDO, which were sustained following repeat treatment. Clinically meaningful improvements in HRQOL were also observed with onabotulinumtoxinA 200U after stratifying by treatment goal category and neurologic disease.

Concluding message
These results demonstrate that the symptom improvement with onabotulinumtoxinA treatment translates into an improvement in HRQOL, which is sustained over two treatments. These results further support the use of onabotulinumtoxinA 200U in patients with NDO and UI who are not adequately managed by anticholinergic medications.

Table: Treatment Goals Among Patients with UI due to NDO and Mean Change from Baseline in Total I-QOL Scores by Treatment Goal

Treatment Goal	Mean Change from Baseline in Total I-QOL Scores Following OnabotulinumtoxinA Treatment	
	Treatment 1	Treatment 2
To be dry	25.7	27.1

To reduce OAB therapies	28.4	27.1
To improve bladder control	32.4	36.4
To have reduced frequency of urination	20.7	26.3
To have reduced incontinence	30.2	33.4
To reduce activity limitations	35.9	37.7
To reduce urgency	29.1	38.4
To improve sleep	30.9	37.8
To improve QOL	27.7	30.9
To improve emotions	29.1	30.5
To reduce other urinary symptoms	26.1	34.5
Other*	18.8	34.4
Overall	26.2	29.9

*Includes 'treatment works', 'renewed bladder', 'positive treatment result', 'save money' and 'stop reflux'.

Disclosures
Funding: Funded by Allergan, Inc. **Clinical Trial:** Yes **Registration Number:** Clinicaltrials.gov NCT00311376 and NCT00461292 **RCT:** Yes **Subjects:** HUMAN **Ethics Committee:** institutional review boards or ethics committees at each study site approved the study **Helsinki:** Yes **Informed Consent:** Yes