

## **CLINICALLY MEANINGFUL IMPROVEMENTS IN URINARY INCONTINENCE AND QUALITY OF LIFE OVER MULTIPLE TREATMENT CYCLES OF ONABOTULINUMTOXINA IN PATIENTS WITH OVERACTIVE BLADDER SYNDROME AND URINARY INCONTINENCE: INTERIM ANALYSIS OF A LONG-TERM EXTENSION STUDY**

### Hypothesis / aims of study

Two pivotal, phase 3, randomised, double-blind, placebo-controlled studies demonstrated that a single treatment of onabotulinumtoxinA 100U significantly reduced urinary incontinence (UI) and was well tolerated in patients with idiopathic overactive bladder syndrome (OAB) syndrome and UI who were inadequately managed with anticholinergic therapy. However, data on the long-term efficacy and safety of onabotulinumtoxinA treatment of OAB from large multicentre studies is needed. Here we report a pre-planned interim analysis of the ongoing extension trial of the phase 3 studies assessing the responders to treatment and safety of onabotulinumtoxinA over multiple treatments.

### Study design, materials and methods

On completion of either of the two phase 3, randomised, double-blind, placebo-controlled, pivotal studies, patients could enter a 3-year extension study (NCT00915525) and receive multiple treatments of intradetrusor onabotulinumtoxinA administered via cystoscopy, avoiding the trigone. The study is still ongoing. Data were integrated across studies; patients receiving  $\geq 1$  onabotulinumtoxinA treatment in the evaluation period were analysed by onabotulinumtoxinA treatment cycle (up to 5 cycles). The timepoint of primary interest was week 12 after each treatment. Assessments included the proportion of patients with  $\geq 50\%$  reduction in UI episodes/day compared to the baseline prior to any study treatment. In addition, health-related quality of life (HRQOL) was assessed using the Incontinence Quality of Life (I-QOL) total summary score and two pre-specified domains (Role Limitations and Social Limitations) of the King's Health Questionnaire (KHQ). The proportion of patients exceeding the minimally important differences (MIDs) of a  $\geq 10$  point increase from baseline for the I-QOL and a  $\geq 5$  point decrease from baseline for each KHQ domain was assessed at week 12 of each treatment cycle. Adverse events (AEs) and use of clean intermittent catheterization (CIC) due to elevated post void residual urine (PVR) were also evaluated.

### Results

For this interim analysis, a total of 825, 558, 253, 113, and 47 patients had received 1, 2, 3, 4, and 5 onabotulinumtoxinA 100U treatments, respectively. At week 12 after each treatment, the proportion of patients with  $\geq 50\%$  reduction in UI episodes/day were 68.2%, 68.5%, 65.2%, 54.8%, and 58.3% in treatment cycles 1-5, respectively. Large improvements from baseline in HRQOL that exceeded the MIDs were seen following each onabotulinumtoxinA treatment. At week 12, 68.9%, 73.2%, 71.4%, 61.9%, and 62.9% of patients exceeded the MID for the I-QOL total summary score in treatment cycles 1-5, respectively. The proportions of patients exceeding the MID for the KHQ Role Limitations domain were 67.3%, 71.8%, 66.7%, 65.5%, and 54.3%; for the Social Limitations domain, 57.5%, 61.9%, 58.0%, 58.3%, and 51.4% of patients exceeded the MID in treatment cycles 1-5, respectively. The most common AEs in each treatment cycle were primarily localized to the urinary tract. Urinary tract infection was observed in 26.9%, 24.2%, 24.5%, 20.4%, and 14.9% of patients, and the AE of urinary retention was reported in 4.0%, 3.4%, 3.2%, 3.5%, and 2.1% of patients in treatment cycles 1-5, respectively. The proportion of patients requiring CIC due to elevated PVR was 4.6%, 4.1%, 4.7%, 5.3%, and 2.1% in onabotulinumtoxinA 100U cycles 1-5. No change in the AE profile was observed over repeated treatments.

### Interpretation of results

This pre-planned interim analysis of data from the ongoing extension of the phase 3 trials of onabotulinumtoxinA in OAB patients with UI who were inadequately managed with anticholinergic medications demonstrated clinically meaningful reductions in UI episodes and improved HRQOL over 5 treatment cycles. A consistent safety profile was also seen, with no new safety signals.

### Concluding message

Repeated onabotulinumtoxinA treatment in OAB patients with UI inadequately managed with anticholinergic medications showed sustained reductions in UI episodes per day, improved HRQOL, and was well tolerated.

### Disclosures

**Funding:** Allergan, Inc. **Clinical Trial:** Yes **Registration Number:** ClinicalTrials.gov, NCT00915525 **RCT:** No **Subjects:** HUMAN **Ethics Committee:** Institutional Review Boards **Helsinki:** Yes **Informed Consent:** Yes