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CLINICALLY MEANINGFUL IMPROVEMENTS IN URINARY INCONTINENCE FOLLOWING LONG-TERM ONABOTULINUMTOXINA TREATMENT IN PATIENTS WITH OVERACTIVE BLADDER SYNDROME: FINAL RESULTS OF A 3.5-YEAR STUDY

Hypothesis / aims of study

OnabotulinumtoxinA (BOTOX®; Allergan, Inc.) 100U is approved for the treatment of urinary incontinence (UI) in patients with overactive bladder (OAB) who were inadequately managed by ≥1 anticholinergic. This approval was based on the results of two, 24-week, phase 3, randomized, placebo-controlled, double-blind trials, which demonstrated that onabotulinumtoxinA significantly reduces UI, improves quality of life, and is well tolerated. Upon completion of the phase 3 trials, patients could continue to receive multiple treatments in a 3-year, prospective, multicenter extension study to assess the long-term efficacy and safety of onabotulinumtoxinA in patients with OAB. Here we present the final results of these patients, with up to 3.5-year follow-up.

Study design, materials and methods

Patients received onabotulinumtoxinA treatments administered via cystoscopy, avoiding the trigone. Patients requested treatment 'as needed' for control of symptoms (100U or 150U). Treatment was administered based on fulfillment of prespecified criteria (≥12 weeks since previous treatment, ≥2 urgency UI episodes over 3 days, and a post-void residual volume of <200 mL). Because patients were on individualized treatment schedules, the total number of treatments received during the study differed among patients. Originally, a dose increase from 100U to 150U was permitted from treatment 3 onwards. After regulatory approval of the 100U dose for OAB, all patients subsequently received only 100U.

Study assessments included change from baseline in UI episodes/day at week 12 following each treatment (co-primary endpoint with Treatment Benefit Scale, not presented here); UI responder rates (proportions of patients with ≥50%, ≥75%, or 100% ['dry'] reductions in UI); proportion of patients with an overall median time to request retreatment (duration of effect) of ≤6 months, >6 to ≤12 months, or >12 months; adverse events (AEs); and initiation of clean intermittent catheterization.

Change in UI episodes/day, duration of effect, and safety data were assessed for the overall population of patients who received 100U in any treatment cycle (overall 100U population; n=829). In order to evaluate the consistency of response to repeat treatments by following the same patients through the study, additional data (change in UI episodes/day and UI responder rates) were assessed in discrete subgroups of patients who received 1 (n=105), 2 (n=118), 3 (n=117), 4 (n=83), 5 (n=46), or 6 (n=33) treatments of only the 100U dose throughout the study (discrete subgroups; n=502).

Results

Of the 829 patients who received ≥1 onabotulinumtoxinA 100U treatment in either of the phase 3 studies or the long-term extension, 51.7% completed the 3.5-year study. Discontinuations due to AEs (5.1%) or lack of efficacy (5.7%) were low. Only 4 patients (0.5%) discontinued due to treatment-related AEs; other reasons for discontinuation were not treatment-related. In the overall population, mean age at baseline was 60.1 ± 13.4 years, 90.3% were female, and patients reported an average of 5.6 ± 3.6 UI episodes/day; baseline characteristics were similar in each of the discrete subgroups. A consistent response with repeat treatment was seen in the overall population; at week 12 following onabotulinumtoxinA 100U treatment, mean decreases of UI episodes/day from baseline were -3.3, -3.6, -3.8, -3.5, -3.3, and -3.1 UI episodes/day for treatments 1-6, respectively.

For each discrete subgroup of patients, mean reductions in UI episodes/day at week 12 were consistent regardless of how many total treatments with 100U were administered: 1 (-3.1); 2 (-2.9, -3.2); 3 (-4.1 to -4.5); 4 (-3.4 to -3.8); 5 (-3.0 to -3.6); or 6 (-3.1 to -4.1). In addition, high proportions of patients achieved ≥50% and ≥75% reduction in UI episodes at week 12 after onabotulinumtoxinA 100U treatment; 64-81% of patients achieved ≥50% reduction and 47-74% of patients achieved ≥75% reduction in daily UI episodes across all subgroups. In 5 of the 6 subgroups, 29-50% of patients achieved 100% reduction after each treatment (the remaining subgroup was 16-36%).

Overall median duration of effect (time to request for retreatment) for onabotulinumtoxinA 100U was 7.6 months. The proportion of patients with a duration of effect ≤6 months, >6 to ≤12 months, and >12 months was 34.2%, 37.2%, and 28.5%, respectively.

De novo clean intermittent catheterization rates due to retention were 4.0%, 1.7%, 1.4%, 1.6%, 0.6%, and 0.8% in the overall population in treatment cycles 1–6, respectively. The most common AEs included urinary tract infection, dysuria, bacteriuria, and urinary retention.

Interpretation of results

This long-term, multicenter study followed patients with OAB and UI for up to 3.5 years and demonstrated that in the overall study population, long-term treatment with onabotulinumtoxinA resulted in clinically meaningful and sustained absolute reductions in UI episodes/day. In addition, in the discrete subgroup analysis in which the same groups of patients were followed across treatments, reductions in UI and the proportions of patients achieving ≥50%, ≥75%, and 100% reduction in UI were consistent from treatment to treatment. The duration of effect results demonstrate that different patients will request retreatment at different time intervals; in this study, almost equal proportions of patients requested retreatment within ≤6 months, >6 to ≤12 months, and >12 months.

Concluding message

Long-term onabotulinumtoxinA treatment provided consistent and sustained improvements in UI in patients with OAB, with a median duration of effect >6 months in about two-thirds of patients and >12 months in almost one-third of patients. OnabotulinumtoxinA was well tolerated, with no new safety signals identified over 3.5 years. These results further support the long-term use of onabotulinumtoxinA in patients whose OAB is inadequately managed by ≥1 anticholinergic.

Disclosures

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