Repeat OnabotulinumtoxinA Treatment in Spinal Cord Injury Patients With Neurogenic Detrusor Overactivity: Final Analysis of 4 Years’ Follow-Up Confirms Sustained Safety and Efficacy

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INTRODUCTION

• Patients with spinal cord injury (SCI) often have neurogenic detrusor overactivity (NDO), which frequently results in urinary incontinence (UI) and elevated risks of urinary tract infections (UTI) that may impair patients’ quality of life (QOL) and increase their risk for the development of renal dysfunction.

• OnabotulinumtoxinA (BOTOX®, Allergan, Inc.) has been shown to be well tolerated and effective in the treatment of NDO due to SCI or multiple sclerosis in two 52-week, phase 3, randomized, placebo-controlled, double-blind trials in patients who were inadequately managed by at least 1 anticholinergic.1,2

• A large, multicenter, extension study has been conducted to investigate the long-term efficacy and safety of onabotulinumtoxinA in patients with NDO.

OBJECTIVE

• To present the final efficacy and safety results from the SCI cohort from the multicenter, long-term study of onabotulinumtoxinA for treatment of UI due to NDO, in which patients were eligible to receive multiple treatments for up to 4 years.

METHODS

Study Design and Participants

• Patients who completed either of the two 52-week, phase 3, randomized studies of onabotulinumtoxinA versus placebo for the treatment of NDO (in which they received up to 2 onabotulinumtoxinA treatments) could enter a 3-year extension study in which they were eligible to receive multiple intradetrusor onabotulinumtoxinA treatments.

• Initially, patients received the same dose of onabotulinumtoxinA they had received in the preceding phase 3 study (200U or 300U), but after regulatory approval of onabotulinumtoxinA 200U for the treatment of UI due to NDO, the trial protocol was amended to allow patients who subsequently received onabotulinumtoxinA 200U if they requested and qualified for re-treatment.

• Patients were treated on an “as needed” basis (based upon patient request/need for re-treatment with onabotulinumtoxinA, as well as fulfillment of predefined criteria [≥1 UI episode within a 3-day diary and ≥1 UI episode within the previous 4 weeks]) Therefore, the total number of treatments needed by each patient during the study varied.

• Study assessments included changes from baseline in UI episodes/day (primary efficacy measure), volume/void, Incontinence Quality of Life (I-QOL) total summary score at week 6 after each treatment; proportions of patients with ≥50% reduction in UI episodes at week 6 after each treatment; and adverse events (AE) (Table 1).

Statistical Methods

• Patient data from the extension study were integrated with their data from the extension study were integrated with their

RESULTS

Patient Disposition and Baseline Demographics

• A total of 157 SCI patients received ≥1 onabotulinumtoxinA treatment over 4 years (onabotulinumtoxinA 200U or 300U), with 62.4% (95% confidence interval: 57.4%, 66.5%) of patients completing the 4-year study. Median duration of effect was calculated for patients who received onabotulinumtoxinA 200U or 300U with complete treatment cycles (n=157). Table 1.

Table 1. Baseline Demographics and Disease Characteristics

<table>
<thead>
<tr>
<th>OnabotA 200U (n=83)</th>
<th>OnabotA 300U (n=74)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>40.7 ± 12.2</td>
</tr>
<tr>
<td>Male gender, n (%)</td>
<td>61 (73.5)</td>
</tr>
<tr>
<td>Duration of NDO, y</td>
<td>8.9 ± 6.9</td>
</tr>
<tr>
<td>Anticholinergic use, n (%)</td>
<td>48 (57.8)</td>
</tr>
<tr>
<td>Using CIC, n (%)</td>
<td>58 (69.1)</td>
</tr>
<tr>
<td>UI episodes/day</td>
<td>6.9 ± 4.2</td>
</tr>
<tr>
<td>Volume/void, mL</td>
<td>201.2 ± 111.0</td>
</tr>
<tr>
<td>Mean total summary score</td>
<td>37.0 ± 19.1</td>
</tr>
</tbody>
</table>

Efficacy Measures

• OnabotulinumtoxinA consistently reduced the number of UI episodes/day. At week 6, mean reductions from baseline in UI episodes/day were −2.7, −2.6, −3.1, −3.0, and −3.3 following onabotulinumtoxinA 200U treatments 1–5, respectively, and were similar with 300U (Figure 1).

• Overall median duration of effect in SCI patients was 8.7 months with onabotulinumtoxinA 200U and 8.3 months for 300U (Figure 4).

• The proportion of SCI patients with ≥50% reduction in UI episodes at week 6 after treatment with onabotulinumtoxinA 200U were 75.3%, 79.7%, 80.6%, 83.3%, and 90.3% (treatments 1–5, respectively), while the proportion of “dry" patients following onabotulinumtoxinA 200U treatment was 40.7%, 42.0%, 41.2%, 58.7%, and 54.5%, respectively. Results with 300U were similar (Table 2).

• Volume/void was consistently increased at week 6 following onabotulinumtoxinA treatment, nearly doubling following treatment. Increases from baseline ranged from 110.1 to 170.0 mL following treatment with onabotulinumtoxinA 200U and from 108.3 to 164.3 mL in the 300U group (Figure 2).

• The long-term efficacy of repeat treatment with onabotulinumtoxinA was supported by a mean of 4.1 UI episodes/day and mean volumes of 123.5 mL at week 6 after each treatment; proportions of SCI patients with ≥50% reduction in UI episodes at week 6 after each treatment; and adverse events (AE) (Table 2).

CONCLUSIONS

• This large, 4-year, prospective, multicenter study demonstrates that improvements in UI, volume/void, and QOL following onabotulinumtoxinA treatment are clinically meaningful and are sustained over a period of up to 4 years in patients with SCI.

• OnabotulinumtoxinA treatments were well tolerated, with no new safety signals identified over 4 years follow-up.

• To our knowledge, these data represent the longest longitudinal follow-up from a large, prospective, multicenter, interventional trial of a UI treatment in SCI patients with NDO who are inadequately managed by 1 anticholinergic medication.

REFERENCES


CLOSURE

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MK, KK, and GJQ receive salary from, and MCM, GJQ, and GKG are in-eligible for, conducted studies funded by, or received honoraria from, Allergan, Inc.; Y2 and Y4 are employees of Allergan, Inc. GS is an employee of Allergan, Ltd. Units of biological activity of onabotulinumtoxinA cannot be compared with or converted into units of any other botulinum toxin product, and onabotulinumtoxinA is not interchangeable with other botulinum toxin preparations.

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