INTRODUCTION

- Many patients develop neurogenic detrusor overactivity (NDO) as a result of neurodegenerative conditions such as multiple sclerosis (MS) or spinal cord injury (SCI).
- NDO frequently results in urinary incontinence (UI) and high detrusor pressures, which can lead to severe damage to the upper urinary tract. UI also significantly impairs patients’ quality of life (QOL).1

- Anticholinergic agents are widely used for the treatment of NDO, although many patients discontinue their use due to lack of efficacy or adverse effects.2

- One potential new treatment is onabotulinumtoxinA (BOTOX®, Allergan, Inc.), which has been shown to significantly decrease UI episodes and improve urodynamic parameters compared with placebo in NDO patients with UI.3

HYPOTHESIS/AIMS OF STUDY

- To evaluate the effects of onabotulinumtoxinA on health-related QOL (HRQOL) in patients with UI due to NDO.

MATERIALS AND METHODS

Study Design and Participants

- Results are presented for 2 pivotal, multicenter, double-blind, randomized, placebo-controlled, phase 3 studies that were identical in study design except for UI episode frequency threshold.

- Studies 19162-515 (NCT00311376) and 19162-516 (NCT00441932): the DIGNITY trials.

- Eligible patients had NDO due to MS or SCI with ≥3 UI episodes per week and were not adequately managed with anticholinergics.4

- Continued use of anticholinergics was permitted.

- Patients received 30 intradetrusor injections (1 ml each) of placebo, onabotulinumtoxinA 200U, or onabotulinumtoxinA 300U, administered cytoscopically via the trigone.5

- Patients could request a second treatment from 12 weeks post first treatment on the basis of the investigator’s judgment (patient had >50% (NCT00311376) or >30% (NCT00441932) reduction from baseline in weekly UI episodes).

- The primary efficacy endpoint in both studies was change in HRQOL measured in weekly UI episodes at week 6 after the first treatment.

Health Outcomes Endpoints

- Health outcomes endpoints were assessed every 6 weeks.

- Incontinence Quality of Life Questionnaire (I-QOL): A validated, disease-specific, 22-item questionnaire designed to measure the impact of UI on patients’ lives.6

- Comprised of domain scores (avoidance and limiting behavior, psychosocial impact, and social embarrassment) and a total score.

- Higher scores reflect better QOL.

- Modified OAB-Patient Satisfaction with Treatment Questionnaire (OAB-PSTQ): A 16-item questionnaire comprised of a 12-item total score and 4 individual items:

- Questions 2–13 comprised the total score and assessed medication impact on various symptoms of OAB and patient dissatisfaction and on ability to interact more freely in social situations, activities, and relationships, and cost.8

- The 4 additional individual items assessed treatment satisfaction, severity of side effects, patients’ achievement of primary treatment goal, and fulfillment of treatment expectations (questions 1, 14, 15, and 16, respectively):

- For questions 1–3, patients responded on the following scale: 1 = very satisfied, 2 = somewhat satisfied, 3 = neutral, 4 = somewhat dissatisfied, 5 = very dissatisfied, and 6 = does not apply.

- For the total score (questions 2–13), decreases from baseline indicate improvement.

- For questions 4 (side effects), the proportion of patients who reported feeling very or somewhat satisfied in the 6-week group was calculated.

- For question 14 (satisfaction), responses were ordered on the following scale: no, mild, moderate, or severe. For questions 15 and 16 (effect of UI on daily activities), patients responded on the following scale: 0 = no, 1 = mild, 2 = moderate, significant, complete. For question 16 (fulfillment of treatment expectations), responses were ordered on the following scale: did not meet, met somewhat, met moderately, met well, exceeded treatment expectations.

RESULTS

Baseline Demographic and Disease Characteristics

- Overall baseline demographics and disease characteristics were balanced across all treatment groups (Table 1).

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Placebo (n=221)</th>
<th>OnabotA 200U (n=222)</th>
<th>OnabotA 300U (n=222)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years), mean (SD)</td>
<td>66.3 (10.4)</td>
<td>66.4 (10.4)</td>
<td>66.7 (10.5)</td>
</tr>
<tr>
<td>Men, %</td>
<td>52.7</td>
<td>51.8</td>
<td>51.3</td>
</tr>
<tr>
<td>Duration of NDO, mean (SD)</td>
<td>2.8 (2.5)</td>
<td>2.7 (2.5)</td>
<td>2.7 (2.5)</td>
</tr>
<tr>
<td>Anticholinergics use, %</td>
<td>91</td>
<td>91</td>
<td>91</td>
</tr>
<tr>
<td>I-QOL score (mean (SD))</td>
<td>73.4 (16.3)</td>
<td>73.3 (16.4)</td>
<td>73.3 (16.3)</td>
</tr>
</tbody>
</table>

Statistical Analyses

- Analyses were performed on the intent-to-treat (ITT) population (defined as all randomized patients).

- An analysis of covariance (ANCOVA) was used to assess differences in I-QOL total and domain scores and OAB-PSTQ total scores between each onabotulinumtoxinA group and placebo, with baseline value as a covariate and treatment group, eligibility (MS or SCI), concurrent anticholinergic use at screening (use vs non-use), and investigator site as fixed effects.

- Proportions of patients in each active treatment group achieving ≥1 point increase above baseline in I-QOL total score were termed responders.

- Comparison between placebo and active treatment was assessed using a Fisher’s exact test or Pearson’s chi-square test as appropriate.

- Painfree comparisons between the onabotulinumtoxinA 200U or 300U and placebo groups were performed using a chi-square test for the individual items of the modified OAB-PSTQ at weeks 6 and 12.

- Placebo-controlled comparison focused on first 2 weeks post-treatment 1, prior to possible repletion.

- For I-QOL scores, a ≥11 point improvement from baseline was considered a responder.

- For OAB-PSTQ scores, a ≥7 point improvement from baseline in total score, or a ≥2 point improvement from baseline in any single domain was considered a responder.

Statistical Analysis

- Mean improvement in I-QOL total scores and all domain scores at weeks 6 and 12 was significantly greater in both the onabotulinumtoxinA 200U and 300U groups compared with placebo (P<0.001 vs placebo for all comparisons), with no clinically relevant differences between onabotulinumtoxinA doses (Figure 1).

- Significantly greater percentages of patients treated with onabotulinumtoxinA 200U and 300U reported they were somewhat or very satisfied with treatment (P<0.001), had significant progress toward or complete achievement of their primary treatment goal (P<0.001 vs placebo), and met or exceeded treatment expectations at weeks 6 and 12 compared with patients who received placebo (P<0.001 vs placebo) (Figure 4).

- Significantly greater percentages of patients receiving onabotulinumtoxinA 200U or 300U had ≥11 point increases in I-QOL total scores at weeks 6 and 12 compared with placebo (P<0.001 vs placebo) (Figure 2).

- Significant greater percentages of patients receiving onabotulinumtoxinA 200U or 300U had ≥11 point increases in I-QOL total scores at weeks 6 and 12 compared with placebo (P<0.001 vs placebo) (Figure 3).

- Percentage of patients reporting no side effects on the OAB-PSTQ at weeks 6 and 12 were high and generally similar among treatment groups (79%–73% for placebo, 84%–86% for onabotulinumtoxinA 200U, and 58%–65% for onabotulinumtoxinA 300U).

- No clinically relevant difference in efficacy was observed between the 2 doses.

CONCLUSIONS

- OnabotulinumtoxinA doses of 200U and 300U provided significant and clinically relevant improvements in QOL in patients with UI due to NDO.

- Higher proportions of onabotulinumtoxinA-treated patients were satisfied with treatment, attained their treatment goals, and reported their expectations were completely met.

- No clinically relevant difference in efficacy was observed between the 2 doses.

REFERENCES


DISCLOSURES

This study and its analyses were sponsored by Allergan, Inc., Irvine, CA, USA. Writing assistance for paper development was provided by Linda M. Wilson and Eulalia Ortega, PhD, of Evidence Scientific Solutions and was funded by Allergan, Inc. M. Chancellor, D. Sussman, G. Del Popolo, P. Po, and W. Wychowski, PhD, of Evidence Scientific Solutions and was funded by Allergan, Inc. M. Chancellor, D. Sussman, G. Del Popolo, P. Po, and W. Wychowski, PhD, of Evidence Scientific Solutions and was funded by Allergan, Inc.

The authors disclose no conflicts of interest.

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