INTRODUCTION

- The efficacy and safety of onabotulinumtoxinA (onabotA) for the treatment of moderate to severe forehead lines in subjects with upper facial lines were evaluated in the FLO-11 (Facial Lines OnabotulinumtoxinA) 116 study.
- The study was a randomized, double-blind, placebo-controlled, 16-week study with a 12-week treatment period and a 4-week follow-up period.
- The primary efficacy endpoint was the change from baseline to maximum elevation in the Subject Forehead Wrinkle Score (FWS) at the end of cycle 1 in the intent-to-treat (ITT) population.

METHODS

- **Subjects:** Included neurotoxin-naive males and females aged ≥18 years who had the following:
  - Five or more moderate to severe forehead lines (FHL) at rest
  - A maximum FWS of 3 or more

- **Randomization:** Randomized to receive onabotA 40 U (cycle 1) or 64 U (cycle 2 and 3) in a 1:1 ratio, followed by a blinded period of 4 weeks with follow-up at 3 and 4 weeks.

- **Outcome Measures:**
  - **Efficacy and Safety:** Primary endpoint was the change from baseline to maximum elevation in the FWS at week 4 in the ITT population.
  - **Secondary Efficacy:** Additional endpoints included the change from baseline to maximum elevation in the FWS at week 4 in the modified ITT (mITT) population.

- **Safety:** Treatment-emergent adverse events (TEAEs), vital signs, urine pregnancy test, and laboratory tests were assessed.

RESULTS

- **Efficacy:**
  - *Significantly better results (P < 0.05) vs placebo:*
    - Lines Outcomes Questionnaire Items 1, 4, and 5 at Day 30 (mITT population)
    - FLO-11 ratings were similar between the two treatment groups (P > 0.05)

- **Safety:**
  - No serious adverse events were reported.
  - TEAEs were generally mild and of a character expected from botulinum toxin and its injection.

ACKNOWLEDGMENTS

- The authors acknowledge the contributions of the investigators, the patients, and the families of the patients.

REFERENCES


FINANCIAL DISCLOSURES

- This study was sponsored by Allergan plc. Medical writing and editorial assistance were provided by Cactus Communications and was funded by Allergan plc. All authors meet the ICMJE criteria for authorship on this manuscript.

CONCLUSIONS

- OnabotulinumtoxinA significantly improved the appearance of FHL when treated with 40 U and 64 U successfully in the ITT and mITT populations.
- The results of this study support the use of onabotulinumtoxinA for the treatment of moderate to severe forehead lines in subjects with upper facial lines.

Safety

- Overall, TEAEs were reported in 66 (23%) of subjects (onabotA 40 U) during the double-blind period and 52 (18%) of subjects (onabotA 64 U) during the follow-up period.
- The most frequently reported TEAEs in both treatment groups were injection site reactions.
- No serious adverse events were reported.
- No clinically meaningful changes in vital signs were reported during the study.

Table 2: Additional Adverse Events Occurring in ≥15% of Subjects in All Treatment Groups

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Placebo 40 U</th>
<th>Placebo 64 U</th>
<th>OnabotA 40 U</th>
<th>OnabotA 64 U</th>
</tr>
</thead>
<tbody>
<tr>
<td>Injection area reactions</td>
<td>20.0%</td>
<td>25.0%</td>
<td>22.0%</td>
<td>18.0%</td>
</tr>
<tr>
<td>Injection site reactions</td>
<td>13.0%</td>
<td>15.0%</td>
<td>34.0%</td>
<td>30.0%</td>
</tr>
<tr>
<td>Sleep disturbances</td>
<td>12.0%</td>
<td>15.0%</td>
<td>18.0%</td>
<td>14.0%</td>
</tr>
<tr>
<td>Headache</td>
<td>2.0%</td>
<td>2.0%</td>
<td>3.0%</td>
<td>2.0%</td>
</tr>
</tbody>
</table>

Figure 1: Fornhead, Glabellar, and Crow’s Feet Lines

Figure 2: Study Design

Figure 3: Subject Demographics and Baseline Characteristics

Figure 4: Responder Archiving Investigator Facial Wrinkle Scale Ratings of Apex Mild for Forehead LineSeverity at Baseline Eyebrow Elevation (ITT population)

Figure 5: Responder Archiving Investigator Facial Wrinkle Scale Ratings of Apex Mild for Forehead LineSeverity at Baseline Eyebrow Elevation (ITT population)

Figure 6: Responder Archiving Investigator Facial Wrinkle Scale Ratings of Apex Mild for Forehead LineSeverity at Baseline Eyebrow Elevation (ITT population)

Figure 7: Patient Images at Maximum Elevation (A) and at Rest (B) Before and After Treatment With OnabotulinumtoxinA at 40 U for Moderate to Severe Forehead Lines

Figure 8: Responder Archiving Investigator Facial Wrinkle Scale Rating of Forehead Line Severity at Baseline Eyebrow Elevation (ITT population)

Figure 9: Responder Archiving Investigator Facial Wrinkle Scale Rating of Forehead Line Severity at Baseline Eyebrow Elevation (ITT population)