OnabotulinumtoxinA for Treatment of Moderate to Severe Horizontal Frontalis Lines and Glabellar Lines From the Subject’s Perspective: Patient-Reported Satisfaction and Impact Outcomes From a Phase 3 Double-Blind Study

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INTRODUCTION

The development of upper facial lines can negatively influence self-perception and may have adverse psychological impacts.1-3 Subject satisfaction with aesthetic treatment reflects successful treatment outcomes, which consequently may be associated with improved self-esteem and body image.4,5 OnabotulinumtoxinA has been used effectively and safely to treat facial lines since the early 1990s.6,7 When treating forehead lines (FHL), concurrent treatment of glabellar lines (GL) is recommended to reduce the risk of eyebrow ptosis by maintaining a balance between pretarsal and depressor muscles (including the procerus and corrugator muscles making up the glabellar complex).8,9

The safety and efficacy of onabotulinumtoxinA for treating FHL with 20 U to the frontalis muscle and 20 U to the glabellar complex was evaluated in a 12-month, phase 3 study.10

— The primary endpoint—proportion of subjects achieving ≥20-grade improvement from baseline on day 30 in investigator and subject frontal Wrinkle Score with photometric unit (FWS) scores of FHL at maximum eyebrow elevation—was met (64.9% vs onabotulinumtoxinA vs 0% vs placebo; P<0.0001).

OBJECTIVE

To present results from a 12-month, phase 3 study on the effects of onabotulinumtoxinA on patient-reported satisfaction and to assess impacts of treatment.

METHODS

Patients

— Neurotoxin-naïve males and females aged ≥18 years with both:
  — Moderate to severe FHL at maximum elevation (as assessed by both investigator and subject using the FWS on day 1 of study, before treatment)
  — Moderate to severe GL at maximum frown (as assessed by the investigator using the FWS on day 1, before treatment)

Study Design

The 12-month, phase 3 study was conducted at 9 sites in the United States, 5 in Canada, and 2 in Europe (Ireland) from October 2014 to April 2016.

The study comprised a 6-month double-blind, placebo-controlled, parallel-group treatment period (cycles 1–180) followed by a 6-month open-label treatment period (days 181–360) (Figure 1)

Eligible subjects were randomized (1:1) to receive a single treatment consisting of onabotulinumtoxinA 40 U (20 U in FHL and 20 U in GL) or placebo administered at 10 injection sites (Figure 2).

OnabotulinumtoxinA 40 U or placebo was given in 0.2 mL at each injection site.

Following the double-blind period, subjects could receive up to 2 open-label treatments with onabotulinumtoxinA using the same 10 injection sites, with all subsequent treatment cycles limited to 2.

Follow-up assessments were made at weeks 1 and 2 after each study treatment; all subjects also had follow-up visits every 30 days from study day 20 through day 360 (Figures 2, 3, and 4).

RESULTS

Patient-Reported Outcome (PRO) Measures

— Subjects completed the Facial Line Satisfaction Questionnaire (FLSQ) and the 11-item Facial Line Outcome Questionnaire (FLO-11) at baseline, on days 1, 14, and 30, then every 30 days through day 360.

— Both PRO instruments were developed, validated, and implemented in accordance with US Food and Drug Administration guidance.6

— The FLSQ (comprising 11 questions at baseline and 13 questions at follow-up) was designed to assess treatment satisfaction and appearance-related impacts associated with FHL and GL from the subject’s perspective.

— FLO-11 assesses subjects’ satisfaction with treatment of their facial lines.

— The IMPACT measures appearance-related and emotional impacts of treatment, including appearance-related age, anger, tiredness, emotional appeal, and stiffness.

— The FLSQ also assesses psychological and appearance-related impacts associated with FHL and GL from the subject’s perspective.

— FLO-11 item 4 evaluates whether subjects feel that they look older than their actual age.

Statistical Analysis

— FLSQ item 5 and Impact Domain and FLO-11 item 4 were included as key secondary endpoints as they reflect each subject’s perception of treatment effects and drive treatment decisions.

— Proportion of subjects mostly or very satisfied on FLSQ item 5 (primary time point: day 90).

— Proportion of subjects mostly or very satisfied on FLSQ Impact Domain, defined by ≥3-point improvement from baseline (primary time point: day 28).

— Proportion of subjects on FLO-11 item 4, defined by ≥3-point improvement from baseline (primary time point: day 28).

— These PROs were evaluated in the intent-to-treat (ITT) population, comprising all randomized subjects.

— Between-group comparisons were conducted using the Cochran–Mantel–Haenszel test, stratified by study site, with statistical significance achieved at P<0.05.

FLSQ Impact Domain

— The responder rate on the FLSQ Impact Domain was significantly greater with onabotulinumtoxinA than placebo on day 30 (73.9% vs 4.8%; P<0.0001) and at the primary time point for this measure on day 90 (80.7% vs 1.0%; P<0.0001) (Figure 4).

— Subject satisfaction with treatment remained significantly higher with onabotulinumtoxinA than placebo on day 30 (90.3% vs 0.7%; P<0.0001; *P<0.0001 for onabotulinumtoxinA vs placebo).

— The responder rate on the FLSQ Impact Domain was significantly greater with onabotulinumtoxinA than placebo at all time points through day 180 (P=0.002) (Figure 4).

FLSQ-11 Item 4

— The responder rate on the FLO-11 item 4 (looking older than actual age) was significantly greater with onabotulinumtoxinA than placebo on day 30 (73.9% vs 11.2%; P<0.0001) and at the primary time point for this measure on day 90 (80.7% vs 1.0%; P<0.0001) (Figure 5).

— The FLO-11 item 4 responder rate remained significantly higher with onabotulinumtoxinA than placebo at all time points through day 180 (P<0.002) (Figure 5).

FLSQ Impact Domain

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CONCLUSIONS

— Subjects were highly satisfied with onabotulinumtoxinA of FHL and GL, which reflects successful treatment in appearance-related and emotional impacts of their facial lines.

— These PRO improvements were sustained for all time points after a single treatment cycle with responder rates maintained with repeated onabotulinumtoxinA treatment.

REFERENCES


ACKNOWLEDGMENTS

This study was sponsored by Allergan plc, Dublin, Ireland. Medical writing and editorial assistance was provided by Dr. Doni Miller, PhD at the Precision Science Group, Paramus, NJ. All authors contributed equally to all aspects of this study and received payment made for authorship.

FINANCIAL DISCLOSURES

All authors disclosed no potential conflicts of interest, financial or otherwise. All authors were paid for their contributions to the study. All authors have been involved in the planning and execution of this study.

Figure 1. Study Design

Figure 2. Injection Sites for OnabotulinumtoxinA Treatment of FHL and GL

Figure 3. Subjects Mostly or Very Satisfied on FLSQ Item 5 Over the 12-Month Study

Figure 4. Responders Achieving ≥20-Point Improvement From Baseline in FLSQ Impact Domain Over the 12-Month Study (subjects with baseline scores ≥20)

Figure 5. Responders Achieving ≥3-Point Improvement From Baseline in FLSQ Impact Domain Over the 12-Month Study (subjects with baseline scores ≥3)