OnabotulinumtoxinA for Platysma Prominence at Maximum Contraction: Safety and Efficacy Results from a Phase 3 Open-Label Repeat Treatment Study

Authors: Deanne MrazMD, FAAD[1]; C. William HankeMD[2]; Ira Papel, MD[3]; Kenneth Beer, MD[4]; Steven Yoelin, MD[5]; Susan Weinkle, MD[6]; Terrence Keaney, MD[7]; Rodney Rohrich, MD[8]; Reva McCaskill, MD[9];Sandhya V. Shimoga, PhD[10];Grace S. Park, DrPH[10];Warren Tong, PharmD[10];René Hopfinger, MS[10]

Author Affiliations: [1]Modern Dermatology of Connecticut, Westport, CT, USA;[2]Laser and Skin Surgery Center of Indiana, Indianapolis, IN, USA;[3]Aesthetic Center at Woodholme, Pikesville, MD, USA;[4]Beer Dermatology, West Palm Beach, FL, USA; [5]Steven Yoelin, MD, Medical Associates, Inc. Newport Beach, CA, USA;[6]Weinkle Dermatology, Bradenton, FL, USA;[7]SkinDC, Arlington, VA, USA;[8]Dallas Plastic Surgery Institute, Dallas, TX, USA;[9]Allergan Aesthetics, an AbbVie company, Irvine, CA, USA; [10]AbbVie Inc., North Chicago, IL, USA

Writing Support: Medical writing support was provided by Rianne Campbell, PhD, of AbbVie Inc. and editorials support was provided by Angela T. Hadsell of AbbVie Inc.; both were funded by AbbVie Inc.

Funding Source: Allergan Aesthetics, an AbbVie company, funded this study and participated in the study design, research, analysis, data collection, interpretation of data, reviewing, and approval of the publication. All authors had access to relevant data and participated in the drafting, review, and approval of this publication. No honoraria or payments were made for authorship.

Authors' Conflicts of Interest Statement: Financial arrangements of the authors with companies whose products may be related to the present report are listed as declared by the authors. Deanne Mraz, C. William Hanke, Ira Papel, Kenneth Beer, Susan Weinkle, and Rodney Rohrich are investigators for Allergan Aesthetics, an AbbVie company. Terrence Keaney and Steven Yoelin are investigators, consultants, and speakers for Allergan Aesthetics, an AbbVie company. Reva McCaskill, Sandhya V. Shimoga, Grace S. Park, Warren Tong, and andRené Hopfinger are full-time employees of AbbVie and may own company stock.

Data Sharing Statement

AbbVie is committed to responsible data sharing regarding the clinical trials we sponsor. This includes access to anonymized, individual, and trial-level data (analysis data sets), as well as other information (eg, protocols, clinical study reports, or analysis plans), as long as the trials are not part of an ongoing or planned regulatory submission. This includes requests for clinical trial data for unlicensed products and indications.

These clinical trial data can be requested by any qualified researchers who engage in rigorous, independent, scientific research, and will be provided following review and approval of a research proposal, Statistical Analysis Plan (SAP), and execution of a Data Sharing Agreement(DSA). Data requests can be submitted at any time after approval in the US and Europe and after acceptance of this manuscript for publication. The data will be accessible for 12 months, with possible extensions considered. For more information on the process or to submit a request, visit the following link: https://vivli.org/ourmember/abbvie then select “Home”.

IRB approval status: This study complied with the Declaration of Helsinki, included written informed consent, and was approved by institutional review boards (Advarra IRB, Columbia, MD, USA and Advarra IRB, Aurora, ON, Canada).

ClinicalTrials.gov:NCT05134649

Patient Consent: Consent for the publication of recognizable patient photographs or other identifiable material was obtained and included at the time of article submission to the journal stating that all patients gave consent with the understanding that this information may be publicly available.

Attachments: CONSORT checklist, research protocol/statistical analysis plan, IRB approval letter, supplemental tables and figures.

Presented in part at: American Society for Dermatology Surgery (ASDS) 2024, China Dermatologist Association (CDA) 2024 Meeting.

ABSTRACT

Background: OnabotulinumtoxinA (onabotA) treatment of prominent platysma muscles demonstrates a safety profile consistent with other onabotA aesthetic indications and effectively improves the appearance of vertical neck bands and jawline definition.

Objective: To evaluate the safety and efficacy of repeatonabotA treatment for improving the appearance of moderate-to-severe platysma prominence.

Methods: Participants received up to 4 onabotA treatments administered ≥3 months apart, including treatment with onabotAor placebo in the double-blind lead-in study.

Results: All treatment-emergentAEs (TEAEs) related to study treatment were mild in severity with no observed trends across treatment cycles. Four participants reported 6 AEs of special interest, including dysphagia (4 events) and facial paresis (2 events). All were mild in severity with no evidence of distant spread of toxin; almost all resolved by the study end and none resulted in discontinuation. The percentages of participants achieving a ≥1-grade improvement at maximum contraction as assessed by clinicians on Day 14 for each treatment cycle were83.6%, 92.0%, 90.0%, and 98.0%and by participants were 82.5%, 90.4%, 87.0%, and 94.0%.

Limitations: This was an open-label study with no placebo control.

Conclusions: Repeat onabotA treatment is well-tolerated and improves platysma prominence for up to 1 year.

Keywords: onabotulinumtoxinA, platysma muscle, lower face, vertical neck bands, neck, jawline, rejuvenation, intramuscular injection, repeat treatment, safety

INTRODUCTION

Prominentplatysma muscles present as distinct vertical neck bands and a loss of jawline definition.[1–3] This condition is a normal result of aging and occurs due to repetitive platysma muscle contractions in conjunction with subcutaneous fat loss and reduced skin elasticity. The platysma is a mimetic muscle used for non-verbal communication, and with age, platysma prominence can become noticeable and bothersome during everyday activities, like smiling or speaking.[1]The appearance of prominent platysma muscles may be misinterpreted as conveying a negative emotional state (e.g., anger, aggression, disgust) which can contribute to negative psychological impacts on an individual's self-esteem and social confidence.[4,5]While surgical treatment options exist, there is growing interest in minimally invasive procedures that improve the appearance and quality of life of patients with prominent platysma muscles.[6]

OnabotulinumtoxinA (onabotA; BOTOX® Cosmetic; Allergan Aesthetics, an AbbVie company, Irvine, CA, USA) is approved to treat aesthetic indications, including most recently FDA approval for the treatment of moderate-to-severe platysma bands.[7,8]In Phase 2and 3 studies, onabotA treatment of platysma prominence demonstrated a favorable benefit-risk profile, offering a new treatment approach for this indication.[9,10]Here, we report study results evaluating the safety and efficacy ofonabotArepeat treatment in adults with moderate-to-severe platysma prominence.

METHODS

Study Design

This Phase 3, multicenter, 8-month, open-label extension (OLE; NCT05134649) study was conducted from November 2021 to August 2023 at 28 sites in the United States and Canada. This OLE study assessed the long-term safety of repeatonabotA treatment in adults with moderate-to-severe platysma prominence at maximum contraction. Eligible participants completed the double-blind, placebo-controlled (DBPC)4-month lead-in study, where they were randomized and received either a single treatment of onabotA or placebo. Full methodological details of the DBPC (NCT04949399), including randomization and blinding, have been published previously.[10] Participantscouldreceive up to 3 additional onabotA treatments(≥84 days apart) in the OLE study.The first OLE onabotA administration occurred at the Day 1 visit, which was the Day 120/study exit visit of the lead-in study. In addition to the Day 14 visit after each onabotA treatment, scheduled monthly visits (Days 30, 60, 90, 120, 150, 180, 210) occurred throughout the study exit (Day 240). Safety and efficacy data were collected from both studies, totaling up to 4 treatments during a 12-month period.

This study adhered to the guidelines and ethical principles in the Declaration of Helsinki and the International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use guidelines. Prior to study initiation, an independent ethics committee and institutional review board reviewed and approved the study protocol at each study site, and all participants provided informed consent.

Participants

Eligible participants for the lead-in study had a BMI between 18 kg/m^2 and 30 $kg/m^2$and be able to correctly and consistently contract their platysma muscles. The severity of platysma prominence was assessed on Day 1 of the DBPC study before treatment administration by the investigator and participant using the Clinician Allergan Platysma Prominence Scale (C-APPS) and the Participant Allergan Platysma Prominence Scale (P-APPS), respectively. Participants had Moderate (Grade 3) to severe (Grade 4) prominence at maximum contraction on both the left and right sides. Severity score on either side were not required to match. Eligible participants were required to be at least *somewhat bothered* on Item 2 [jawline] and Item 1 [vertical neck bands] of the Bother Assessment Scale – Platysma Prominence (BAS-PP) on Day 1 of the DBPC study.

For the OLE study, participants were reassessed on Day 1 of the studyto determine whether they metinclusion and exclusioncriteria. Exclusions include any adverse events of special interest (AESIs) related to study treatment during the DBPC period, increased medical risk after exposure to onabotA, or medical conditions that could interfere with study assessments.

Study Treatment

Trained aesthetic investigators administered onabotAas a series of superficial intramuscular injections into the platysma muscles. The onabotAdose was tailored to the severity of platysma prominence prior to each treatment (**Supplementary Figure 1).** A fixed dose of 16 U of onabotA was administered to the upper segment of the platysma muscle at the jawline below the mandibular margin as 4 injections per side (0.05 mL or 2 U per injection, approximately 1-2 cm apart). An additional 5 U was administered to each continuous vertical neck as 5 injections per band(1 or 2 bands per side, 0.025 mL or 1 U per injection, approximately 1-2 cm apart). Depending on the total number of continuous vertical neck bands (2, 3, or 4), a total dose of 26 U, 31 U, or 36 U of onabotA was administered at each treatment visit.[9,10]

Assessments

Safety of repeat onabotA treatment was monitored throughout the study viaadverse events (AEs) and vital signs. Treatment-emergent AEs (TEAE) were defined as any AE with an onset that occurs after the first dose of the study drug.The primary endpoint was the incidence of TEAEs throughout the study.

The efficacy of repeat onabotA treatment was evaluated by investigators and participants using the C-APPS and P-APPS respectively, each on a 5-point scale (1=Minimal, 2=Mild, 3=Moderate, 4=Severe, 5=Extreme). Details regarding both scales have been published previously.[5,9,10] Platysma prominence severity was assessed on the left and right sides independently at maximum contraction. Exploratory efficacy endpoints included achievement of ≥1-grade improvement from baseline on C-APPS or P-APPS. Efficacy assessments were conducted on days 14 (primary time point in DBPC study), 30, 60, 90, and 120 for Cycle 1; on days 14, 30, 60, and 90 for Cycles 2 and 3; and on days 14, 30, and 60 for cycle 4.

Standardized Photography

Standardized facial photographs (Canfield Scientific, New Jersey, USA) were taken at each treatment visits, Day 14 after treatment and scheduled monthly visits (ie, Days 30, 60, 90, 120, 150, 180, 210, 240).

Statistical Analysis

Safety and efficacy analyses considered onabotA treatment cycles from both the DBPC lead-in and OLE study. The participants who received at least 1 onabotA treatment either in the lead-in study or in OLE study were used for safety and efficacy analyses.

The number and percentage of participants experiencing at least 1 AE were used to present an overview of AEs throughout a particular treatment cycle or throughout the study. Descriptive statistics were used to summarize efficacy measures.

RESULTS

Participant Demographics

Of 408 participants from the DBPC study, 292 were enrolled in the OLE study with the majority of participants (89.7%) completing the OLE study. Among the 30 discontinued participants, the primary reason for discontinuation was withdrawal by participant (4.8%, n = 14), followed by lost to follow-up (4.1%, n = 12) **(Supplementary Figure 3)**. No participant discontinued due to an AE (0%).

A total of 350 participants in the DBPC and OLE studies received at least 1treatment of onabotA; these participants had a mean (SD)age of 49.3(9.70)years and were mostly female (94.0%), White (90.6%), and with Fitzpatrick skin types II/III (74.3%)(**Supplementary Table 1**). Baseline severity based on C-APPS assessment was severe on both sides for the majority of subjects (54%) prior to treatment cycle 1. A decreasing trend was observed over subsequent cycles, and only 37% of the participants were severe on both sides prior to treatment cycle 4 (**Supplementary Table 2**).

Safety and Tolerability

The percentage of participants experiencing any TEAEswas similar across treatment cycles (Cycle 1, 23.4%; Cycle 2,16.8%; Cycle 3,14.1%; Cycle 4, 20.4%), with 33.7% of participants reporting any TEAE throughout all onabotA treatment cycles (**Table 1**). No clinically meaningful trends in TEAEs based on age, race, or ethnicity were detected. A total of 97 participants out of 350 (27.7%)experienced a TEAE, all were mild in severity and the most common TEAEs across all onabotA treatment cycles being COVID-19 infection (8.9%).

AcrossonabotA treatment cycles, a total of 7.1% of participants reported TEAEs that were considered by the investigator to be treatment-related (**Table 2:** Cycle 1, 3.1%; Cycle 2, 4.1%; Cycle 3, 1.7%; Cycle 4, 9.3%);all were mild in severity.The most frequently reported treatment-related TEAEs were injection-site bruising (3.7%) and injection-site hemorrhage (1.7%). There was no evidence of the distant spread of toxin throughout the study.

Four participants experienced a total of 6 AESIsduring the OLE study. AESI events (1.1%)included dysphagia (0.9%) and facial paresis (0.6%), all mild in severity with 5 out of 6 events resolving spontaneously by the end of the study (**Supplementary Table 3**). Four events of mild dysphagia reported by 3 participants were described as involving either solids alone or both solids and liquids. The severity of platysma prominence for three of these participants was assessed as severe on both sides and one was assessed as moderate on both sides based on C-APPS. One participant experienced mild dysphagia in Cycles 2 and 3, while the other 2 participants experienced mild dysphagia in Cycle 2. All dysphagia events started within 3 weeks afteronabotA treatment and lasted between 2 to 71 days. Two participants experienced mild facial paresis, 1 of which reported both mild facial paresis and mild dysphagia in Cycle 2, with the facial paresis resolving after 127 days. The second participant reported mild facial paresis during Cycle 4, which was ongoing at the end of the study. Based on participant photos, both events of facial paresis manifested as asymmetrical smiles and were not present at rest. No trends were found in the percentage of participants reporting at least 1 AESI across all treatment cycles. No clinically meaningful changes from baseline in the mean vital sign values were identified.

Efficacy

The percentage of participants achieving ≥1-grade improvement at maximum contraction from baseline on Day 14 using C-APPS was 83.6%, 92.0%, 90.0%, and 98.0% and using P-APPS was 82.5%, 90.4%, 87.0%, and 94.0% at Treatment Cycle 1 through 4(**Figure 1; Supplementary Figure 2**). While efficacy peaked at day 14 of each treatment cycle, improvements in the appearance of platysma muscle prominence were still seen throughoutthe duration of each treatment cycle.

DISCUSSION

This study demonstrates that repeatonabotAtreatment, using a tailored dose based on baseline severity and precise injection technique, resulted in an acceptable safety profile consistent with other onabotA aesthetic indications. Moreover, repeatonabotA treatment led to consistent improvements in the appearance of vertical neck bands and jawline definition. These improvements were observedby both clinicians and participants.

The most common treatment-related TEAEs were mild, local, and related to the injection procedure, which was also observed in other aesthetic onabotAindications.[10–13]No new onabotA safety signals were observed during this study. This favorable safety profile can be attributed tothe dosing paradigm developed for the platysma prominence indication. A tailored dose (26, 31, or 36 U) based on platysma prominence presentation or severity, delivered at low injection volumes (0.05 and 0.025 mL) as superficial intramuscular injections with much of the dose (16 U) delivered below the jawline as opposed to the anterior neck. Precise injection technique is important to avoid adverse events as the platysma is a paper-thin muscle complex that lies just beneath the skin, with the anterior portion positioned superficial to deeper strap muscles of the neck involved in swallowing and breathing. This injection paradigm minimizes risk to these critical structures while still demonstrating efficacy across all measures.[9]

In this study, 0.9% of participants experienced dysphagia and 0.6% experienced facial paresis. These events may occur due to local toxin spread or inadvertent injections into deeper muscles, affecting muscles such as the pharyngeal muscles to cause dysphagia or reaching the depressor labii inferioris muscle, leading to asymmetrical smile or facial paresis. A good understanding of anatomy with precise injection placement is critical to preventing AEs related to the underlying muscles within the area of interest. Notably, all AESIs were mild in severity and 5 out of 6 events were resolved by the end of the study. Furthermore, one participant chose to receive additional onabotA treatment after their dysphagia was resolved. The remaining participants were not able to receive additional treatments because their AEs occurred orresolved near the end of the study. In addition,2 of the 3 participants who experienced dysphagia had possible confounding factors. One participant, with a 2-day duration of dysphagia, had Sjogren's syndrome, an autoimmune disorder known to cause swallowing issues.[15] Another participant who experienced 2 mild dysphagia events (durations of 71 days and 59 days), had a history of ankyloglossia. This medical condition, which was disclosed by the participant only after the second event, may have predisposed the patient to swallowing difficulties.[14] It is critical to highlight that these dysphagia events had no interference with the participant's daily activities. These cases emphasize the importance of careful assessment of a patient's medical history before onabotA treatment to ensure well-tolerated and favorable outcomes. Furthermore, it is important to capture detailed baseline photographs prior to onabotA treatment to ensure proper documentation for baseline facial symmetry.

Efficacy improvements were consistent across multiple treatment cycles, similar to results seen with repeat onabotA treatment for other indications.[12,16]The responder rates were determined by assessing severity at maximum contraction, when onabotA effects are most prominent.[7,17]Similar to prior studies examining onabotA treatment for platysma prominence, the peak effect foronabotA treatment in the neck occurred at Day 14 of each treatment cycle.[9,10,13]Additionally, these results illustrate that onabotA's effects in the platysma muscle last up to 3 to 4 months in each repeat treatment cycle.[10,13]These results further demonstrate that intramuscular onabotAtreatment of the platysma muscle reduces targeted muscle activity and improves the appearance of vertical neck bands and jawline definition.

There are several limitations to this study. Most participants were female and White, reducing the generalizability to broader populations. Additionally, the OLE study did not include a placebo control, as the primary focus was to assess the long-term safety of repeat onabotA treatments.[9,13,18] Lastly, the number of participants eligible to receive the fourth onabotA treatment may have been limited by the study duration and study design. Not all participants received onabotA treatment in the DBPC study and therefore, were only eligible to receive up to a maximum of 3 treatments. Participants were also required to return to Grade 3 or 4 on the C-APPS to be eligible for re-treatment, and participants were not allowed to receive treatment beyond Day 180 of the OLE study.

CONCLUSIONS

RepeatonabotA treatment demonstrated an acceptable safety profile consistent with other aesthetic indications. Tailoring onabotA treatment to the severity of a patient's prominent platysma muscle delivered an optimal benefit-risk profile; treatment was well-tolerated and effective in reducing the appearance of vertical neck bands while improving jawline definition over the course of multiple treatment cycles.

Abbreviations and Acronyms

AESI: adverse event of special interest

C-APPS: Clinician Allergan Platysma Prominence Scale

DBPC: Double-blind, placebo-controlled

ITT: intent-to-treat

OLE: Open-label extension

OnabotA: onabotulinumtoxinA

P-APPS: Participant Allergan Platysma Prominence Scale

PDSOT: possible distant spread of toxin

PP: platysma prominence

TEAE: treatment-emergent adverse event

Acknowledgments

Allergan Aesthetics, an AbbVie company, and the authors would like to thank the participants, study sites, and study investigators, as well as the employees of AbbVie Inc., including Elisabeth Lee and other team members, who were involved in this clinical trial. The design, study conduct, and financial support for the study were provided by Allergan Aesthetics, an AbbVie company. AbbVie participated in the interpretation of data, review, and approval of the publication. Medical writing support was provided by Rianne Campbell, PhD, of AbbVie Inc. and editorial support was provided by Angela T. Hadsell of AbbVie Inc.; both were funded by AbbVie Inc.

REFERENCES

1. Chen DL, Cohen JL. Botulinum Toxin-A Chemical Denervation for Platysmal Bands: Maximal Dosing Considerations. *J drugs Dermatol : JDD*. 2015;14(9):931.2. Brandt FS, Boker A. Botulinum toxin for rejuvenation of the neck. *Clin Dermatol*. 2003;21(6):513-520. doi:10.1016/j.clindermatol.2003.11.004

3. Matarasso A, Matarasso SL, Brandt FS, Bellman B. Botulinum A Exotoxin for the Management of Platysma Bands. *Plast Reconstr Surg*. 1999;103(2):645-652. doi:10.1097/00006534-199902000-00043

4. Michaud T, Gassia V, Belhaouari L. Facial dynamics and emotional expressions in facial aging treatments. *J Cosmet Dermatol*. 2015;14(1):9-21. doi:10.1111/jocd.12128

5. Garcia J, Whyte J, Gauthier M, Foster B, Foley C, Patel V. Development and Validation of Patient-Reported Outcome Measures for Platysma Prominence. Presented at: ISPOR Global Conference; 2010.

6. Matarasso A. Managing the Components of the Aging Neck From Liposuction to Submentalplasty, to Neck Lift. *Clin Plast Surg*. 2014;41(1):85-98. doi:10.1016/j.cps.2013.09.013

7. Carruthers JD, Lowe NJ, Menter MA, Gibson J, Eadie N, Group BGLIS. Double-Blind, Placebo-Controlled Study of the Safety and Efficacy of Botulinum Toxin Type A for Patients with Glabellar Lines. *Plast Reconstr Surg*. 2003;112(5):21S-30S. doi:10.1097/01.prs.0000076504.79727.62

8. An AbbViecompany. Botox Cosmetic [package insert]. Published online 2024.

9. Rohrich RJ, Bertucci V, Dayan S, et al. “Efficacy and Safety of OnabotulinumtoxinA for the Treatment of Platysma Prominence: A Randomized Phase 2 Dose-Ranging Study.” *Plast Reconstr Surg*. Published online 2024. doi:10.1097/prs.0000000000011472

10. Fabi S, Biesman B, George R, et al. 54237 Treating Platysma Prominence with OnabotulinumtoxinA: Safety and Efficacy Results from a Phase 3 Multicenter, Randomized, Double-blind, Placebo-Controlled Study. *J Am Acad Dermatol*. 2024;91(3):AB93. doi:10.1016/j.jaad.2024.07.376

11. Carruthers J, Rivkin A, Donofrio L, et al. A Multicenter, Randomized, Double-Blind, Placebo-Controlled Study to Evaluate the Efficacy and Safety of Repeated OnabotulinumtoxinA Treatments in Subjects With Crow’s Feet Lines and Glabellar Lines. *Dermatol Surg*. 2015;41(6):702-711. doi:10.1097/dss.0000000000000357

12. Moers-Carpi M, Carruthers J, Fagien S, et al. Efficacy and Safety of OnabotulinumtoxinA for Treating Crow’s Feet Lines Alone or in Combination With Glabellar Lines. *Dermatol Surg*. 2015;41(1):102-112. doi:10.1097/dss.0000000000000220

13. Shridharani SM, Ogilvie P, Couvillion M, et al. Improving Neck and Jawline Aesthetics WithOnabotulinumtoxinA by Minimizing Platysma Muscle Contraction Effects: Efficacy and Safety Results in a Phase 3 Randomized, Placebo-Controlled Study. *Aesthetic Surg J*. Published online 2024:sjae220. doi:10.1093/asj/sjae220

14. Dydyk A, Milona M, Janiszewska-Olszowska J, Wyganowska M, Grocholewicz K. Influence of Shortened Tongue Frenulum on Tongue Mobility, Speech and Occlusion. *J Clin Med*. 2023;12(23):7415. doi:10.3390/jcm12237415

15. Mathews SA, Kurien BT, Scofield RH. Oral Manifestations of Sjögren's Syndrome. *J Dent Res*. 2008;87(4):308-318. doi:10.1177/154405910808700411

16. Carruthers A, Carruthers J, Fagien S, Lei X, Kolodziejczyk J, Brin MF. Repeated OnabotulinumtoxinA Treatment of Glabellar Lines at Rest Over Three Treatment Cycles. *Dermatol Surg*. 2016;42(9):1094-1101. doi:10.1097/dss.0000000000000704

17. Harii K, Kawashima M. A Double-Blind, Randomized, Placebo-Controlled, Two-Dose Comparative Study of Botulinum Toxin Type A for Treating Glabellar Lines in Japanese Subjects. *Aesthetic Plast Surg*. 2008;32(5):724. doi:10.1007/s00266-008-9199-6

18. Fabi S, Humphrey S, Biesman B, et al. Improvement of Platysma Prominence WithOnabotulinumtoxinA: Safety and Efficacy Results From a Randomized, Double-Blinded, Placebo-Controlled Phase 3 Trial. *J Am Acad Dermatol*. Published online 2024. doi:10.1016/j.jaad.2024.10.027

TABLES

Table 1. Reported TEAEs in the safety population.

	OnabotA Cycle 1 n=350	**OnabotA Cycle 2 n=268**	**OnabotA Cycle 3 n=177**	**OnabotA Cycle 4 n=54**	**All OnabotA Cycles n=350**
Treatment-emergent adverse events (TEAE), n (%)	82 (23.4%)	45 (16.8%)	25 (14.1%)	11 (20.4)	118 (33.7%)
TEAE related to study treatment, n (%)	11 (3.1%)	11 (4.1%)	3 (1.7%)	5 (9.3%)	25 (7.1%)
Mild	11 (3.1%)	11 (4.1%)	3 (1.7%)	5 (9.3%)	25 (7.1%)
Moderate	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Severe	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
TEAE related to study procedure, n (%)	11 (3.1%)	10 (3.7%)	2 (1.1%)	5 (9.3%)	24(6.9%)
TEAE related to study drug, n (%)	3 (0.9%)	4 (1.5%)	1 (0.6%)	0 (0.0%)	7 (2.0%)
Treatment-emergent serious adverse events (TESAE), n (%)	3 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	3 (0.9%)
TESAE related to study treatment, n (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
TEAE leading to study drug	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

discontinuation, n (%)					
All deaths, n (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

OnabotA, onabotulinumtoxinA. TEAE, treatment-emergent adverse event.

Table 2. TEAEs related to study treatment.

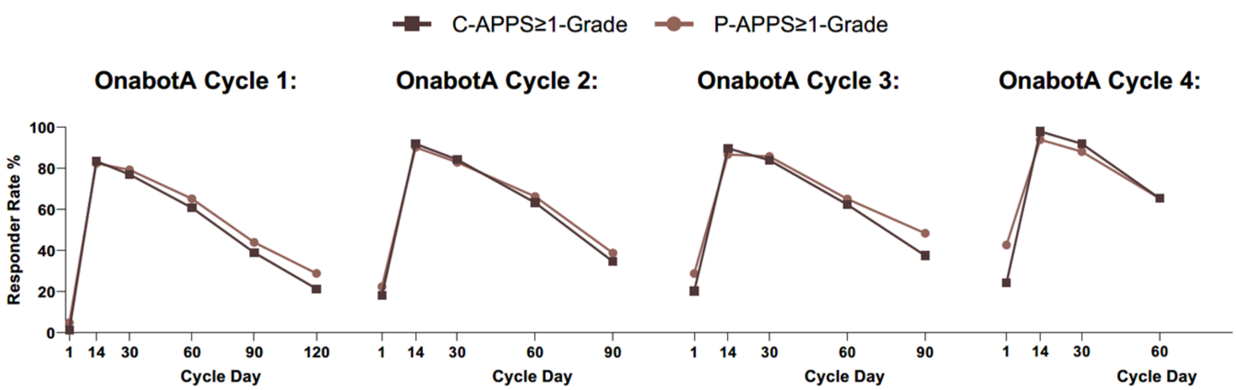
	OnabotA Cycle 1 n=350	**OnabotA Cycle 2 n=268**	**OnabotA Cycle 3 n=177**	**OnabotA Cycle 4 n=54**	**All OnabotACycles N=350**
Participants with at least 1treatment-related TEAE	11 (3.1%)	11 (4.1%)	3 (1.7%)	5 (9.3%)	25 (7.1%)
Gastrointestinal disorders	0 (0.0%)	3 (1.1%)	1 (0.6%)	0 (0.0%)	3 (0.9%)
Dysphagia	0 (0.0%)	3 (1.1%)	1 (0.6%)	0 (0.0%)	3 (0.9%)
General disorders and administration site conditions	10 (2.9%)	7 (2.6%)	2 (1.1%)	4 (7.4%)	20 (6.8%)
Injection-site bruising	4 (1.1%)	5 (1.9%)	2 (1.1%)	3 (5.6%)	13 (3.7%)
Injection-site hemorrhage	4 (1.1%)	1 (0.4%)	0 (0.0%)	1 (1.9%)	6 (1.7%)
Injection-site pain	2 (0.6%)	1 (0.4%)	0 (0.0%)	0 (0.0%)	2 (0.6%)

Injection-site swelling	0 (0.0%)	0 (0.0%)	1 (0.6%)	0 (0.0%)	1 (0.3%)
Musculoskeletal and connective tissue disorders	1 (0.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
Muscle tightness	1 (0.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
Nervous system disorders	1 (0.3%)	2 (0.7%)	0 (0.0%)	1 (1.9%)	4 (1.1%)
Facial paresis	0 (0.0%)	1 (0.4%)	0 (0.0%)	1 (1.9%)	2 (0.6%)
Dizziness	0 (0.0%)	1 (0.4%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
Headache	1 (0.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.3%)

OnabotA, onabotulinumtoxinA. TEAE, treatment-emergent adverse event.

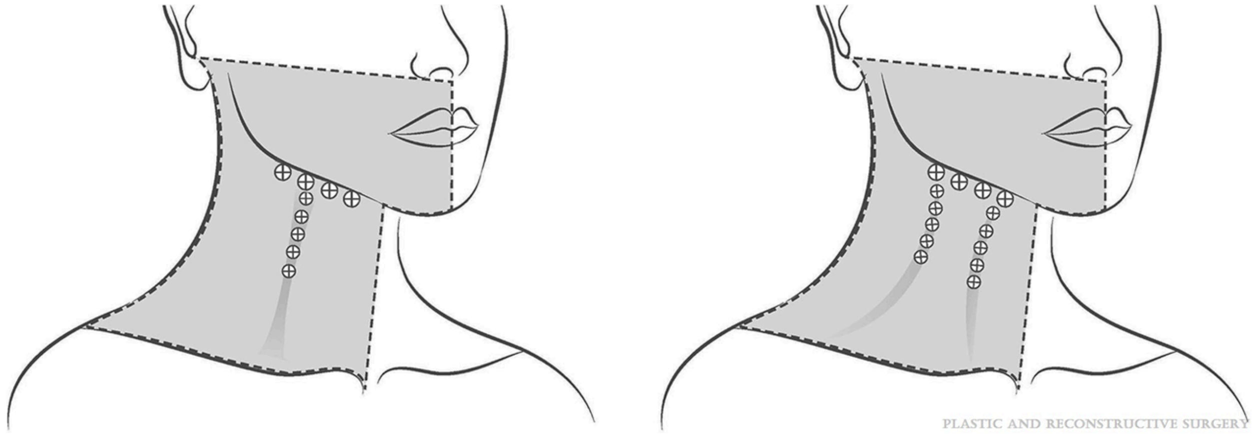
FIGURES

Figure 1. Percentage of participants that achieved $\geq$1-grade improvement from baseline based on either the investigator's assessment using the Clinician-Allergan Platysma Prominence Scale(C-APPS) or participant's self-assessment using the Participant Allergan Platysma Prominence Scale (P-APPS)at maximum contraction throughoutonabotA treatment cycles 1 through 4(intent-to-treat population).

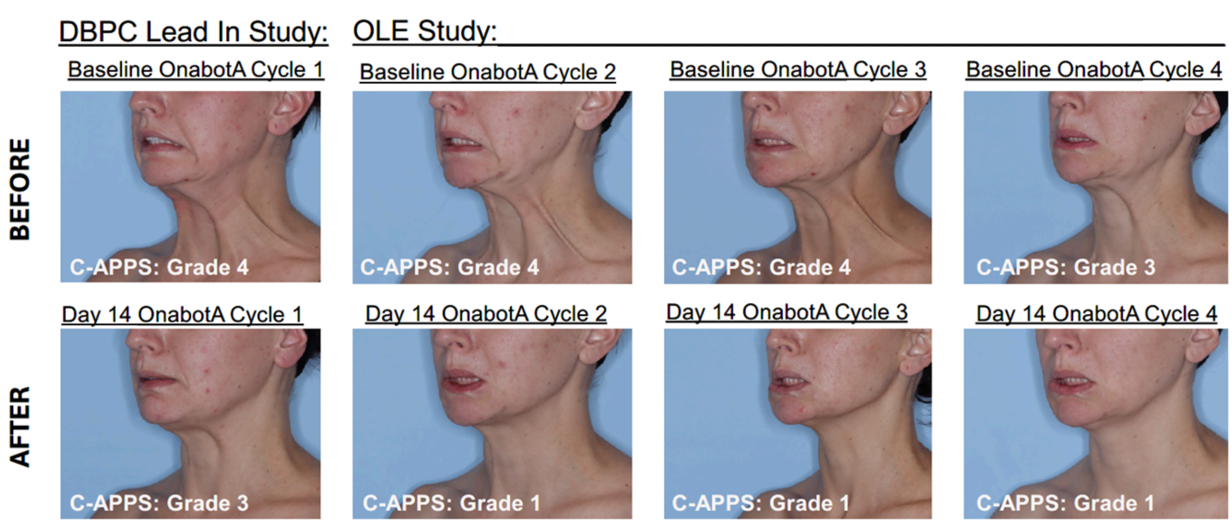


OnabotA, onabotulinumtoxinA.

Supplementary Figure 1. Injection pattern diagram. The number of bands treated per side depends on the severity of the condition. Diagram initially published by Rohrich et al.[9] Used with permission from Wolters Kluwer Health, Inc. (Waltham, MA).

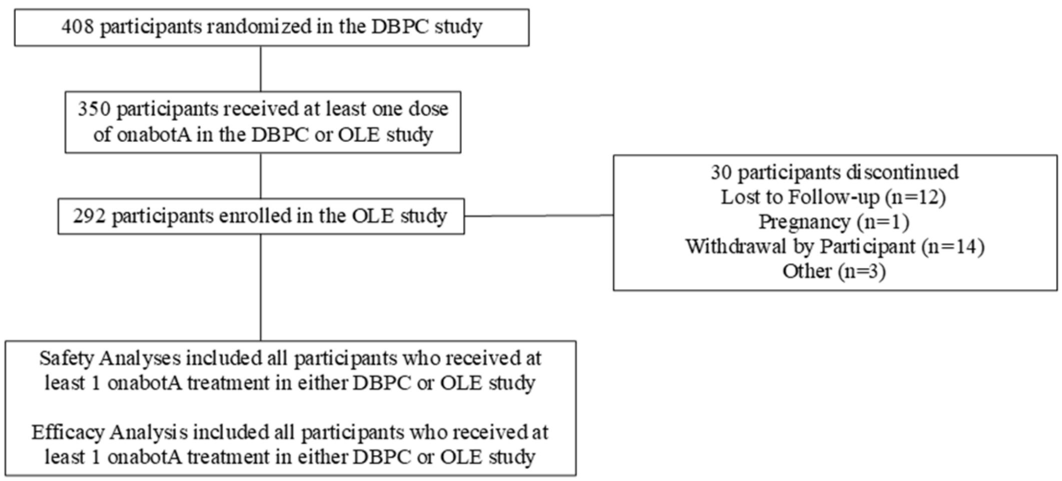


Supplementary Figure2. Representative images of a 34-year-old female participant show the improvement in platysma prominence at maximum contraction, assessed by the C-APPS scale, across 4 treatment cycles. Initially rated as Grade 4 on her left side at baseline, she improved to Grade 3 by Day 14 of Cycle 1 following onabotA treatment. At the baseline of Cycle 2, her condition returned to Grade 4, and achieved Grade 1 by Day 14. She returned to Grade 4 at baseline of Cycle 3 and improved to Grade 1 at Day 14. At the baseline of Cycle 4, she was rated as Grade 3 and achieved Grade 1 at Day 14.



DBPC, double-blind, placebo-controlled. OnabotA, onabotulinumtoxinA. C-APPS, Clinician Allergan Platysma Prominence Scale.

Supplementary Figure 3. Diagram flow of study participants. DBPC: Double-blind, placebo-controlled; OLE, open-label extension; onabotA, onabotulinumtoxinA



Supplementary Table 1. Baseline Demographics and Clinical Characteristics of Participants.

	Total **N=350**
Mean age, in years (SD)	49.3 (9.70)
Sex, n (%)	
Male	21 (6.0%)
Female	329 (94.0%)
Race, n (%)	
Asian	18 (5.1%)
Black or African American	15 (4.3%)
White	317 (90.6%)
Ethnicity, n (%)	
Hispanic	43 (12.3%)
Not Hispanic or Latino	307 (87.7%)
Fitzpatrick skin type, n (%)	
I	19 (5.4%)
II	134 (38.3%)
III	126 (36.0%)
IV	50 (14.3%)
V	13 (3.7%)
VI	8 (2.3%)

OnabotA, onabotulinumtoxinA. C-APPS, Clinician Allergan Platysma Prominence Scale. P-APPS, Participant Allergan Platysma Prominence Scale.

Supplementary Table 2. Platysma Prominence Baseline Severity Rating for Each OnabotA Treatment Cycle.

Platysma Prominence Severity Rating	**OnabotATreatment Cycle 1 Baseline (N=350)**	**OnabotA Treatment Cycle 2 Baseline (N=268)**	**OnabotA Treatment Cycle 3 Baseline (N=177)**	**OnabotA Treatment Cycle 4 Baseline (N=54)**
C-APPS at maximum contraction				
Grade 3 on both sides	72 (20.6%)	86 (32.1%)	54 (30.5%)	19 (35.2%)
Grade 3 on one side, Grade 4 on other side	85 (24.3%)	61 (22.8%)	44 (24.9%)	15 (27.8%)
Grade 4 on both sides	189 (54.0%)	113 (42.2%)	74 (41.8%)	20 (37.0%)
Others	4 (1.1%)	8 (3.0%)	5 (2.8%)	0 (0.0%)
P-APPS at maximum contraction				
Grade 3 on both sides	73 (20.9%)	81 (30.2%)	52 (29.4%)	20 (37.0%)
Grade 3 on one side, Grade 4 on the other side	91 (26.0%)	71 (26.5%)	48 (27.1%)	6 (11.1%)
Grade 4 on both sides	177 (50.6%)	93 (34.7%)	55 (31.1%)	18 (33.3%)
Others	9 (2.6%)	23 (8.6%)	22 (12.4%)	10 (18.5%)

Supplementary Table 3. Adverse Events of Special Interest.

Participant	Relevant Medical History	Dose/ Treatment cycle	Verbatim term	Onset since recent treatment	Duration (days)	Severity/ related	Outcome	Received onabotA treatment for PP after AE was resolved?
1	Sjogren's syndrome	36 U/ onabotAcycle 2	Dysphagia with solids only	Day 11 (study day 220)	2	Mild/ related	Recovered	No
2	-	36 U/ onabotAcycle 2	Dysphagia with solids and liquids	Day 3 (study day 232)	28	Mild/ related	Recovered	No
	-		Facial paresis (lower left side)	Day 3 (study day 232)	127	Mild/ related	Recovered	No
3	-	26 U/ onabotAcycle 4	Facial paresis right side	Day 5 (study day 306)	>50	Mild/ related	Ongoing at study end	No
4	Ankyloglossia	36 U/ onabotAcycle 2	Dysphagia with solids and liquids	Day 15 (study day 225)	71	Mild/ related	Recovered	Yes

		26 U/ onabotAcycle 3	Dysphagia with solids and liquids	Day 21 (study day 322)	59	Mild/ related	Recovered	No

OnabotA, onabotulinumtoxinA.PP, Platysma Prominence.