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AbobotulinumtoxinA for the Treatment of Moderate-to-Severe Glabellar Lines: A Randomized, Dose-Escalating, Double-Blind Study

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ABSTRACT

Objective: To evaluate the efficacy and safety of AbobotulinumtoxinA (ABO) dose escalation in the correction of moderate-to-severe glabellar lines.

Design: Phase 2, 36-week, multicenter, randomized, dose-ranging, double-blind, placebo-controlled study.

Methods: Adults with moderate-to-severe glabellar lines received a single ABO treatment, dosed at 50, 75, 100, or 125 U, or placebo. Primary endpoint was week 4 composite ≥2-grade responder rate among those achieving a severity score of 0 (none) or 1 (mild) at maximum frown, evaluated using concurrent investigator and subject assessments. Secondary endpoints included ≥1-grade severity improvement, duration of effect, and reporting of treatment-emergent adverse events (TEAEs).

Results: Overall, 399 subjects were included (88.2% were female). Week 4 composite ≥2-grade ABO responder rate was 80.0% (50 U), 88.8% (75 U), 90.0% (100 U) and 95.1% (125 U), versus 2.6% with placebo ($P<0.001$). Responder rate (≥1-grade) ranged between 53% (50 U) and 69% (125 U) at week 24 and between 18% (50 U) and 31% (125 U) at week 36. Median time (weeks) to return to baseline severity/worse, among those scoring 0 (none) or 1 (mild), was 32.3 (50 U), 34.3 (75 U), 36.0 (100 U) and 36.6 (125 U), versus 23.7 (placebo). ABO-related TEAEs were reported in 4% of subjects (80% were mild). No seroconversion to ABO neutralizing antibodies was seen.

Conclusion: A single ABO treatment provided rapid and effective improvements in glabellar line severity at all doses. Higher doses tended to demonstrate elevated response rates and longer duration of effect. All ABO doses were well-tolerated with low TEAE incidence.

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INTRODUCTION

Botulinum toxin type A treatment remains a cornerstone of facial aesthetic treatments.[1,2] AbobotulinumtoxinA (ABO) has demonstrated efficacy, safety and subject satisfaction in the treatment of facial lines in randomized trials and real-world observational studies.[3-6] ABO is available as Dysport® in the United States and Azzalure® in Europe (Ipsen Biopharm Limited, UK).[7,8] The 50 Speywood unit (50 U) dose, currently licensed for correction of moderate-to-severe glabellar lines, has been shown to effectively reduce glabellar line severity for durations extending to 5 months.[7-11] However, data suggest that higher doses of botulinum neurotoxin type-A products may lengthen treatment effect, without impacting safety.[2,12,13] Joseph et al 2016 demonstrated that a single ABO 120 U treatment provided a prolonged treatment effect, compared with the 50 U

dose.[12] Investigator assessments revealed median duration of response to be 150 days (21.4 weeks) overall and 165 days (23.6 weeks) when treating moderate glabellar lines.[12] Respective investigator and subject assessments showed that 61.9% and 66.7% maintained ≥1-grade improvements from baseline at day 150.[12] However, subject numbers were small (n=30) and further studies are required to establish the influence of ABO dosing on longevity of aesthetic effect.[12]

The evolving evidence base for ABO may support individualized approaches to treatment, based on specific requirements (eg, facial anatomy, muscle activity pattern, muscle mass).[13,14] The current study aimed to examine the impact of increasing dose on the efficacy, safety and durability of a single ABO treatment for the correction of moderate-to-severe glabellar lines.

MATERIALS AND METHODS

Study Design

A 36-week, Phase 2, multicenter, randomized, dose-ranging, double-blind, placebo-controlled study was conducted at 10 centers across the United States between November 2018 and July 2020 (NCT03736928). The study complied with the principles of the Declaration of Helsinki (1964) and subsequent amendments and the International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use Good Clinical Practice (GCP). Subjects provided written informed consent. Ethical approval was obtained from relevant institutional review boards (IRBs).

Study Population

Males/females (aged 18–65 years) were included with moderate-to-severe glabellar lines, assessed at maximum frown using the investigator live assessment (ILA) photographic scale and the subject self-assessment (SSA) static categorical scale. Both scales used a 4-point grading system: 0 (none), 1 (mild), 2 (moderate), and 3 (severe).

Subjects were excluded if they had received prior facial treatment with botulinum toxin (within 9 months), had a history of facial surgery or aesthetic procedures, or known allergy to any component of study product or to cow's milk protein. Other exclusion criteria included history or presence of eyelid or eyebrow ptosis, amblyopia, cancerous/pre-cancerous lesions or radiation in the glabellar region, facial nerve palsy, and the presence of inflammation, active infection, or skin disorder near to or in the glabellar region. Women who were pregnant, planning a pregnancy, or breastfeeding could not enroll.

Study Treatment

Study vials containing ABO 300 U or placebo lyophilized powder were reconstituted with 1.5, 1.0, 0.75, or 0.60 mL of preservative-free NaCl 0.9% for injection, corresponding to four ABO doses: 50 U (10 U/0.05 mL injection), 75 U (15 U/0.05 mL injection), 100 U (20 U/0.05 mL injection), or 125 U (25 U/0.05 mL injection). At baseline (day 0), subjects were randomized (4:1) to receive either ABO or placebo, given as a 0.25 mL total volume (0.05 mL per injection site) at 5 pre-specified sites in the glabellar region; 2 in each corrugator muscle and 1 in the procerus muscle. Stepwise enrollment was applied for the two highest doses. Subjects were assessed post-treatment at day 2, week 1, and week 2, and then monthly at week 4 through week 36.

Primary Efficacy Endpoint

Primary endpoint was week 4 composite ≥2-grade responder rate. Responders were defined as those achieving a glabellar line severity score of 0 (none) or 1 (mild) and at least a 2-grade improvement from baseline at maximum frown on both the ILA and SSA scales concurrently.

Secondary Efficacy Endpoints

Secondary efficacy endpoints, evaluated at maximum frown during all post-treatment visits, comprised responder rate among subjects achieving a score of 0 (none) or 1 (mild) (assessed on ILA and SSA scales individually), and responder rate for subjects with ≥1-grade improvement from baseline (ILA scale only). Subject diary cards reported time to onset of treatment effect (days 1–7). Duration of response was assessed at maximum frown for those achieving scores of 0 (none) or 1 (mild) (ILA and SSA scales concomitantly) and reported as the time to loss of 0 (none) or 1 (mild) score and the time taken to return to baseline score/worse. Participants also completed the subject satisfaction questionnaire.

Safety Endpoints

Treatment-emergent adverse events (TEAEs) were reported. Blood samples were taken at baseline (prior to treatment) and at week 36 or in cases of early termination from the study and were tested for the presence of neutralizing antibodies against ABO.

Statistical Analysis

Statistical analyses were performed using the SAS® system (Version 9.4) and compared responder rate data at all study visits from ABO-treated groups against placebo group data, with *P* values calculated using Fisher's Exact Tests and exact confidence intervals using the Chan and Zhang method. The study was not powered to examine statistical differences in efficacy between ABO doses. Confidence intervals (CI) were 2-tailed and constructed at a confidence level of 95%. Primary and secondary efficacy variables were analyzed using the intent-to-treat (ITT) population; all subjects randomized and treated with study product. Kaplan-Meier methods were used to evaluate time to onset and duration of treatment effect. The safety population was identical to the ITT population.

TABLE 1.

Baseline Demographics and Characteristics (ITT Population)						
	AbobotulinumtoxinA					
	Placebo (N=78)	50 U (N=80)	75 U (N=80)	100 U (N=80)	125 U (N=81)	Total (N=399)
Age (years)						
Mean (SD)	47.6 (11.50)	49.4 (9.54)	50.2 (10.33)	46.3 (11.52)	48.4 (10.22)	48.4 (10.68)
Range	25–65	22–65	25–64	22–65	23–65	22–65
Gender, n (%)						
Female	68 (87.2)	72 (90.0)	71 (88.8)	68 (85.0)	73 (90.1)	352 (88.2)
Male	10 (12.8)	8 (10.0)	9 (11.3)	12 (15.0)	8 (9.9)	47 (11.8)
Race, n (%)						
American Indian/ Alaska Native	1 (1.3)	0	0	0	0	1 (0.3)
Asian	1 (1.3)	0	2 (2.5)	0	5 (6.2)	8 (2.0)
Black/African American	4 (5.1)	4 (5.0)	7 (8.8)	5 (6.3)	6 (7.4)	26 (6.5)
Native Hawaiian/Other Pacific Islander	0	1 (1.3)	1 (1.3)	0	2 (2.5)	4 (1.0)
White	71 (91.0)	72 (90.0)	67 (83.8)	72 (90.0)	66 (81.5)	348 (87.2)
Other	1 (1.3)	2 (2.5)	2 (2.5)	3 (3.8)	1 (1.2)	9 (2.3)
Multiple	0	1 (1.3)	1 (1.3)	0	1 (1.2)	3 (0.8)
Ethnicity, n (%)						
Not Hispanic or Latino	56 (71.8)	55 (68.8)	61 (76.3)	58 (72.5)	61 (75.3)	291 (72.9)
Hispanic or Latino	22 (28.2)	25 (31.3)	19 (23.8)	22 (27.5)	20 (24.7)	108 (27.1)
Fitzpatrick Skin Type score, n (%)						
I	5 (6.4)	1 (1.3)	0	1 (1.3)	0	7 (1.8)
II	17 (21.8)	27 (33.8)	21 (26.3)	21 (26.3)	20 (24.7)	106 (26.6)
III	33 (42.3)	32 (40.0)	33 (41.3)	28 (35.0)	28 (34.6)	154 (38.6)
IV	19 (24.4)	14 (17.5)	12 (15.0)	21 (26.3)	19 (23.5)	85 (21.3)
V	0	4 (5.0)	8 (10.0)	4 (5.0)	8 (9.9)	24 (6.0)
VI	4 (5.1)	2 (2.5)	6 (7.5)	5 (6.3)	6 (7.4)	23 (5.8)
Baseline ILA at maximum frown, n (%)						
Moderate	24 (30.8)	32 (40.0)	28 (35.0)	22 (27.5)	22 (27.2)	128 (32.1)
Severe	54 (69.2)	48 (60.0)	52 (65.0)	58 (72.5)	59 (72.8)	271 (67.9)
Baseline SSA at max. frown, n (%)						
Moderate	23 (29.5)	24 (30.0)	18 (22.5)	22 (27.5)	26 (32.1)	113 (28.3)
Severe	55 (70.5)	56 (70.0)	62 (77.5)	58 (72.5)	55 (67.9)	286 (71.7)

Abbreviations: IIT, intention to treat; ILA, investigator live assessment; SSA, subject self-assessment; SD, standard deviation

RESULTS

Study Population

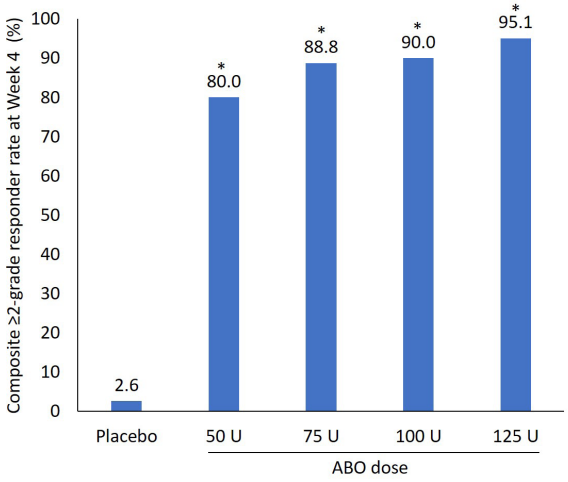
In total, 401 subjects were randomized and 399 received ABO or placebo. Each of the ABO 50, 75 and 100 U groups included 80 subjects, 81 received the ABO 125 U dose, and 78 were given placebo. Overall, 369 (92.0%) randomized subjects completed the study. One subject withdrew due to concerns relating to the COVID-19 pandemic, 14 discontinued prematurely for other reasons and 15 individuals were lost to follow-up.

Table 1 shows baseline demographics and characteristics. Most subjects were female (88.2%) and White (87.2%). Mean (standard deviation [SD]) age was 48.4 (10.68) years (range, 22–65 years). The majority had severe glabellar lines when assessed using ILA (67.9%) and SSA (71.7%) scales.

Primary Endpoint

Week 4 composite ≥2-grade responder rate with ABO 50, 75,

FIGURE 1. Composite ≥2-grade responder rate at week 4 after administration of ABO or placebo (ITT population).



*P<0.001 versus placebo for all ABO doses. Composite responder defined as subject achieving a glabellar line severity score of 0 or 1 and ≥2-grade improvement from baseline on both ILA and SSA scales concurrently. Abbreviations: ABO, AbobotulinumtoxinA; ITT, intention to treat; ILA, investigator live assessment; SSA,subject self-assessment.

100 and 125 U treatment was 80.0%, 88.8%, 90.0% and 95.1%, respectively, versus 2.6% with placebo (P<0.001; Figure 1).

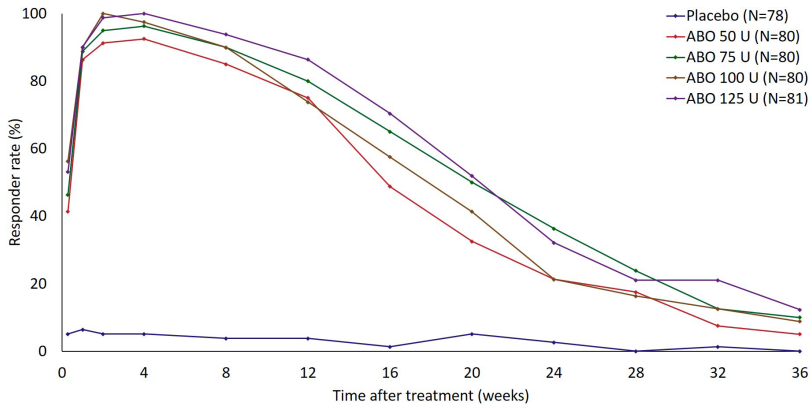
Secondary Efficacy Endpoints

Figure 2A shows the ILA responder rate at all post-treatment visits for subjects scoring 0 (none) or 1 (mild) at maximum frown. Respective day 2 responder rates with ABO 50, 75, 100, and 125 U were 41.3%, 46.3%, 56.3%, and 53.1%, versus 5.1% with placebo (P<0.001). Week 4 ABO responder rates with ABO 50, 75, 100, and 125 U were 92.5%, 96.3%, 97.5%, and 100%, respectively, versus 5.1% with placebo (P<0.001). Week 24 respective responder rates with ABO 50, 75, 100, and 125 U were 21.3%, 36.3%, 21.3%, and 32.1%, versus 2.6% with placebo (P<0.001). Respective week 36 responder rates with ABO 50, 75, 100 and 125 U were 5.0% (P=0.120), 10.0% (P=0.007), 8.8% (P=0.014), and 12.3% (P=0.001), versus 0 with placebo. Similar results were reported for SSA scale assessments (Figure 2B).

Figure 3 shows ILA responder rates for subjects achieving ≥1-grade improvement from baseline. Respective day 2

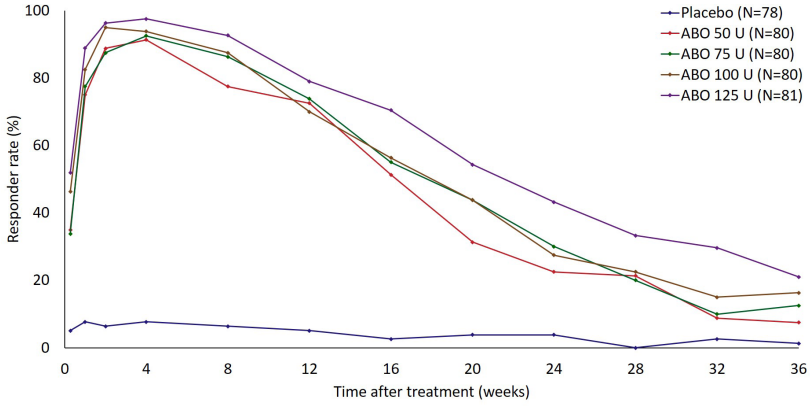
FIGURE 2. Responder rate among subjects achieving glabellar line severity scores of 0 (none) or 1 (mild) at maximum frown (ITT population). (A) ILA 4-point photographic scale (B) SSA 4-point categorical scale.

(A)



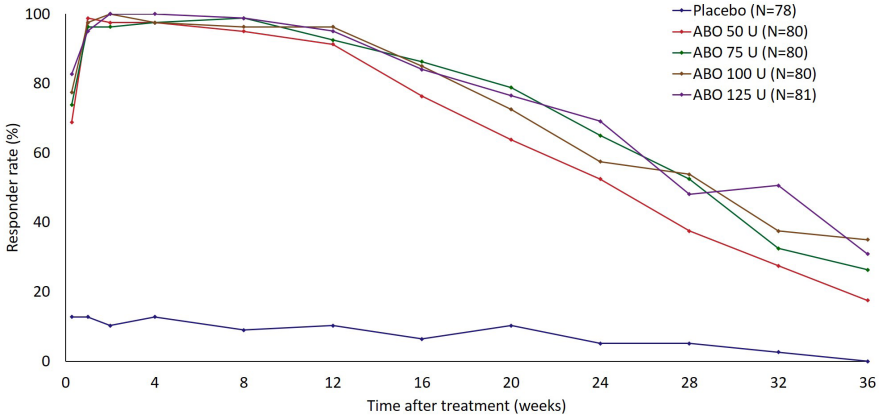
Statistically significant responder rate (none [0] or mild [1]) versus placebo through week 28 with ABO 50 U (P<0.001) and through week 36 with ABO 75 U (P=0.007), 100 U (P=0.014) and 125 U (P=0.001). Responder defined as a subject achieving a glabellar line severity score of 0 or 1 from baseline on the ILA scale. Post-treatment study visits were conducted on day 2, week 1, week 2, week 4, week 8, week 12, week 16, week 20, week 24, week 28, week 32 and week 36. Abbreviations: ABO, AbobotulinumtoxinA; ITT, intention to treat; ILA, investigator live assessment.

(B)



Statistically significant responder rate (none [0] or mild [1]) versus placebo through week 28 with ABO 50 U (P<0.001) and through week 36 with ABO 75 U (P=0.009), 100 U (P=0.001) and 125 U (P<0.001). Responder defined as a subject achieving a glabellar line severity score of 0 or 1 from baseline on the SSA scale. Post-treatment study visits were conducted on day 2, week 1, week 2, week 4, week 8, week 12, week 16, week 20, week 24, week 28, week 32 and week 36. Abbreviations: ABO, AbobotulinumtoxinA; ITT, intention to treat; SSA, subject self-assessment.

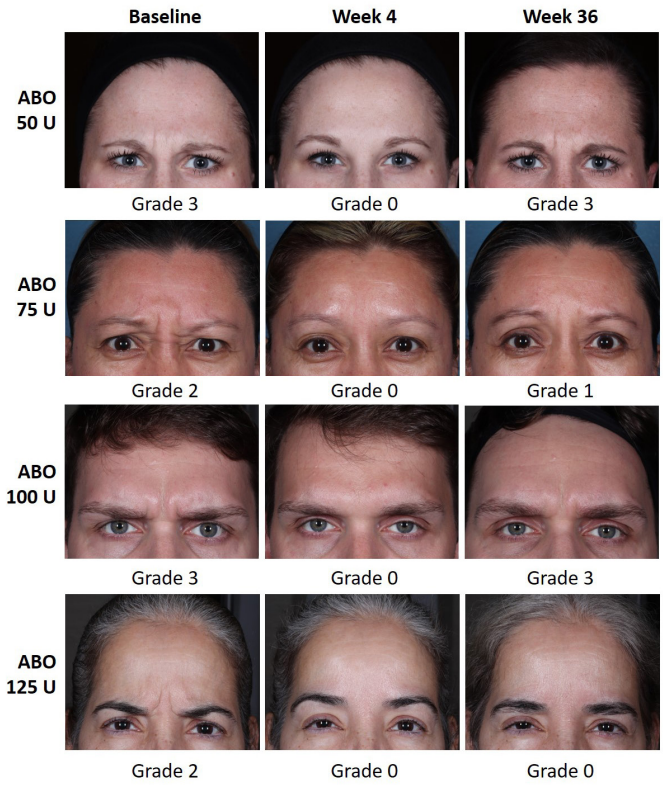
FIGURE 3. Responder rate among subjects achieving ≥1 grade improvement in glabellar line severity score at maximum frown. ILA 4-point photographic scale assessment (ITT population).



P<0.05 versus placebo for all ABO doses through Week 36. Responder defined as a subject achieving an improvement in glabellar line severity score of ≥1 grade from baseline on the ILA scale. Post-treatment study visits were conducted on day 2, week 1, week 2, week 4, week 8, week 12, week 16, week 20, week 24, week 28, week 32 and week 36. Abbreviations: ABO, AbobotulinumtoxinA; ITT, intention to treat; ILA, investigator live assessment.

responder rates with ABO 50, 75, 100, and 125 U were 68.8%, 73.8%, 77.5% and 82.7%, versus 12.8% with placebo (*P*<0.001). Week 4 respective responder rates with ABO 50, 75, 100 U were all 97.5%, and 100% with 125 U, versus 12.8% with placebo (*P*<0.001). Week 24 responder rates with ABO 50, 75, 100, and 125 U were 52.5%, 65.0%, 57.5%, and 69.1%, respectively, versus 5.1% with placebo (*P*<0.001). Respective week 36 responder rates with ABO 50, 75, 100, and 125 U were 17.5%, 26.3%, 35.0%, and 30.9%, versus 0 responders with placebo (*P*<0.001). Figure 4 shows photographic results at baseline, week 4, and week 36, assessed using the ILA scale.

FIGURE 4. ILA scale photographic assessment at maximum frown at baseline, week 4 and week 36.



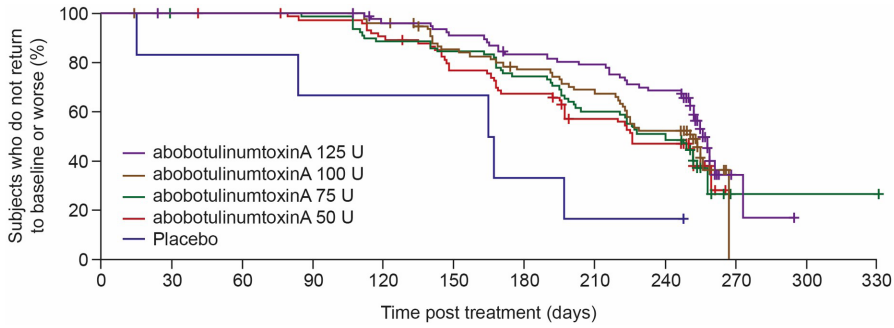
Abbreviations: ABO, AbobotulinumtoxinA; ILA, investigator live assessment.

Median time to onset of ABO treatment effect was 2 days, regardless of dose. Onset of ABO treatment effect was reported at day 1 for 25.6% (50 U), 35.4% (75 U), 30.0% (100 U) and 41.3% (125 U), versus 8.0% with placebo.

The median time (weeks) to loss of 0 (none) or 1 (mild) score (ILA and SSA scales concurrently) with ABO 50, 75, 100 and, 125 U was 20.7, 24.0, 23.3 and 27.4, respectively, versus 17.8 with placebo. For the same subjects, the median time (weeks) for the glabellar line severity score to return to baseline/worse with ABO 50, 75, 100 and 125 U was 32.3, 34.3, 36.0, and 36.6, respectively, versus 23.7 with placebo (Figure 5). For those achieving a score of 0 (none) or 1 (mild) on the ILA scale, median time (weeks) to return to baseline score with ABO 50, 75, 100 and 125 U was 27.4, 30.3, 31.9, and 35.9, versus 13.7 with placebo. For those achieving a score of 0 (none) or 1 (mild) on the SSA scale, respective median time (weeks) to return to baseline severity score with ABO 50, 75, 100, and 125 U was 28.1, 31.9, 31.6, and 35.9, versus 16.0 with placebo.

Subject satisfaction questionnaires reported natural-looking results in each ABO group at week 4 (>97%), week 24 (>95%), and week 36 (>89%). Most were satisfied/very satisfied with their appearance at week 4 (>94%), week 24 (>83%), and week 36 (>67%), regardless of ABO dose. ABO-treated subjects were satisfied/very satisfied with aesthetic outcomes in the treatment area at week 4 (>98%), week 24 (>81%), and week 26 (>67%).

FIGURE 5. Kaplan-Meier plot showing time to return to baseline glabellar line scores/worse on ILA and SSA scales concurrently for subjects achieving a score of 0 (none) or 1 (mild) (ITT population).



Abbreviations: ITT, intention to treat; ILA, investigator live assessment; SSA, subject self-assessment.

ABO-treated subjects reported feeling better/much better about themselves at week 4 (>75%), week 24 (>61%), and week 36 (>39%). Irrespective of ABO dose, most subjects (>91%) wanted to receive the same treatment again at week 36 and indicated that they would recommend the treatment to family/friends.

Safety Endpoints

Overall, 87 TEAEs were reported by 61 ABO-treated subjects. Ten individuals receiving placebo reported 14 TEAEs during the study. Fifteen TEAEs, reported by 13 (4%) ABO-treated subjects and one (1.3%) placebo group participant were related to treatment (Table 2). Most treatment-related TEAEs (80%) were mild, with the remainder being of moderate severity. With the exception of one event (mild dry eye), all treatment-related TEAEs resolved during the study. The most common ABO-related TEAEs were mild headache (1.2%) and eyelid ptosis (1.2%). One subject had mild ptosis in each of the 75 U and 125 U groups, and two subjects had moderate ptosis in the 100 U group (Table 2). All ptosis cases occurred during the first 16 days post-treatment, and all events resolved (median duration: 75 days). No treatment-related TEAEs were reported to be serious and none resulted in premature study discontinuation. There were no incidents of seroconversion to ABO neutralizing antibodies during the study.

TABLE 2.

Summary of Reported Related Treatment-Emergent Adverse Events (Safety Population)

System Organ Class Preferred Term	AbobotulinumtoxinA					
	Placebo (N=78) n (%)	50 U (N=80) n (%)	75 U (N=80) n (%)	100 U (N=80) n (%)	125 U (N=81) n (%)	Total ABO (N=321) n (%)
Subjects with ≥1 related TEAE*	1 (1.3)	3 (3.8)	2 (2.5)	5 (6.3)	3 (3.7)	13 (4.0)
Eye disorders	0	1 (1.3)	1 (1.3)	2 (2.5)	1 (1.2)	5 (1.6)
Eyelid ptosis	0	0	1 (1.3)	2 (2.5)	1 (1.2)	4 (1.2)
Dry eye	0	1 (1.3)	0	0	0	1 (0.3)
Gastrointestinal disorders	0	0	0	0	1 (1.2)	1 (0.3)
Nausea	0	0	0	0	1 (1.2)	1 (0.3)
General disorders and administration site conditions	0	1 (1.3)	0	1 (1.3)	0	2 (0.6)
Injection site bruising	0	1 (1.3)	0	0	0	1 (0.3)
Injection site hematoma	0	0	0	1 (1.3)	0	1 (0.3)
Injection site swelling	0	0	0	1 (1.3)	0	1 (0.3)
Nervous system disorders	1 (1.3)	1 (1.3)	1 (1.3)	2 (2.5)	1 (1.2)	5 (1.6)
Headache	1 (1.3)	1 (1.3)	1 (1.3)	1 (1.3)	1 (1.2)	4 (1.2)
Migraine	0	0	0	1 (1.3)	0	1 (0.3)
Skin and subcutaneous tissue disorders	0	1 (1.3)	0	0	0	1 (0.3)
Ecchymosis	0	1 (1.3)	0	0	0	1 (0.3)

*TEAE onset occurring on/after study treatment date. A subject reporting ≥1 event per category was counted once in that category.
Abbreviations: TEAE, treatment-emergent adverse event; ABO, AbobotulinumtoxinA

DISCUSSION

A single ABO treatment provided rapid and high composite responder rates when administered at doses ranging between 50–125 U for moderate-to-severe glabellar lines. Line severity was reduced to grade 0 (none) or 1 (mild) for all responders. Although the study was not powered to examine statistical differences between ABO doses, there was a tendency toward higher response rates and longer duration of aesthetic effect over approximately 6 and 9 months with dose escalation. Incidence of TEAEs was consistently low across all ABO doses and comparable with previous studies examining the safety of the licensed dose.[2-6,16-19] Subject satisfaction was high for all ABO doses, with natural looking results reported alongside a desire to receive repeat treatment.

Week 4 composite ≥2-grade responder data showed statistically significant improvements in glabellar line severity versus placebo (P<0.001), irrespective of the ABO dose given. All ABO groups achieved week 4 composite ≥2-grade responder rates ≥80%, with rates reaching 95% with ABO 125 U. These data reflect previous studies examining the safety and efficacy of variable ABO dosing and support the case for further investigations exploring individualization of treatment according to specific client requirements/characteristics (eg, muscle mass, sex).[10,14,15,19,20]

Median time to onset of treatment effect was 2 days for all ABO doses and most subjects (69–83%) achieved ≥1-grade improvement from baseline at day 2 (ILA scale), comparing favorably with previous data.[16-19] As highlighted in other studies, recipients can observe benefits with ABO treatment from 24 hours.[16,19] Onset of ABO treatment effect at day 1 ranged between 26% (50 U) and 41% (125 U), suggesting that the higher dose may provide more rapid effect.

Single ABO treatments generally provide visible glabellar line improvements for approximately 4–5 months, but emerging data suggest that elevated doses of botulinum toxin extend the duration of effect.[9-12,21] Hypotheses based on non-clinical data infer that efficacy duration is conferred by the neurotoxin light chain, with degradation taking longer where higher quantities are present.[11,22] Our results indicate that ABO doses up to 125 U can prolong treatment durability in practice as approximately one-third maintained improvements of ≥1-grade from baseline at week 36 (approximately 9 months). For those achieving a score of 0 (none) or 1 (mild), the median time taken to return to baseline severity ranged between 27 (50 U) and 36 (125 U) weeks for investigator assessments, and 28 (50 U) to 36 (125 U) weeks with subject self-assessments. Although direct comparisons between toxin treatments are not possible, these data suggest that treatment potency and duration may be enhanced with relatively conservative increases in ABO dosing, while greater magnitudes of dose escalation have been required to achieve similar results with other toxins.[21] ABO treatment satisfaction remained high through week 36 (approximately 9 months); beyond previously reported expectations for a single treatment (≤6 months post-injection).[23] The ability to extend treatment efficacy without impacting safety could influence the frequency of repeat treatments required over time.

All ABO doses were generally well tolerated. Treatment-related TEAEs were mild to moderate in intensity and had resolved at the end of the study period. No serious treatment-related TEAEs were reported and there were no incidences of remote spread of toxin effect recorded during the study.

CONCLUSION

A single ABO treatment, administered at doses ranging from 50–125 U, provided rapid and effective improvements in glabellar line severity. Higher ABO doses tended to provide increased response rates and longer duration of aesthetic effect over a 36-week period. All ABO doses were well-tolerated with low incidence of TEAEs and high levels of subject satisfaction.

DISCLOSURES

Dr. Joseph is an investigator and paid speaker for Galderma. Dr. Moradi is a paid consultant and clinical trial investigator for Galderma. Dr. Lorenc is an investigator for Galderma. Dr. Coleman is an investigator for Galderma. Dr. Ablon is an investigator for Galderma. Dr. Kaufman-Janette is a paid advisory board consultant and clinical trial investigator for Galderma. Dr. Cox is an investigator and paid advisory board member for Galderma. Dr. Campbell is an investigator for Galderma. Dr. Dayan is a paid consultant and speaker for Galderma and research support for Galderma. Dr. Berg is an employee of Galderma. Dr. Munavalli is an investigator for Galderma.

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