TWO ON-LABEL INJECTION VOLUMES OF ABOBOTULINUMTOXINA (ABO) PRODUCE SIMILAR SAFETY AND EFFICACY RESULTS WHEN USED TO TREAT MODERATE TO SEVERE GLABELLAR LINES

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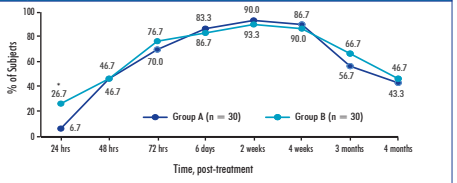
INTRODUCTION

- Two injection volumes (0.05 mL and 0.08 mL) of Dysport® (abobotulinumtoxinA [ABO]; manufactured by Ipsen Biopharm Ltd, Wrexham, UK), reconstituted in either 1.5 mL or 2.5 mL of sterile preservative-free 0.9% sodium chloride for injection USP, respectively, are approved for the treatment of glabellar lines (GLs)[1]
- Even though both injection volumes are approved for reconstitution in the US label, many injectors tend to believe that with the higher dilution volumes of neurotoxins, the greater risk of toxin spread or other unwanted safety issues[2]
- This study aimed to show both injection volumes result in similar efficacy and safety profiles

Figure 1. Representative Photographs - Subject 138-003

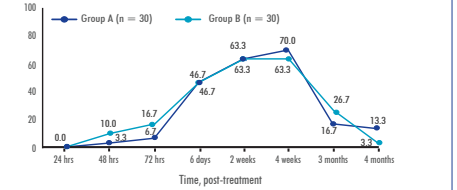
Figure 2. Proportion of Composite Responders

2a) Proportion of composite responders with at least a 1-point reduction from baseline in GLSS, maximum frown (n = 60); mITT Population



Group A (1.5 mL) – 0.05 mL/injection; Group B (2.5 mL) – 0.08 mL/injection; *P=.0377, Group A compared to Group B; Composite Responders = based on combined subject and blinded evaluator assessments; mITT = modified intent to treat

2b) Proportion of composite responders with at least a 2-point reduction from baseline in GLSS, maximum frown (n = 60); mITT Population



Group A (1.5 mL) – 0.05 mL/injection; Group B (2.5 mL) – 0.08 mL/injection; Composite Responders = based on combined subject and blinded evaluator assessments; mITT = modified intent to treat

SUBJECTS and METHODS

Subject Selection and Methods

- This 120 day, multi-center, randomized, subject- and evaluator-blinded study enrolled subjects with moderate Glabellar Line Severity Scores (GLSS=2) to severe (GLSS=3) who were naïve to botulinum toxin treatment in the facial area
- Subjects were randomized (by age, gender, blinded evaluator GLSS) to receive either 0.05 mL/injection (Group A) or 0.08 mL/injection (Group B). Subjects received 1 treatment which consisted of 5 injections in the glabellar area. Each subject received a total of 50 U (10 U/injection site) of ABO.

Primary Efficacy Endpoint

- The proportion of composite responders (defined as subjects who achieved at least a 1-point reduction from baseline in the GLSS at maximum frown, based on the combined blinded evaluator and subject assessments), at 30 days post-treatment using a validated 4-point photographic scale[3] for evaluators and a static 4-point categorical scale for subjects

Secondary Endpoints

- Subject and blinded evaluator assessment for Onset of Effect (OOE) at all time points
- The proportion of ≥1-point and ≥ 2-point composite responders at each study visit, by evaluating the GLSS change from baseline (subject, blinded evaluator, and treating investigator assessments)
- Treating investigator satisfaction at day 30 using 5-point Likert scale
- Subject satisfaction with appearance and naturalness of results using a subject questionnaire and 5-point Likert scale (1=strongly disagree; 5=strongly agree) at 30 and 120 days post-treatment
- Evaluation of treatment emergent adverse events (TEAEs) reported during the study

Table 1. Summary of Treatment-Emergent Adverse Events (TEAEs)

	Group A (n=30)	Group B (n=30)
Number of Subjects with ≥ 1 TEAE, n (%)	3 (10)	3 (10)
Number of Subjects with Related TEAE, n (%)*	2 (6.7)	1 (3.3)
Vision blurred	1 (3.3)	0 (0)
Injection site pain	1 (3.3)	0 (0)
Injection site swelling	1 (3.3)	0 (0)
Headache	2 (6.7)	0 (0)
Migraine	1 (3.3)	0 (0)
Dry skin	1 (3.3)	0 (0)
Skin hyperpgimentation	0 (0)	1 (3.3)
Number of Subjects with Not Related TEAE, n (%)	1 (3.3)	2 (6.7)
Seasonal allergies	1 (3.3)	0 (0)
Bronchitis	0 (0)	1 (3.3)
Nasopharyngitis	0 (0)	1 (3.3)
Dermatitis contact	1 (3.3)	0 (0)

Safety Population = 60 subjects; Group A (1.5 mL) – 0.05 mL/injection; Group B (2.5 mL) – 0.08 mL/injection. Counts reflect the number of subjects experiencing TEAEs, not the number of TEAEs.

*One subject had multiple events: headache, migraine, injection site pain, and injection site swelling

REFERENCES

1. Dysport®. Prescribing Information. Fort Worth, TX: Galderma Laboratories, L.P., 2016.
2. Trindade De Almeida AR, Secco LC, Carruthers A. Handling botulinum toxins: an updated literature review. *Dermatol Surg.* 2011 Nov;37(11):1553-1565.
3. Honeck P, Weiss C, Sterry S, Gladys study group, et al. Reproducibility of a four-point clinical severity score for glabellar frown lines. *Br J Dermatol.* 2003;149:306-310.

RESULTS

Demographics

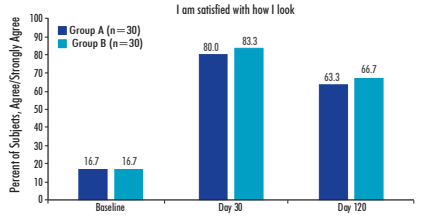
- Sixty subjects (24-64 years old; mean age of 45.8 years) were enrolled. Subjects were primarily female (86.7%) and Caucasian (96.7%) with moderate (25%) and severe (75%) GLLS scores at maximum frown (baseline).

Glabellar Line Severity Scores

- 46.7% of subjects achieved at least a 1-point reduction in GLSS (based on combined subject and blinded evaluator assessments) within 48 hours using either injection volume, this increased to 88.3% overall by 30 days post-treatment (Figure 1, representative photographs)
- At 48 hours post-treatment, 46.7% of subjects in both treatment groups were composite responders with an increase to 70.0% (Group A) and 76.7% (Group B) by 72 hours post-treatment (Figure 2a). The only statistically significant difference between treatments was noted at 24 hours post-treatment, where 26.7% of subjects in Group B were considered composite responders compared to only 6.7% in Group A ($P=.0377$; Figure 2a)
- At 30 day post-treatment, 90.0% of subjects in Group A and 86.7% of subjects in Group B were considered composite responders (Figure 2a)
- For Group A composite responders at day 30, 70.0% achieved at least a 2-point reduction from baseline in GLSS. For Group B composite responders at day 30, 63.3% achieved at least a 2-point reduction from baseline in GLSS (Figure 2b).

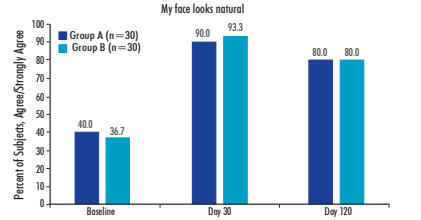
Figure 4. Subject Satisfaction at Days 30 and 120, Relative to Baseline (n=60) – mITT Population

4a) Subject Satisfaction, Satisfaction with Overall Look



Group A (1.5 mL) – 0.05 mL/injection; Group B (2.5 mL) – 0.08 mL/injection; mITT = modified intent to treat

43b) Subject Satisfaction, Natural Looking Appearance



Group A (1.5 mL) – 0.05 mL/injection; Group B (2.5 mL) – 0.08 mL/injection; mITT = modified intent to treat

Onset of Effect

- As early as 24 hours post-treatment, OOE was reported for 30.0% of subjects (based on combined subject and blinded evaluator assessments) with no significant difference between treatment groups. Within 48 hours, 73.3% of subjects had reported OOE.
- Within 24 hours post-treatment, 26.7% of subjects in Group A and 33.3% of subjects in Group B experienced OOE (based on subject and blinded evaluator assessments); this increased to 76.7% and 70.0% within 48 hours post-treatment, respectively (Figure 3).

Treating Investigator Satisfaction

- Investigators reported high satisfaction for both treatments

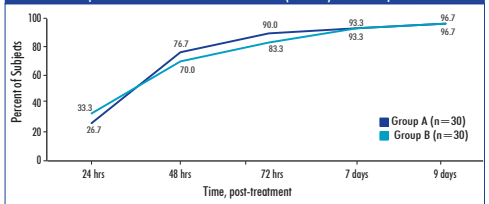
Subject Satisfaction

- At 30 days post-treatment, the majority of subjects (80.0% Group A, 83.3% Group B) agreed or strongly agreed they were satisfied with how they looked compared to baseline (16.7% Group A, 16.7% Group B) and most subjects remained in agreement at day 120 (63.3% Group A, 66.7% Group B; Figure 4a)
- At 30 days post-treatment, the majority of subjects (90.0% Group A, 93.3% Group B) agreed or strongly agreed that treatment provided a natural looking appearance compared to baseline (40.0% Group A, 36.7% Group B) and most subjects remained in agreement at day 120 (80.0% Group A, 80.0% Group B; Figure 4b)

Safety

- A total of 13 treatment emergent adverse events (TEAEs) were reported in 6 subjects (3 subjects from each treatment group); 9 TEAEs reported in 3 subjects were assessed as related to treatment (2 subjects in Group A, 1 subject in Group B; Table 1)
- No SAEs were reported and both treatments were well-tolerated

Figure 3. Proportion of Subjects Who Achieved Onset of Effect (OOE), Based on Combined Subject and Blinded Evaluator Assessments (n = 60) – mITT Population



1.5 mL = 0.05 mL/injection, n=30; 2.5 mL = 0.08 mL/injection, n=30; mITT = modified intent to treat

SUMMARY

- The study results demonstrated that treatment of moderate-to-severe GLs with either on-label injection volume resulted in almost identical efficacy and safety profiles, rapid onset of effect, and provided a high degree of clinician and subject satisfaction.
- Responder rates for each treatment group were generally similar among all evaluations with the exception of ≥ 1-point composite responders at maximum frown at Day 2 (~ 24 hours post-treatment) where ABO 2.5 mL treatment group (Group B) had a statistically significant larger number of responders compared to ABO 1.5 mL treatment group (Group A; $P = .0377$).
- High levels of subject satisfaction with appearance and natural looking outcome were maintained through Day 120.
- Both treatments provided a natural looking aesthetic outcome and were found to be safe and well tolerated. The results of this study demonstrated that the higher injection volume produced similar effects for improvement of GL severity and did not result in increased safety concerns compared to the lower volume.

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