Efficacy and Safety of IncobotulinumtoxinA in the Treatment of Upper Facial Lines: Results from a Randomized, Double-Blind, Placebo-Controlled, Phase III Study

P6.10

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BACKGROUND

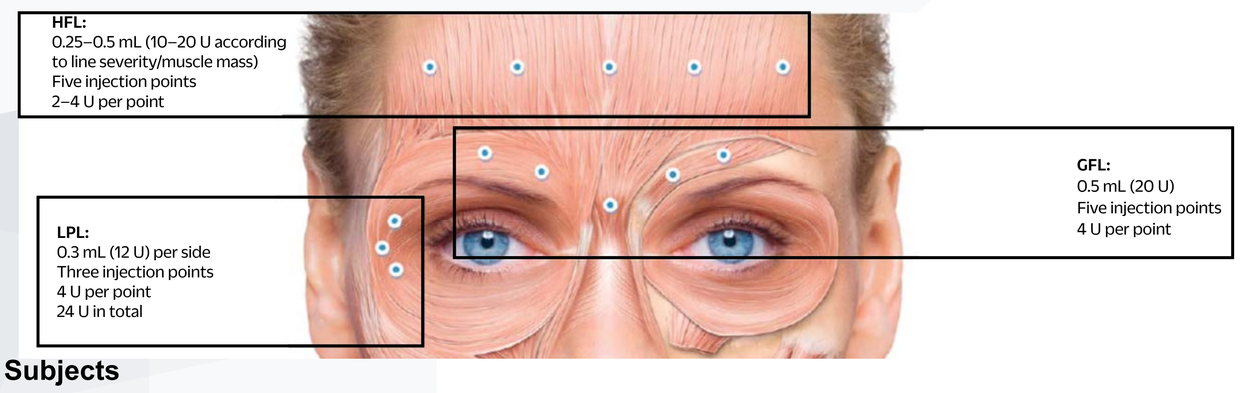
- In clinical practice, multiple areas of the upper face (glabellar frown lines [GFL], horizontal forehead lines [HFL], and lateral periorbital lines [LPL]) are often treated together using botulinum toxin
- Here we report efficacy and safety of repeated incobotulinumtoxinA injections for the treatment of UFL in a prospective, randomized, double-blind, placebo-controlled, phase 3 study.
- IncobotulinumtoxinA (Xeomin®, Merz Pharmaceuticals, GmbH) was the first toxin approved in Europe for combined treatment of upper facial lines (UFL: GFL+HFL+LPL) based upon the results of this study..

METHODS

Study design

- Healthy subjects with moderate-to-severe UFL (using the Merz Aesthetics Scales [MAS]) received placebo (n=51) or 54–64U of incobotulinumtoxinA (n=105) administered to the GFL (20U), HFL (10–20U), and LPL (24U) (**Figure 1**).

Figure 1. Division of the total administered dose of incobotulinumtoxinA (54-64 U) across the 3 aesthetic areas.



Subjects

- All subjects had HFL, GFL, and symmetrical LPL of moderate-to-severe intensity at maximum contraction, as assessed by the investigator using the 5-point MAS

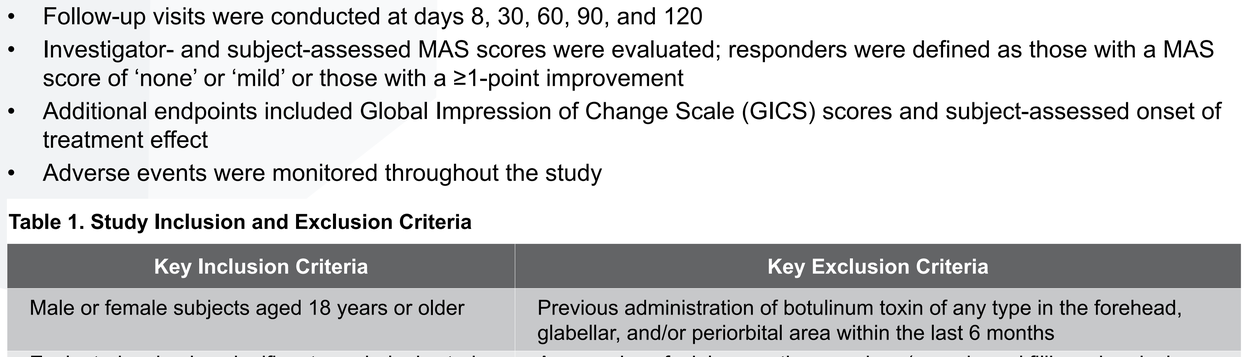
Study Assessments

- At Visit 1 (screening visit, completed from 14 to 3 days before baseline), each subject underwent eligibility assessment for study inclusion.
  - At baseline (Day 1, Visit 2), subjects were randomized and incobotulinumtoxinA or placebo was administered.
- Follow-up visits were conducted at days 8, 30, 60, 90, and 120
- Investigator- and subject-assessed MAS scores were evaluated; responders were defined as those with a MAS score of 'none' or 'mild' or those with a ≥1-point improvement
- Additional endpoints included Global Impression of Change Scale (GICS) scores and subject-assessed onset of treatment effect
- Adverse events were monitored throughout the study

Table 1. Study Inclusion and Exclusion Criteria

Key Inclusion Criteria	Key Exclusion Criteria
Male or female subjects aged 18 years or older	Previous administration of botulinum toxin of any type in the forehead, glabellar, and/or periorbital area within the last 6 months
Evaluated as having significant psychologic strain according to the FLQA-k assessment tool	Any previous facial cosmetic procedure (e.g., dermal filling, chemical peeling, photo rejuvenation) in the forehead, glabellar, and/or periorbital areas within the last 8 months
GFL, HFL, and symmetric LPL of moderate-to-severe intensity at maximum contraction, as assessed by the investigator using the 5-point MAS	Any previous insertion of permanent material in the forehead, glabellar, and/or periorbital area (regardless of the time between previous treatment and this study)
Stable medical condition	Any facial cosmetic procedure planned for within the study period
Use of a highly effective method of birth control (for women of childbearing potential)	Very severe lines (GFL, HFL, and/or LPL) at maximum contraction, as assessed by the investigator using the MAS
	Inability to substantially lessen UFL by physically spreading them apart
	Any previous surgery/existing scars in the treatment areas
	Marked facial asymmetry
	Pregnancy or lactation
	Known hypersensitivity to the study medication

Figure 2. Patient flow diagram.



CONCLUSIONS

- **IncobotulinumtoxinA demonstrated significant efficacy in treating GFL, HFL, and LPL separately and combined, as well as a good safety profile.**
- **The effects were maintained for up to 120 days, and the treatment was well tolerated.**

RESULTS

- In total, 240 subjects were screened and 156 randomized (**Figure 2**). Baseline MAS scores for each treatment area are presented in **Table 2**.
- Investigator-assessed scores of "none" (0) or "mild" (1) on the MAS for GFL, HFL, and LPL at maximum contraction on Day 30 demonstrated a significant treatment effect of incobotulinumtoxinA, with a higher response rate among the incobotulinumtoxinA group compared with the placebo group ($p < .0001$, **Figure 3**).
- Similarly, the response rate for the sum of investigator-assessed MAS scores for the 3 treated areas (GFL, HFL plus LPL) at maximum contraction on Day 30 was higher in the incobotulinumtoxinA group compared with the placebo group ($p = .0001$).

Table 2. Baseline Severity of GFL, HFL, and LPL According to the MAS (Investigator's Rating at Maximum Contraction)

		IncobotulinumtoxinA Group (n = 105)	*Placebo Group (n = 51)*
Treatment Area	***Baseline Severity (MAS Score)***	***n* (%)**	***n* (%)**
GFL	Moderate (2)	32 (30.5)	13 (25.5)
	Severe (3)	73 (69.5)	38 (74.5)
HFL	Moderate (2)	18 (17.1)	13 (25.5)
	Severe (3)	87 (82.9)	38 (74.5)
LPL*	Moderate (2)	28 (26.7)	14 (27.5)
	Severe (3)	76 (72.4)	37 (72.5)

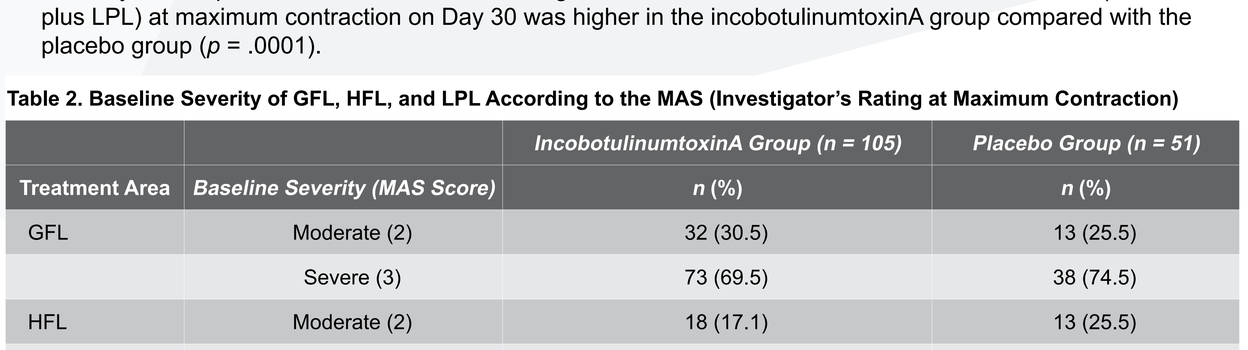
*One subject in the incobotulinumtoxinA group with very severe lines is not included here.MAS scores: 0 = no lines; 1 = mild lines; 2 = moderate lines; 3 = severe lines; 4 = very severe lines.

Table 3. Proportion of Subjects With a "Much Improved" (Increase of 2 Points) or "Very Much Improved" (Increase of 3 Points) Score on the GICS at Day 30—Observed Cases

	IncobotulinumtoxinA Group (n = 105) Proportion (%)	*Placebo Group (n = 51) Proportion (%)*	*p (Logistic Regression Model)*
Investigator's rating	86.4	2.1	<0.0001
Subject's rating	77.7	2.1	<0.0001

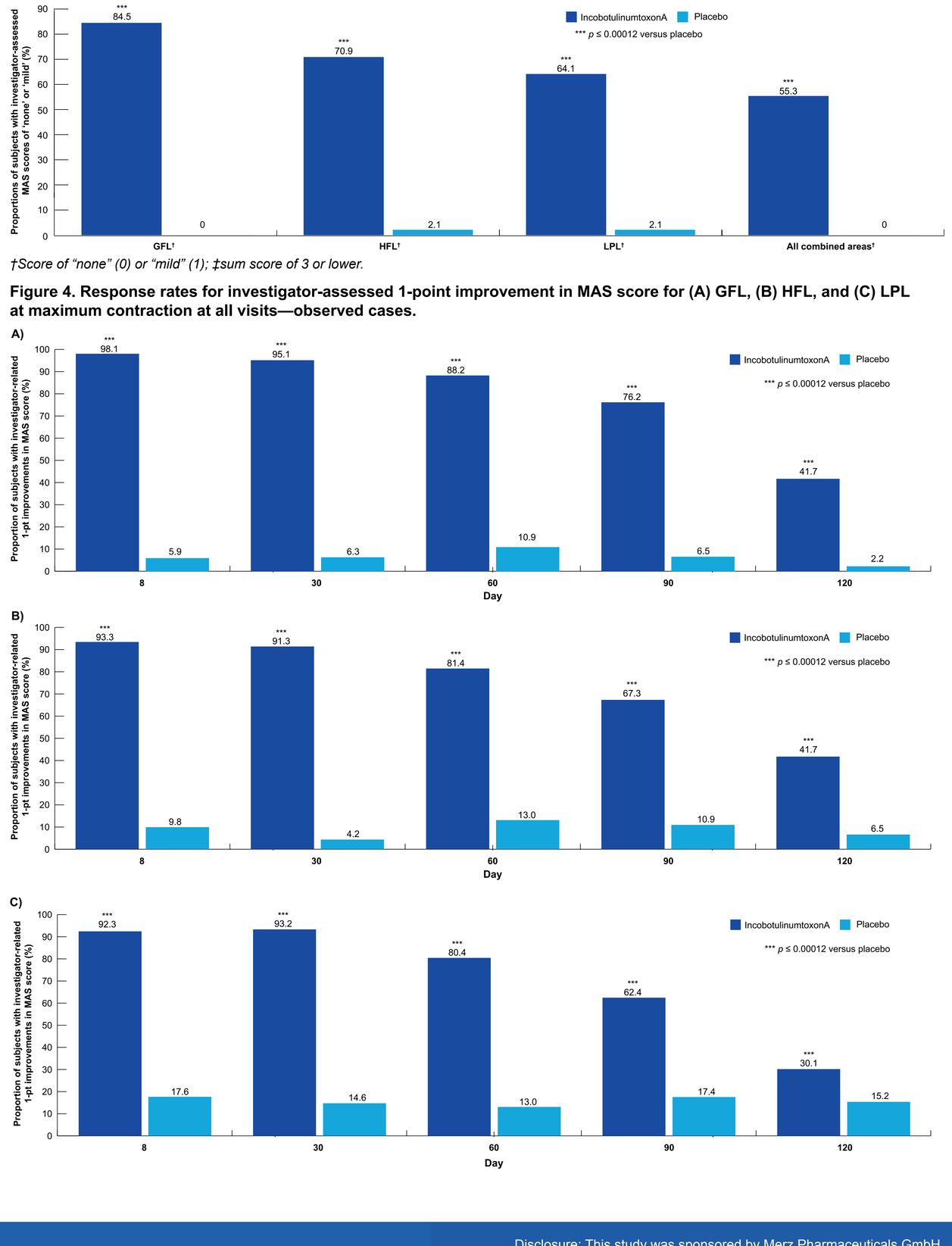
Logistic regression model (including investigational site and treatment group as factors) for the treatment area combination (GFL, HFL plus LPL). Rating according to the GICS: 23 = very much worse; 22 = much worse; 21 = minimally worse; 0 = no change; 1 = minimally improved; 2 = much improved; 3 = very much improved.

Figure 3. Response rates for investigator-assessed scores of "none" (0) or "mild" (1) on the 5-point MAS for GFL, HFL, and LPL and a sum score of 3 or lower in the UFL combination at maximum contraction on Day 30—observed cases, FAS.



†Score of "none" (0) or "mild" (1); ‡sum score of 3 or lower.

Figure 4. Response rates for investigator-assessed 1-point improvement in MAS score for (A) GFL, (B) HFL, and (C) LPL at maximum contraction at all visits—observed cases.



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