Safety and Efficacy of IncobotulinumtoxinA for the Treatment of Upper Facial Lines: Results from the Open-Label Extension Period of a Phase III Study

P6.16

Martina Kerscher[1]; Simon A. Connolly[2]; Bernard Biwer[3]; Petra Weissenberger[4]; Philippe Kestemont[5]; Ernst M. Noah[6]; Gerhard Sattler[7]; Patrick Trevidic[8]

[1]Division of Cosmetic Science, University of Hamburg, Germany; [2]Regency Medical Clinic, Glasgow, United Kingdom; [3]Private Practice, Ludwigshafen, Germany; [4]Merz Pharmaceuticals GmbH, Frankfurt am Main, Germany; [5]Clinique Esthétique St George, Nice, France; [6]Red Cross Hospital, Department for Plastic, Reconstructive and Aesthetic Surgery, Kassel, Germany; [7]Rosenparkklinik, Darmstadt, Germany; [8]Expert2Expert, Paris, France

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
- IncobotulinumtoxinA (Xeomin®, Merz Pharmaceuticals, GmbH) was the first toxin approved in Europe for combined treatment of upper facial lines (UFL: GFL+HFL+LPL).
  - This approval was based upon the main period (MP) of a double-blind, placebo controlled, phase 3 study[1]
- Here we report efficacy and safety of repeated incobotulinumtoxinA injections for the treatment of UFL in an open-label extension (OLEX) period of the phase 3 European approval study.

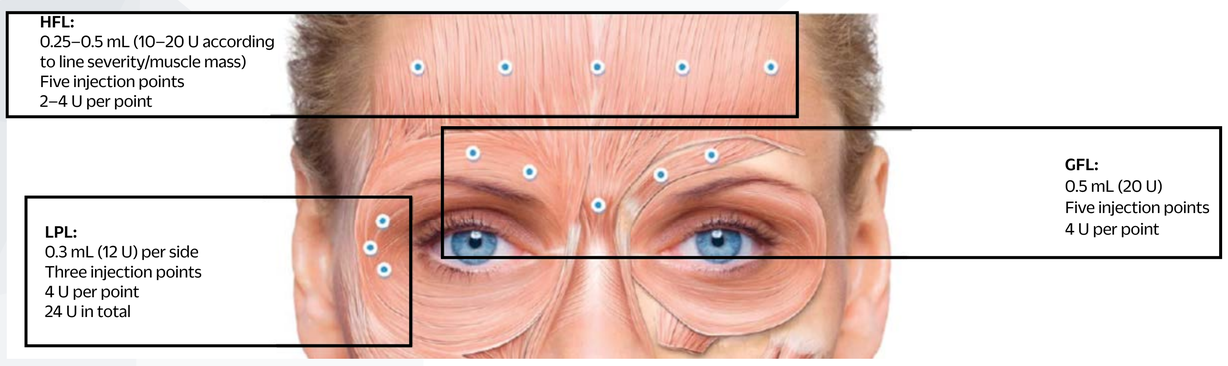
[1]*Dermatol Surg* 2015; 41:1149-1157

METHODS

Study design

- In the MP, subjects with moderate-to-severe UFL (using the Merz Aesthetics Scales [MAS]) received one treatment with placebo (n=51) or 54–64U of incobotulinumtoxinA (n=105) administered to the GFL (20U), HFL (10–20U), and LPL (24U).
- In the OLEX, all subjects (n=139) received one treatment with 54–64U of incobotulinumtoxinA (**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
- Full inclusion and exclusion criteria for the MP have been published previously[1]
- To be included in the OLEX, subjects had to return to at least moderate severity (MAS) in all 3 treated areas intensity following the MP

Study Assessments

- Follow-up visits were conducted at days 8, 30, 75, 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 subjectassessed onset of treatment effect
- Adverse events were monitored throughout the study

RESULTS

- Rapid, significant responses were observed in individual treated areas and all treated areas combined.
- At Day 30 of the OLEX, the proportions of responders (ie, score of 'none' or 'mild') were 80.1%, 77.2%, and 66.9% for GFL, HFL, and LPL, respectively.
- 88.2% and 83.8% of subjects were assessed by the investigator and subject, respectively, as "much improved or "very much improved" on the GICS at Day 30.
- Onset of effect was rapid, with high response rates observed by 8 days.
- IncobotulinumtoxinA was well tolerated throughout the MP and OLEX, with no increase in adverse events with repeat injection.

Table 1. Baseline Demographics and Severity of UFL

	OLEX (n = 139)
Sex, *n* (%)	
Female	122 (87.8)
Male	17 (12.2)
Age, yrs	
Mean (SD)	47.6 (9.9)
Range	23-82
Ethnicity, *n* (%)	
White	136 (97.8)
Black/African American	2 (1.4)
Other	1 (0.7)
BMI, kg/m^2	
Mean, (SD)	23.8 (3.5)
Severity–GFL, *n* (%)*†	
Moderate	59 (43.4)
Severe	76 (55.9)
Severity–HFL, *n* (%)*¡	
Moderate	58 (42.6)
Severe	74 (54.4)
Severity–LPL, *n* (%)*§	
Moderate	58 (42.6)
Severe	76 (55.9)

*Includes only the 136 subjects who had at least 1 post-baseline value during the OLEX period. †One subject with mild lines not shown. ¡Three subjects with mild lines and 1 with very severe lines not shown. §One subject with mild lines and 1 with very severe lines not shown.
BMI, body mass index; GFL, glabellar frown lines; HFL, horizontal forehead lines; LPL, lateral periorbital lines; OLEX, open-label extension; SD, standard deviation.

Table 2. Percentage of Subjects Achieving an Improvement of ≥1 Point From the Last Assessment Before OLEX Injection on the MAS (Investigator's Rating) at Maximum Contraction

	Responders (≥ 1-Point Improvement)		
	GFL (%)	*HFL* (%)	*LPL* (%)
Day 8	94.1	91.9	87.4
Day 30	92.6	91.9	88.2
Day 75	84.6	78.5	73.1
Day 120	58.2	47.0	45.5

GFL, glabellar frown lines; HFL, horizontal forehead lines; LPL, lateral periorbital lines; MAS, Merz Aesthetic Scales; OLEX, open-label extension.

Table 3. Percentage of Subjects Achieving an Improvement of ≥1 Point From the Last Assessment Before OLEX Injection on the MAS (Subject's Rating) at Maximum Contraction

	Responders (≥ 1-Point Improvement)		
	GFL (%)	*HFL* (%)	*LPL* (%)
Day 8	88.9	91.9	84.4
Day 30	88.2	93.4	81.6
Day 75	78.5	76.2	62.3
Day 120	50.7	49.3	46.3

GFL, glabellar frown lines; HFL, horizontal forehead lines; LPL, lateral periorbital lines; MAS, Merz Aesthetic Scales; OLEX, open-label extension.

Table 4. Percentage of Subjects Achieving a Score of "Much Improved" or "Very Much Improved" on the GICS

	n/N (%)
Investigator's rating	120/136 (88.2)
Subject's rating	114/136 (83.8)

Figure 2. Responders at Maximum Contraction (Investigator-Assessed). Responders were those with a score of "none" or "mild" on the MAS; for the combined area, responders were defined as those with a sum score ≤3 for all 3 facial areas.

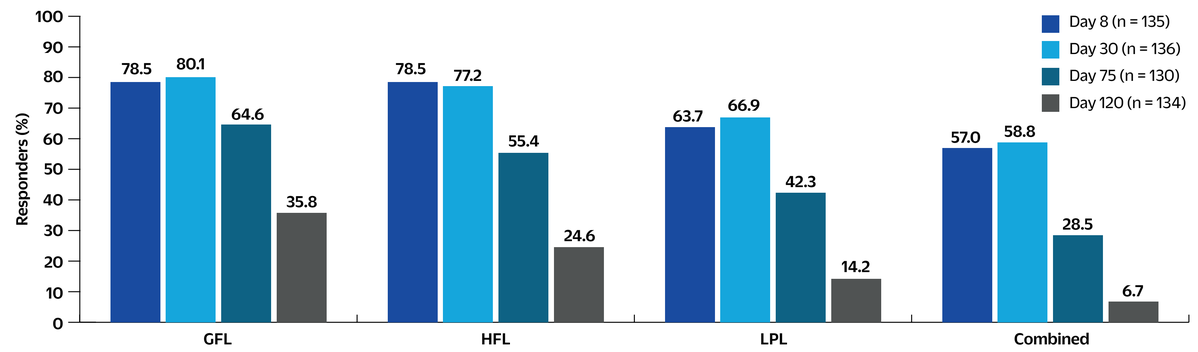


Figure 3. Responders at Maximum Contraction (Subject-Assessed). Responders were those with a score of "none" or "mild" on the MAS; for the combined area, responders were defined as those with a sum score ≤3 for all 3 facial areas.

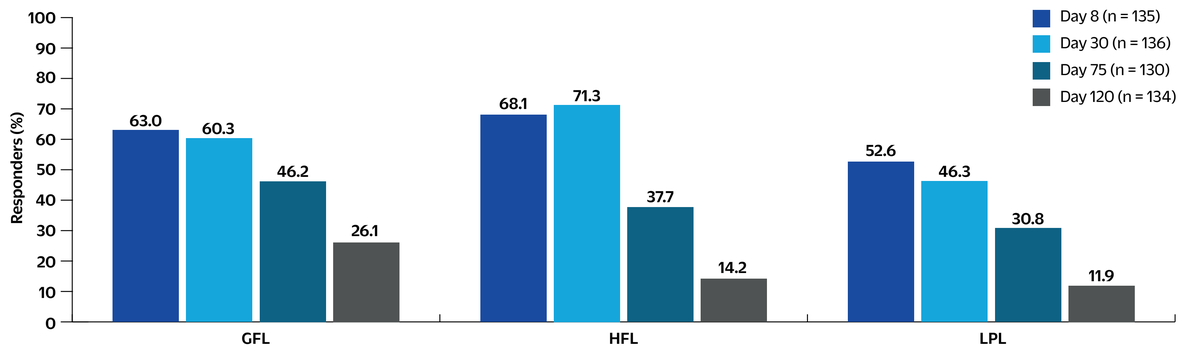


Table 5. Summary of TEAEs in the OLEX

n (%)	*Previous Xeomin (N = 94)*	*Previous Placebo (N = 45)*	*Total (N = 139)*
Any TEAE	44 (46.8)	20 (44.4)	64 (46.0)
Treatment related	14 (14.9)	8 (17.8)	22 (15.8)
TEAE of special interest	3 (3.2)	2 (4.4)	5 (3.6)
Treatment related	2 (2.1)	2 (4.4)	4 (2.9)
Serious TEAE	1 (1.1)	0 (0.0)	1 (0.7)
Treatment related	0 (0.0)	0 (0.0)	0 (0.0)
TEAE leading to discontinuation	0 (0.0)	0 (0.0)	0 (0.0)

OLEX, open-label extension; TEAE, treatment-emergent adverse event.

CONCLUSIONS

- **IncobotulinumtoxinA is effective and well tolerated for the combined treatment of upper facial lines.**
- **There was no increase in adverse events with repeat injection.**

Disclosure: This study was sponsored by Merz Pharmaceuticals GmbH.