

Reduced Psychosocial Burden and High Patient Satisfaction Associated With Glabellar Lines Treatment With LetibotulinumtoxinA: BLESS Phase 3 Trials

Michael H. Gold, MD*

Gold Skin Care Center, Tennessee Clinical Research Center, Nashville, Tennessee

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Introduction

- Hyperfunctional glabellar frown lines can transmit facial miscues that may adversely affect emotional communication, increase perceived age, and diminish psychosocial functioning, emotional wellbeing, and self-confidence¹⁻³
- Patient-reported outcome (PRO) assessments after glabellar line treatment with botulinum neurotoxin type A injections have demonstrated benefits for self-esteem, age perception, and quality of life (QoL) across multiple domains⁴⁻⁷
- LetibotulinumtoxinA is approved by the US Food and Drug Administration for the treatment of moderate-to-severe glabellar lines associated with corrugator and/or procerus muscle activity in adults⁸
- Approval was based on the BLESS III pivotal phase 3 trial, in which letibotulinumtoxinA demonstrated good tolerability with a rapid onset of action and high, sustained efficacy in the treatment of moderate-to-severe glabellar lines⁹
- The impact of letibotulinumtoxinA treatment on psychosocial wellbeing, QoL, and age perception was investigated in a large pooled dataset

Objectives

- Evaluate the efficacy of letibotulinumtoxinA in mitigating the negative psychological impact associated with moderate-to-severe glabellar frown lines
- Assess patient satisfaction with treatment outcomes
- Investigate correlations between PRO measures and glabellar line severity

Methods

- Data were pooled from BLESS III (NCT03985982) and two other identical phase 3 trials (BLESS I [NCT02677298] and BLESS II [NCT02677805])
- Each trial assessed the efficacy and safety of letibotulinumtoxinA (total of 20 U injected across 5 sites) in the treatment of moderate-to-severe glabellar lines, through one double-blind placebo-controlled cycle followed by up to 3 open-label active treatment cycles
- The primary end point was defined as the proportion of patients with a Glabellar Line Severity (GLS) score of 0 or 1 and improvement of ≥ 2 points in GLS score at maximum frown at week 4 of the first treatment cycle compared with baseline as rated by a composite of both investigators' and patients' assessments
- An integrated analysis using pooled BLESS data was conducted on secondary PRO end points in the full analysis set; statistical analysis methods are summarized in **Table 1**
- Correlations between PRO measures and glabellar line severity scores with letibotulinumtoxinA treatment were evaluated using a Pearson correlation test

Table 1. BLESS Pooled Analysis: PRO Assessment Instruments and Statistical Methods

	Primary (Composite)	Key Secondary			Additional Secondary
End point description	Response: Proportion of patients with GLS score of 0 or 1 and improvement of ≥ 2 points in GLS score at maximum frown at week 4 of the first treatment cycle vs baseline (investigators' + patients' assessments)	Psychological impact assessment at week 4	Glabellar lines severity at week 4	Age perception at week 4	Patient treatment satisfaction at week 4
Validated assessment instrument	GLS scale (0 = none, 1 = mild, 2 = moderate, and 3 = severe)	Modified Skindex-16 GL-QoL Scale (5-point scale: Total score 0-9 = mild, 10-18 = moderate, 19-28 = severe)	FACE-Q Appraisal of Lines Between Eyebrows Scale (7-item standardized scale on a 4-point scale: higher score = better outcome)	FACE-Q Age Appraisal Visual Analog Scale (single-item question, analyzed as a continuous variable)	FACE-Q Satisfaction With Outcome Scale (6-item instrument)
Statistical method for group comparison	Analyzed with a generalized Cochran-Mantel-Haenszel test using a 1-sided significance level (α) of 0.025	Domain and overall scores compared using the Wilcoxon rank sum test	Statistically compared using Wilcoxon rank sum test	Statistically compared using Wilcoxon rank sum test	Analyzed descriptively

FACE-Q = Facial Assessment and Cosmetic Evaluation; GL-QoL = Glabellar Line Quality of Life; PRO = patient-reported outcomes.

Results

Demographics

- A total of 1272 patients were randomized and treated across the three BLESS trials; of these, 1188 (93%) completed the initial double-blind treatment cycle and 1087 (85%) completed the entire study (**Table 2**)

Table 2. Key Demographics and Baseline Characteristics

BLESS Pooled Data	LetibotulinumtoxinA (n=955)	Placebo (n=317)	Overall (N= 1272)
Age, mean (SD), y	50.5 (11.61)	49.6 (11.51)	50.3 (11.59)
Female, n (%)	881 (92.3)	280 (88.3)	1161 (91.3)
Psychological impact,* n (%)			
Mild	128 (13.4)	56 (17.7)	184 (14.5)
Moderate	437 (45.8)	152 (47.9)	589 (46.3)
Severe	390 (40.8)	109 (34.4)	499 (39.2)
Glabellar Line Scale,* n (%)			
1	1 (0.1)	0 (0)	1 (<0.1)
2	236 (24.7)	90 (28.4)	326 (25.6)
3	718 (75.2)	227 (71.6)	945 (74.3)

*Modified Skindex-16 GL-QoL Scale overall score at baseline, where 0-9 = mild, 10-18 = moderate, and 19-28 = severe.
*Composite GLS score at baseline, where 0 = none/minimal, 1 = mild, 2 = moderate, and 3 = severe.

Psychological Impact of LetibotulinumtoxinA Treatment

Patient Satisfaction

- On the FACE-Q Satisfaction With Outcome Scale, patients receiving letibotulinumtoxinA were more highly satisfied with their treatment results than those who received placebo (**Table 3**)

Table 3. Percentage of Agreement With Patient Satisfaction Statements

	"I am pleased with the result"	"The result was just as expected"	"The result turned out great"	"I was surprised how good I looked in the mirror"	"The result looked fantastic"	"The result is miraculous"
LetibotulinumtoxinA	84.6%	79.0%	77.5%	73.9%	71.6%	62.4%
Placebo	8.5%	8.8%	5.4%	6.3%	4.4%	3.5%
P value	<.001	<.001	<.001	<.001	<.001	<.001

HRQoL Assessment

- QoL improvements from baseline were significantly greater for letibotulinumtoxinA-treated patients than for those treated with placebo
 - Absolute mean (SD) improvements from baseline to week 4 for the overall Modified Skindex-16 GL-QoL score were -33.84 (29.72) versus -1.37 (18.78), respectively (where negative scores indicate improvement; $P<.001$), with comparable differences in individual emotional and social functioning domains (**Figure 1A**)

Glabellar Line Appraisal

- For the FACE-Q Appraisal of Lines Between Eyebrows Scale, letibotulinumtoxinA showed significantly greater absolute mean improvement from baseline to week 4 versus placebo (40.8 [27.05] vs. -1.2 [17.68]; $P<.001$) (**Figure 1B**)

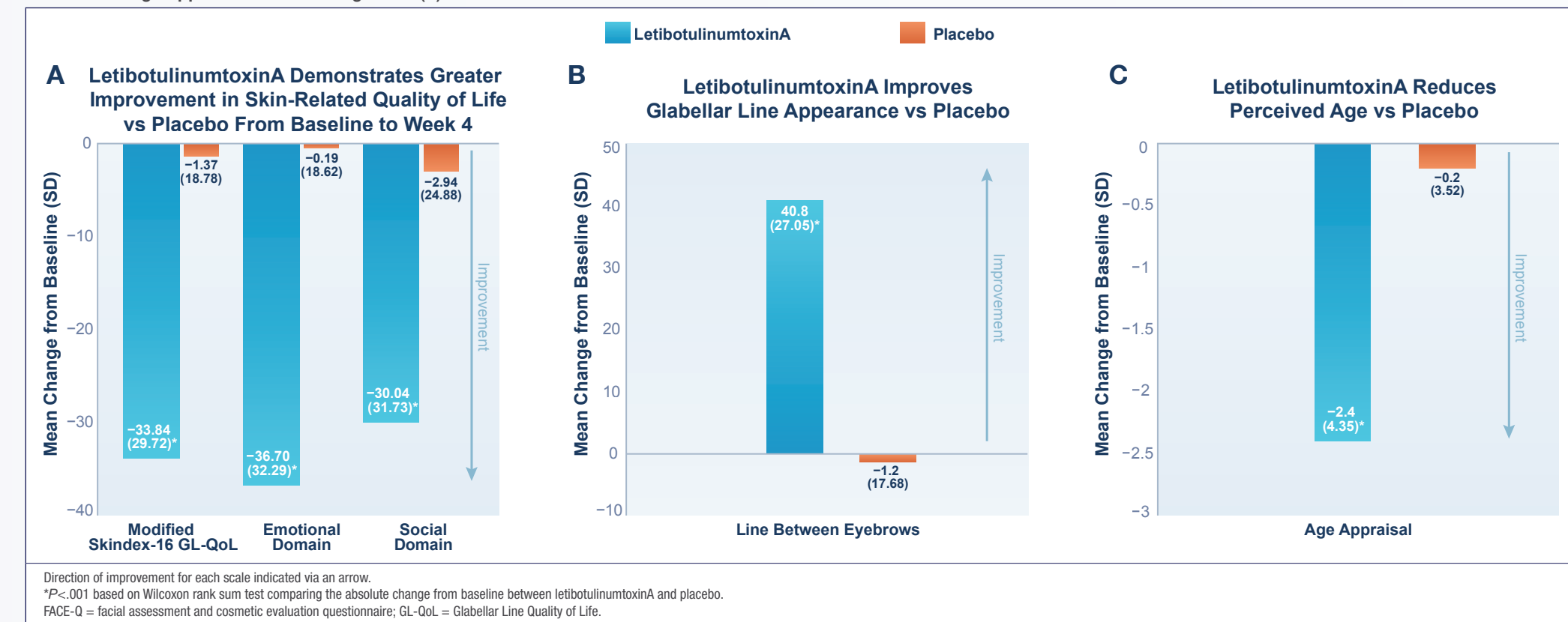
Perceived Age

- On the FACE-Q Age Appraisal Visual Analog Scale assessment, the absolute mean (SD) perceived age change from baseline to week 4 was 2.4 (4.35) years younger than actual age for letibotulinumtoxinA patients compared with 0.2 (3.52) years younger for placebo patients ($P<.001$; **Figure 1C**)

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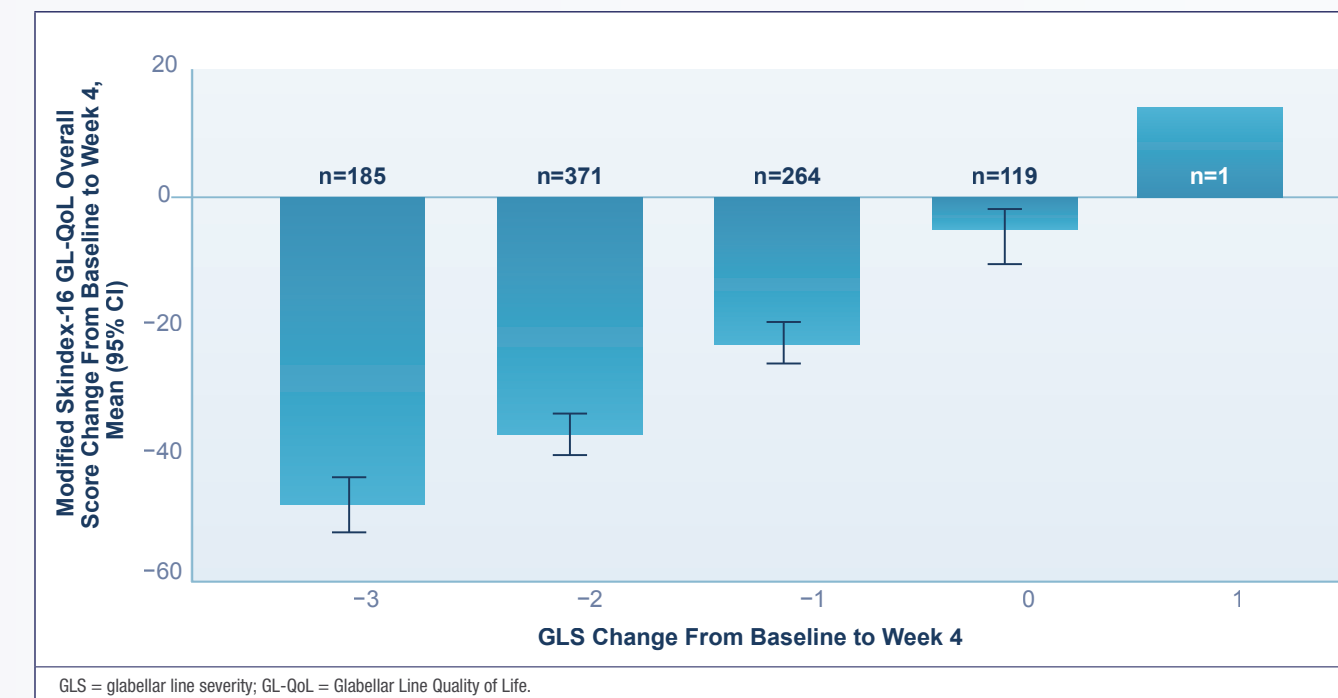
Figure 1. Mean Change From Baseline to Week 4 as Measured by the Modified Skindex-16 GL-QoL Scale (A), FACE-Q Appraisal of Lines Between Eyebrows Scale (B), and FACE-Q Age Appraisal Visual Analog Scale (C)



Correlation Between Changes in Glabellar Line Severity and Psychosocial QoL

- In patients receiving letibotulinumtoxinA, improvements in glabellar line severity were positively correlated with improvements in all measures of psychosocial impact at week 4
 - Improvement in line severity as assessed by the GLS (from severe [3] to none [0]) correlated positively with magnitude of improvement on both the Modified Skindex-16 GL-QoL Scale overall score (**Figure 2**) and the FACE-Q Appraisal Lines Between Eyebrows Scale
 - Greater glabellar line severity improvement was associated with younger self-perceived age after treatment with letibotulinumtoxinA

Figure 2. Correlation Between Change in Glabellar Line Severity at Week 4 and Psychosocial QoL in LetibotulinumtoxinA-treated Patients



GLS = glabellar line severity; GL-QoL = Glabellar Line Quality of Life.

Conclusions

- In this integrated analysis of phase 3 clinical trial data, letibotulinumtoxinA significantly improved the negative psychosocial burden associated with moderate-to-severe glabellar lines
 - This improvement was strongly correlated with improvement in glabellar line severity
- LetibotulinumtoxinA-treated patients reported improved QoL overall and in social and emotional domains, perceived themselves to look younger, and reported feeling highly satisfied with their treatment results

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Disclosures

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