Letybo® for Orbicularis Oculi (Crow's Feet): Evidence-based Treatment and Dosing

RELEVANT PRESCRIPTION INFORMATION LABEL INFORMATION

The information provided relates to a use for Letybo® (letibotulinumtoxinA-wlbg) that is not approved by the US Food and Drug Administration (FDA).

CLINICAL DATA

A search of the published medical literature was conducted regarding Letybo® and treatment of the orbicularis oculi (Crow's Feet and/or Lateral Canthal Lines (LCL)).

The relevant citations referenced in this communication are listed below. The hyperlinks to publicly available abstracts are included. Findings resulted in peer-consensus statements and a non-inferiority Phase III clinical trial, some of which may not be reflective of findings from outcomes in a broader population, and should be considered when evaluating the data.

Some references cited in this response may discuss additional treatment areas and Botulinum toxin products that were not specified in this Medical Information Request.

Letybo® is an acetylcholine release inhibitor and a neuromuscular blocking agent indicated for the temporary improvement in the appearance of moderate to severe glabellar lines associated with corrugator and/or procerus muscle activity in adult patients. Hugel Inc. and BENEV Inc. do not endorse the use of Letybo® in a manner not consistent with the approved label.

Units of biological activity of Letybo® cannot be compared to nor converted into Units of any other botulinum toxin or any toxin assessed with any other specific assay method.

CITATIONS

1. Letybo® Prescribing Information, 2024.
2. Choi HS, Wang J, Tauber D, et al. Consensus Recommendations for Treatment of the Upper Face With LetibotulinumtoxinA. Plast Aesthet Nurs (Phila). 2024;44(4):239-250. doi:10.1097/PSN.0000000000000585 https://pubmed.ncbi.nlm.nih.gov/39348312/
3. Liu S, Cong L, Pongprutthipan M, et al. Use of LetibotulinumtoxinA for Aesthetic Treatment of Asians: A Consensus. *Aesthet Surg J*. 2023;43(11):NP962-NP974. doi:10.1093/asj/sjad151 https://pmc.ncbi.nlm.nih.gov/articles/PMC10575620/
4. Yoo KH, Park SJ, Han HS, Won CH, Lee YW, Kim BJ. Randomized, double-blind, active-controlled, multicentre, phase III clinical trial with two stages to assess the safety and efficacy of letibotulinum toxin a vs. onabotulinum toxin a for subjects with moderate to severe crow's feet. J Eur Acad Dermatol Venereol. 2021;35(7):1587-1594. doi:10.1111/jdv.17217 https://pubmed.ncbi.nlm.nih.gov/33721365/

REVIEW OF RESEARCH AND CLINICAL PRACTICE INFORMATION | TABLE OF CONTENTS

Choi et al. 2024[2] is an expert consensus that provides guidelines for treating facial lines of the upper face with letibotulinumtoxinA. The members of the consensus provided recommendations for injection sites, dosages, and injection techniques using letibotulinumtoxinA and considered relevant anatomy, patient assessment and selection, and individual variations to evaluate clinical strategies for minimizing complications.

Liu et al. 2023[3] is an expert consensus statement that provides clinical guidance on the aesthetic use of Letybo® (letibotulinumtoxinA-wlbg) for treating wrinkles, contour adjustment, and facial lifting in Asian patients. The publication highlights the importance of understanding facial musculature, patient preferences, and botulinum toxin pharmacology to optimize treatment. It underscores that cultural nuances, such as the preference for natural-looking results among Asian patients, inform injection techniques and dosing strategies. The panel recommends starting with conservative dosing, individualizing treatment plans, and adjusting based on patient feedback to achieve high satisfaction. This guidance is especially relevant for applications including orbicularis oculi (Crow's feet) treatment, where anatomical knowledge and precision are critical.

Yoo et al. 2021[4] was a multicenter, randomized, double-blind, active-controlled phase III clinical trial comparing letibotulinumtoxinA (LeBA) to onabotulinumtoxinA (OnBA) for treating crow's feet lines (CFL). A total of 240 subjects were randomized to either the test (LeBA) or control (OnBA) group. At week 4, the response rate of primary efficacy assessment was 69.75% and 68.33% in the test (LeBA) and control (OnBA) groups, respectively, without a significant difference. This study showed that LeBA was as effective and safe as OnBA for the treatment of CFL at the same doses.

Consensus Recommendations For Treating Lateral Canthal Lines with LetibotulinumtoxinA[2]: Lateral canthal lines are frequently treated with neurotoxin injections to reduce the activation of the orbicularis oculi muscle during facial expressions.

To explore the clinical research and references below, please review the cited publication.

Overview and Anatomy[2]: Lateral canthal lines, also known as *crow's feet*, are wrinkles originating from the outer corners of the eyes. These lines are considered to be an initial indication of the aging process. Lateral canthal lines can become permanent as a result of the aging process, sun exposure, and alterations in skin structure (de Maio et al., 2017). Facial wrinkles in this region are typically more noticeable than other types of facial wrinkling, especially during smiling, possibly due to the lack of sebaceous glands in this area (Tamatsu et al., 2015). One of the primary muscles of the periocular region is the superficial orbicularis oculi muscle, which is a broad, flat, elliptical muscle that comprises the orbital and palpebral portions. This intricate sphincteric muscle surrounds the eye and assists in closure of the palpebral fissure. It originates at the medial palpebral ligament, forms a complete elliptical shape around the eye, and attaches at the same point of origin (D'Souza & Ng, 2020). Lateral canthal lines are caused by the repetitive contraction of the orbicularis oculi muscle. Treatment with letiBoNT-A reduces lateral canthal lines by decreasing the activity of the orbicularis oculi muscle. Notably, the contractions of the zygomatic muscles that facilitate speech and facial expressions may also contribute to the formation of the lower canthal lines (Signorini et al., 2022). The zygomaticus major muscle is connected to the inferolateral edge of the orbicularis oculi muscles and has its origin situated beneath the orbicularis oculi muscles (Tremolada et al., 1994).

Patient Evaluation[2]: To examine the orbicularis oculi muscles, the aesthetic practitioner should instruct the patient to tightly close their eyes. The practitioner should evaluate the patterns of the lateral canthal lines and the position of the eyebrows when the patient's face is at rest and during a maximal smile. Kane et al. (2015) suggested identifying four

distinct patterns of the lines: full, upper, lower, and lateral patterns. The diversity of patterns and distributions of the lateral canthus lines suggests the necessity for using tailored injection points and standardized doses of neurotoxin to improve the effectiveness of treatment and ensure patient satisfaction (Braccini et al., 2023). Additionally, it is crucial to assess the presence of bunny lines (vertical and diagonal lines that appear on the bridge of the nose and on either side of the nose) and discuss any potential treatment of these lines with the patient before the procedure. This is particularly important because after treatment, some patients may develop muscle compensation that exacerbates these lines (Kim et al., 2015).

Injection Sites[2]: When treating lateral canthus lines, the consensus panel recommends aesthetic practitioners implement a 6-point (i.e., 3 points per side) intramuscular injection as shown in Figure 3, specifically targeting the lateral orbicularis oculi muscles (Lee et al., 2019; Yi et al., 2022b).

Dosage[2]: The expert panel members recommend injecting 4 units of letiBoNT-A into six injection points (i.e., three points on each side; equating to a total of 24 units), specifically targeting the lateral orbicularis oculi muscles (Yoo et al., 2021).

Potential Complications | Diplopia[2]: Using neurotoxin to treat the periorbital area may lead to notable complications, including diplopia (double vision). If the toxin spreads to unintended areas, such as the lateral rectus muscle innervated by the abducens nerve, it can result in paresis and diplopia. To minimize the risk for diplopia, practitioners should administer the injections at a superficial depth, while maintaining a distance of 1 cm from the orbital border and 1.5 cm from the lateral canthus.

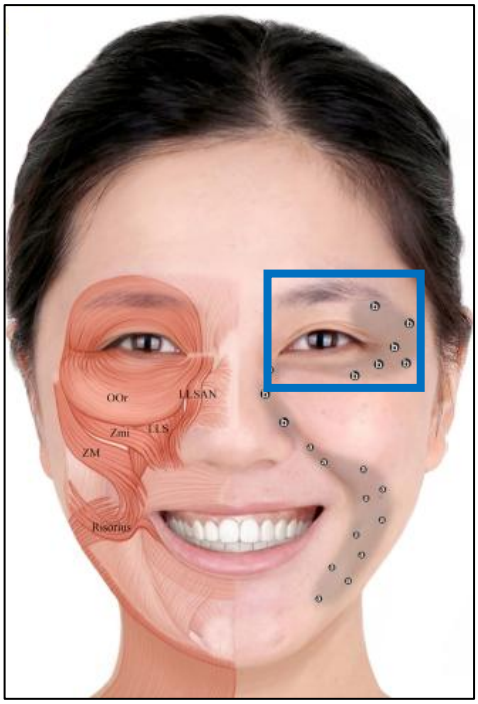
FIGURE 3[2]. Injection points for treating lateral canthal lines with Letibotulinum toxinA (letiBoNT-A; Letybo, Hugel, Inc., Chuncheon, South Korea). When injecting letiBoNT-A for treatment of lateral canthus lines, aesthetic practitioners should use a total of six injection points (i.e., three points on each side), that specifically target the lateral orbicularis oculi muscles. The initial injection should be administered a minimum of 1.5–2 cm temporal to the lateral canthus and just temporal to the orbital rim. The following two injections should be administered 1–1.5 cm above and below the initial injection point, at a 30° medial angle.

Relaxation of the Zygomaticus Muscle[2]: After treatment of the lateral canthus lines, some patients may experience difficulty in raising one side of the upper lip when smiling. This is due to the unintended relaxation of the zygomaticus major muscle that occurs during treatment of the orbicularis oculi muscle (Matarasso & Matarasso, 2001) To prevent this issue, practitioners must be cautious when injecting in the lateral canthal region, ensuring that the injections are not placed inferiorly. The expert panel recommends that practitioners not inject below the horizontal line connecting the infraorbital rim to the superior point of the ear canal and that they not administer injections superficially into the subcutaneous layer.

Patient Follow-Up[2]: To evaluate the efficacy of the initial treatment, the panel recommends a follow-up appointment 14 days after the treatment. Notably, in a multicenter, double-blind, randomized controlled trial to compare treatment of lateral canthus lines with letiBONT and onabotulinum toxin A in 240 participants, Yoo et al. (2021) found significant differences between the groups suggesting that letiBoNT offered better improvement than onabotulinum toxin A; however, the overall results did not show significant difference between the groups.

Use of LetibotulinumtoxinA for Aesthetic Treatment of Asians: A Consensus[3]

To explore the clinical research and references below, please review the cited publication.



Crow's Feet[3]: The orbicularis oculi is a large, thin sphincter whose contraction produces periocular wrinkles. The glabellar complex and nasal dorsalis sometimes contribute to wrinkles by acting as synergistic muscles. At the superior lateral canthal level, the orbicularis oculi is antagonistic to the frontalis. The goal is to evenly weaken the orbicularis oculi and its synergistic muscles while maintaining the dynamic balance between the orbicularis oculi and its antagonistic muscles.

FIGURE 1C[3] | Anatomy and Injection for Crow's Feet Treatment with LetibotulinumtoxinA in Asian Patients (adapted from Liu et al. 2023*). Treatment of Crow's Feet: 0.5 to 2 U/point (blue box). *Figure 1C has been adapted to present only the specific data relevant to this Standard Response Letter.

Anatomy[3]: The orbicularis oculi muscle is an elliptical muscle consisting of orbital and palpebral parts. The orbital part concentrically encircles the orbit, including the depressor supercilii, whereas the palpebral portion, with finer muscle fibers than the orbital part, sweeps across the eyelid anterior to the orbital septum (preseptal part of the palpebral portion) and arises from the medial palpebral ligament (pretarsal part of the palpebral portion). Its contraction causes the pretarsal roll and crow's feet.

Injection Technique[3]: Multipoint intradermal injections provide a more precise and uniform toxin action to the orbicularis oculi (Figure 1C; blue box). Pretreatment evaluation and delicately controlled dosage in the orbital orbicularis muscle and around the insertion of the zygomaticus major are critical for infraorbital rhytids. The frontalis should be balanced if an eyebrow elevation is unwanted. It should be noted that the injection only focuses on the lateral portion of the orbital part, which may lead to an increase in wrinkles at the medial orbit and nasal dorsum portions.

Table 2[3] | Consensus Recommendations for Crow's Feet Treatment With LetibotulinumtoxinA in Asian Patients (adapted from Liu et al. 2023*).

Indication	Target muscle	Injection points (n)	Dose per injection point (units)	Typical total dose range (units)	Preferred injection level
Crow's feet	Orbicularis oculi	10-25 (nmd)	0.25-2 (nmd)	5-25/side (nmd)	ID, SC

The dose shown in this table is for females, and the dose for males is 20% to 30% higher than that for females. ID, intradermal; IM, intramuscular; md, microdroplet; nmd, nonmicrodroplet; SC, subcutaneous
*Table 2 has been adapted to present only the specific data relevant to this Standard Response Letter.

Randomized, double-blind, active-controlled, multicentre, phase III clinical trial with two stages to assess the safety and efficacy of letibotulinum toxin a vs. onabotulinum toxin a for subjects with moderate to severe crow's feet[4]

To explore the clinical research and references below, please review the cited publication.

Selection of Subjects and Study Design[4]:

This was a randomized, double-blind, controlled Phase III trial conducted in two stages. Eligible subjects were adults aged 19–65 years with moderate-to-severe crow's feet lines (CFL) at maximum smile and with facial symmetry. Key exclusion criteria included hypersensitivity to study product components, recent facial procedures involving the crow's feet area (within 48 weeks), pregnancy or breastfeeding, and medical conditions that could increase the risk of adverse events.

In Stage 1, 30 subjects were enrolled and assessed by an independent data monitoring committee for safety at 4 weeks. Following review and absence of safety concerns, Stage 2 proceeded with an additional 210 subjects enrolled. All participants were randomized 1:1 to receive LeBA (letibotulinumtoxinA) or OnBA (onabotulinumtoxinA) and were followed over a 16-week period, with assessments conducted at baseline and at weeks 4, 8, 12, and 16. Safety and efficacy analyses were conducted on the pooled population from both stages.

Treatment[4]: The subjects were randomly assigned to the test or control group (1 : 1). The test group was administered LeBA (Botulax® or Letybo®, Hugel Inc., Chuncheon, Korea); the control group was administered OnBA (Botox®, Allergan Inc., Irvine, CA,USA). The investigator and subjects were blinded to the administered types of drugs. Double-blinding was maintained for both the investigator and the subject to avoid bias in the assessment of the treatment effects and adverse events. One vial (50 U) of each LeBA or OnBA was diluted with 1.25 mL of 0.9% sterile normal saline (4 U/0.1 mL). The diluted drugs [0.1 mL (4 U)] were injected intramuscularly to the outer side of the orbicularis oculi muscles at three sites per side (a total of six sites on both sides with 24 U) using a 31-gauge needle.

Efficacy Asessement[4]: *Primary efficacy assessment.* To verify the non-inferiority of LeBA to the reference drug (OnBA), we evaluated the proportion of responders with severe crow's feet at the maximum smile test after 4 weeks of treatment with the investigational products. An improvement was defined as 0 (none) or 1 (mild) at the 4-week evaluation. The evaluation of CFL was recorded as 0 (none) to 3 (severe) according to the Facial Wrinkle Scale (FWS) for left and right CFL of the Photo Guideline (Table 1a).

Secondary efficacy assessment. To assess the efficacy and safety of LeBA relative to the reference drug (OnBA), the rate of response to each of the listed criteria was evaluated. At the maximum smile, an improvement was considered if the severity at the time of evaluation was 0 (none) or 1 (mild). At the resting state, an improvement was recorded if wrinkles improved by more than one step relative to the appearance before treatment.

Investigator's evaluation of wrinkles caused by CFL. The investigator assessed changes from baseline at the maximum smile at weeks 8, 12 and 16 and at rest at weeks 4, 8, 12 and 16. The evaluation of CFL was recorded as 0 (none) to 3 (severe) according to the FWS for left and right CFL of the Photo Guideline (Table 1a).

Independent evaluators' evaluation of wrinkles caused by CFL. This evaluation was performed at the maximum smile and rest at weeks 4, 8, 12 and 16 from the baseline according to the photo evaluation performed by an independent evaluator. A photo evaluation of the CFL was conducted by three external independent investigators. All

three independent evaluators agreed on a specific assessment before it was deemed the grade of the subject.

Self-evaluation of wrinkle improvement by subjects with CFL (subject's global assessment). Self-evaluation of the subjects' improvement at the maximum smile and rest at weeks 4, 8, 12 and 16 from baseline was performed as instructed: the investigator asked the subjects about improvements in their wrinkles. The answers were derived using a nine-step range [- 4 (100% worsened) to +4 (100% improvement)] for the left and right CFL. If the grade was +2 (50% improvement) or higher, the appearance of wrinkles was reported to be improved (Table 1b).

Investigation of subject's satisfaction with CFL change (subject's satisfaction assessment). The investigator asked the subjects about their satisfaction with their CFL change following treatment with the investigational product. The satisfaction level of the subjects was graded in seven steps [grade 1 (very dissatisfied) to grade 7 (very satisfied)]; a level of grade 6 or higher (satisfied, very satisfied) showed that the subject was satisfied (Table 1c).

Safety assessments. Adverse events were collected, evaluated and classified as local or systemic adverse events. Adverse events were reported if there was a significant change observed on physical examination after the investigational product was administered; any change needed to correspond to the definition of an adverse event.

Results[4]: In stage 1, 30 subjects were screened and treated in both groups. In stage 2, 240 subjects were screened and randomly assigned to the study groups [119 subjects in the LeBA group (test group) and 121 subjects in the OnBA group (control group)] including the Phase I population. the mean age (mean ± SD) was 48.68 ± 7.48 years in the test group and 47.65 ± 6.61 years in the control group. No characteristic was significantly different between the test and control groups.

Primary Efficacy Assessment[4]: According to the investigator's on-site evaluation of the FAS population, the rate of improvement in CFL at the maximum smile after 4 weeks of treatment was 69.75% (83/119 subjects) in the test group and 68.33% (82/120 subjects) in the control group. Accordingly, the difference in the improvement rate between the test and control groups was 1.41% [95% two-sided confidence interval (-10.31, 13.14)], and the lower limit of the 97.5% one-sided confidence interval (-10.31%) was greater than -18%. These findings suggest that the test group was noninferior to the control group (Table 2). In the PPS, the improvement rate was 68.97% (80/116 subjects) in the test group and 68.33% (82/120 subjects) in the control group. Accordingly, the difference in the improvement rate between the test and control groups was 0.63% [95% two-sided confidence interval (-11.21, 12.47)]. Further, the lower limit of the 97.5% one-sided confidence interval (-11.21%) was found to exceed -18%, confirming that the test group was non-inferior to the control group (Table 2).

Table 2 | Ratio of subjects whose both eyes satisfy conditions of improvement of crow's feet lines (CFL) at the maximum smile, as evaluated by the investigator 4 weeks after administration

Full Analysis Set	**LeBA *N* = 119**	**OnBA *N* = 120**
Improved †	83 (69.75)	82 (68.33)
Treatment Difference		
Difference† (Two-sided 95% CI)	1.41 (-10.31, 13.14)	
Non-Inferiority	Yes	
Per-protocol set	**LeBA *N* = 116**	**OnBA *N* = 120**
Improved†	80 (68.97)	82 (68.33)
Treatment Difference		
Difference† (Two-sided 95% CI)	0.63 (-11.21, 12.47)	
Non-Inferiority	Yes	

Number of subjects for each item (%). CFL, Crow's feet line; CI, confidence interval; LeBA, letibotulinumtoxinA; N, number of subjects; OnBA, onabotulinumtoxinA.

†Improved = CFL Facial Wrinkle Scale (FWS) is 0 or 1 for both eyes, Not improved = crow's feet line FWS is 2 or 3. ‡Improvement rate in the test group - Improvement rate in the control group

Secondary Efficacy Assessment[4]: Evaluation by the investigator Based on the investigator's evaluation at 8, 12 and 16 weeks of the FAS population, the rate of improvement at the maximum smile was 57.98% (69/119 subjects), 38.66% (46/119 subjects) and 18.49% (22/119 subjects) in the test group and 55.00% (66/120 subjects), 31.67% (38/120 subjects) and 14.17% (17/120 subjects) in the control group, respectively. There was no significant difference between the groups at any point (Fig. 2). The results of the PPS population were similar to those of the FAS population. The results obtained at the rest state were similar and showed a tendency to decrease over time in both groups without significant between group differences at all visits.

Evaluation by an independent evaluator. Based on the evaluation performed by the independent evaluator at 4, 8, 12 and 16 weeks for the FAS population, the rate of improvement at the maximum smile was 80.67% (96/119 subjects), 55.46% (66/119 subjects), 28.57% (34/119 subjects) and 12.61% (15/119 subjects) in the test group and 78.33% (94/120 subjects), 50.83% (61/120 subjects), 35.00% (42/120 subjects) and 12.50% (15/120 subjects) in the control group, respectively. There was no significant difference between the groups at any time point (Table 3). The results of the PPS population were similar to those of the FAS population. Differences in improvement rates between the groups at-rest state were significant at 12 (63.03% vs. 48.33% in FAS, 62.07% vs. 48.74% in PPS) and 16 weeks (54.62% vs. 35.00% in FAS, 53.91% vs. 35.59% in PPS, Table 3). However, no significant difference was observed at 4 and 8 weeks.

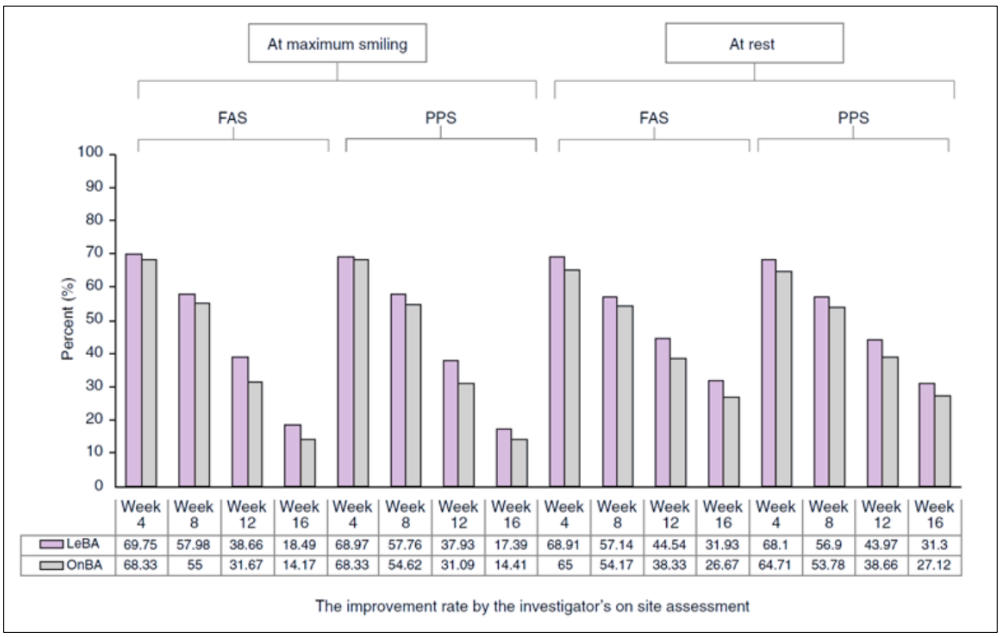


Figure 2 Response rate of crow's feet lines (CFL) at the maximum smile and rest according to the investigator's assessment. The results of the per-protocol set (PPS) analysis are presented to the right. (LeBA, letibotulinumtoxin A; OnBA. onabotulinum toxin A).

Table 3 | Crow's Feet Line (CFL) Improvement Rate According to the Independent Evaluator

	Full Analysis Set			Per-Protocol Set		
	LeBA *N* = 119	**OnBA *N* = 120**	**P-value**	**LeBA *N* = 116**	**OnBA *N* = 119**	**P-value**
Improvement§ rate, Week 4						
The Maximum Smile	96 (80.67)	94 (78.33)	0.6543†	94 (81.03)	93 (78.15)	0.5836†
Rest	95 (79.83)	90 (75.00)	0.3718†	92 (79.31)	90 (75.63)	0.4998†
Improvement§ rate, Week 8						
The Maximum Smile	66 (55.46)	61 (50.83)	0.4734†	64 (55.17)	60 (50.42)	0.4657†
Rest	81 (68.07)	70 (58.33)	0.1188†	78 (67.24)	70 (58.82)	0.1815†
Improvement§ rate, Week 12						
The Maximum Smile	34 (28.57)	42 (35.00)	0.2860†	32 (27.59)	41 (34.45)	0.2554†
Rest	75 (63.03)	58 (48.33)	0.0223†	72 (62.07)	58 (48.74)	0.0399†
Improvement§ rate, Week 16						
The Maximum Smile	15 (12.61)	15 (12.50)	0.9804†	13 (11.30)	15 (12.71)	0.7411†
Rest	65 (54.62)	42 (35.00)	0.0023†	62 (53.91)	42 (35.59)	0.0049†

CFL, Crow's feet line; LeBA, letibotulinumtoxin A; N, number of subjects, number of subjects for each item (%); OnBA, onabotulinumtoxin A.
§Improved = Facial Wrinkle Scale (FWS) of CFL was 0 or 1, Not improved = FWS of CFL was 2 or 3. Comparison between groups: Pearson's chi-square test (†) or Fisher's exact test (‡).

Self-evaluation by the subjects. Based on the evaluation performed by the subjects in FAS, the responder rate at the maximum smile was only significantly different between the groups at week 8 (93.27% vs. 83.81% in FAS, 93.14% vs. 83.65% in PPS). Except for these results, the difference in the response rates between the two groups was not significant and showed a tendency to decrease over time in both groups. The results of the PPS population were similar to those of the FAS population. The results of the at-rest states tended to be similar in both groups without significant between-group differences at all visits.

Subject satisfaction. Based on the FAS population, the respective subject satisfaction rates at 4, 8, 12 and 16 weeks were 92.44% (110/119 subjects), 89.92% (107/119 subjects), 71.43% (85/119) and 54.62% (65/119 subjects) in the test group and 89.17% (107/120 subjects), 80.00% (96/120 subjects), 63.33% (76/120 subjects) and 43.33% (52/120 subjects) in the control group, respectively. The differences between the groups

were significant only at 8 weeks (89.92% vs. 80% in FAS, 89.66% vs. 79.83% in PPS). The results of the PPS population were similar to those of the FAS population.

Safety outcomes. Two cases (1.68%, 2/119 subjects) of adverse events at the local injection sites were reported in the test group; both events were designated as local adverse drug reactions, not serious local adverse events. The following serious adverse events occurred after drug administration: 'diplopia' of 'eye disorders' in the test group [0.84% (1/119 subjects, one case)] and 'malignant fibrous histiocytoma' of 'neoplasms benign, malignant and unspecified (incl. cysts and polyps)' in the control group [0.83% (1/121 subjects, one case)]. None of these serious adverse events were found to be related to the investigational product.

Discussion[4]:

LetibotulinumtoxinA (LeBA) is a 900 kDa type A botulinum neurotoxin complex approved in South Korea for multiple indications. This study evaluated its safety and efficacy for CFLs.

LeBA met the predefined non-inferiority criteria compared to onabotulinumtoxinA (OnBA) at the 4-week primary endpoint, with comparable improvement rates (69.75% vs. 68.33%). These rates align with previously reported CFL outcomes for other BoNT-A products across different populations.

Secondary analyses showed similar trends between treatment arms over the 16-week follow-up period. However, isolated timepoints demonstrated statistically significant differences favoring LeBA, particularly: Week 12 and 16 (at rest, photo-based assessments) and Week 8 (subject-reported outcomes (satisfaction and perceived efficacy with LeBA)

While these findings may suggest a trend toward enhanced durability or patient-perceived benefit with LeBA, the study concludes that LeBA is non-inferior to OnBA for CFL treatment.

One serious adverse event (diplopia) occurred in the LeBA group but was determined to be unrelated to treatment following ophthalmologic and neurologic evaluation. Recovery occurred within 2 weeks, and the case was reported to and acknowledged by the MFDS as not treatment-related. No significant differences in the rate or type of adverse events were observed between groups.

Limitations include a homogeneous Korean study population and a relatively short 16-week observation period. Longer-term and more diverse studies may be needed to fully understand the safety and durability profile of LeBA across populations.

Approved Indication for Letybo®

Letybo® (letibotulinumtoxinA-wlbg) is an acetylcholine release inhibitor and a neuromuscular blocking agent indicated for the temporary improvement in the appearance of moderate to severe glabellar lines associated with corrugator and/or procerus muscle activity in adult patient[1].

Important Safety Information:

WARNING: DISTANT SPREAD OF TOXIN EFFECT

Postmarketing safety data from other approved botulinum toxins suggest that botulinum toxin effects may be observed beyond the site of local injection. The symptoms are consistent with the mechanism of action of botulinum toxin and may include asthenia, generalized muscle weakness, diplopia, ptosis, dysphagia, dysphonia, dysarthria, urinary incontinence, blurred vision and breathing difficulties. These symptoms have been reported hours to weeks after injection. Swallowing and breathing difficulties can be life threatening and there have been reports of death related to spread of toxin effects. In unapproved uses and approved indications, symptoms consistent with spread of toxin effects have been reported at doses comparable to or lower than the maximum recommended total dose. LETYBO is not approved for any conditions other than glabellar lines. Patients or caregivers should be advised to seek immediate medical care if swallowing, speech or respiratory difficulties occur.

Letybo is contraindicated in individuals with known hypersensitivity to any botulinum toxin preparation or to any of the components in the LETYBO formulation and/or have an infection at the injection site.

The potency Units of Letybo® are specific to the preparation and assay method utilized. Letybo® is not equivalent to other preparations of botulinum toxin products, and therefore, Units of biological activity of Letybo® cannot be compared to nor converted into Units of any other botulinum toxin products assessed with any other specific assay method.

This response contains information that is not included in the approved Product Information label. Hugel Inc. and BENEV Inc. do not endorse the use of its products in a manner not consistent with the approved label. For approved products, please refer to the full Prescribing Information for additional information. The Prescribing Information label for Letybo® is available at: bit.ly/3UbRZtP