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IncobotulinumtoxinA for Glabellar Frown Lines in Chinese Subjects: A Randomized, Double-blind, Active-Controlled Phase-3 Study

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Background: This study evaluated the efficacy and safety of IncobotulinumtoxinA 20 U for treatment of glabellar frown lines in Chinese subjects.
Methods: This was a prospective, randomized, double-blind, active-controlled, phase-3 study conducted in China. Subjects with moderate to severe glabellar frown lines at maximum frown were randomized to receive IncobotulinumtoxinA (N = 336) or OnabotulinumtoxinA (N = 167).
Results: For the primary efficacy endpoint at day 30, response rates at maximum frown (score "none" or "mild") on the Merz Aesthetic Scales Glabella Lines – Dynamic were comparable between IncobotulinumtoxinA (92.5%) and OnabotulinumtoxinA (95.1%) per investigator's live rating. Noninferiority of IncobotulinumtoxinA versus OnabotulinumtoxinA was successfully demonstrated, as the two-sided 95% confidence interval of −0.97% to 0.43% for the difference in Merz Aesthetic Scales-based response rates (−0.27%) lay completely above the predefined noninferiority margin of −15%. For the secondary efficacy endpoints assessed at day 30, Merz Aesthetic Scales-based response rates (score "none" or "mild") at maximum frown were similarly comparable between both groups per subject (>85%) and independent review panel (>96%) rating. Per Global Impression of Change Scales, greater than 80% of subjects and greater than 90% of investigators in both groups rated treatment results as at least "much improved" at day 30 compared with baseline. Safety profiles were consistent between groups; IncobotulinumtoxinA was well tolerated, and no new safety concerns were identified in Chinese subjects.
Conclusion: IncobotulinumtoxinA 20 U is safe and effective for treatment of moderate to severe glabellar frown lines at maximum frown in Chinese subjects and is noninferior to OnabotulinumtoxinA 20 U. *(Plast Reconstr Surg Glob Open 2023; 11:e4956; doi: 10.1097/GOX.0000000000004956; Published online 26 May 2023.)*

INTRODUCTION

IncobotulinumtoxinA (Xeomin, Bocouture; Merz Pharmaceuticals GmbH, Frankfurt am Main, Germany) is a highly purified botulinum toxin A (BoNT/A) preparation providing active toxin without complexing proteins[1] and is approved to treat glabellar frown lines (GFL) in the United States[2] and European Union.[3] In the EU, IncobotulinumtoxinA is further approved to treat upper facial lines, the simultaneous treatment of GFL, lateral canthal lines, and horizontal forehead lines.[3] Although clinical investigations supporting the use of IncobotulinumtoxinA for GFL treatment were conducted mainly in White populations,[4–6] GFL are also a common aesthetic concern for Asian patients.[7,8] Recent prospective investigation indicated favorable efficacy and safety of IncobotulinumtoxinA for GFL treatment in a small cohort of BoNT/A-naïve and BoNT/A-experienced Asian subjects,[9] similar to results from postmarket and retrospective analyses in this population.[10,11]

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The current work describes the first randomized controlled trial evaluating the efficacy and safety of IncobotulinumtoxinA for GFL treatment in Chinese subjects. This phase-3 study was designed to establish noninferiority of IncobotulinumtoxinA compared with OnabotulinumtoxinA (Botox, Allergan plc, Dublin, Ireland), already approved for GFL treatment in China.[12] Previous investigations conducted in Europe and North America demonstrate that IncobotulinumtoxinA 20 U is equivalent/noninferior to OnabotulinumtoxinA 20 U for GFL correction.[13,14] Consistent with prior studies, the current work provides evidence of comparability between IncobotulinumtoxinA and OnabotulinumtoxinA for GFL treatment in the Chinese population.

Takeaways

Question: Is IncobotulinumtoxinA a safe and effective treatment for glabellar frown lines in Chinese subjects?

Findings: This prospective, randomized, double-blind, active-controlled, phase-3 study was conducted at 11 sites in China. Investigator's live ratings at day 30 indicated high (>92%) response rates in IncobotulinumtoxinA and OnabotulinumtoxinA groups. Results demonstrated efficacy of IncobotulinumtoxinA for glabellar frown line treatment in Chinese subjects and its noninferiority to OnabotulinumtoxinA. IncobotulinumtoxinA was safe and well tolerated in Chinese subjects, with reported events consistent with its known safety profile, and no new concerns identified.

Meaning: IncobotulinumtoxinA is safe and effective for treatment of moderate to severe glabellar frown lines in Chinese subjects.

SUBJECTS AND METHODS

Study Design

This prospective, randomized, double-blind, active-controlled, phase-3 study was conducted at 11 sites in China (chinadrugtrials.org.cn identifier: CTR20171186) in compliance with Chinese Good Clinical Practice, the Declaration of Helsinki, and Chinese regulatory requirements. This clinical study was registered under Chinadrugtrials Registry (registration identification number and date registered: CTR20171186; 30-OCT-2017; registry URL: https://www.wuxuwang.com/linchuang/dceaa9f4-a185-11ea-82b4-00163e0eafb3). Before initiation, the protocol was approved by an independent ethics committee. Subjects provided written informed consent before any study-related procedures. Subjects were randomized 2:1 to receive injection with IncobotulinumtoxinA 20 U or OnabotulinumtoxinA 20 U using current prescribing information.[2,3,15] After treatment, subjects entered a 120 ± 7 day observation period, with five follow-up visits to monitor efficacy and safety at 8 ± 3, 30 ± 7, 60 ± 7, 90 ± 7, and 120 ± 7 days postinjection.

Study Subjects

Eligible subjects included male and female Chinese outpatients (aged ≥18 to ≤65 years), with moderate to severe (score: 2 or 3) GFL at maximum frown per investigator live rating on the five-point Merz Aesthetics Scales (MAS) Glabella Lines – Dynamic. Key exclusion criteria were: BoNT treatment (any serotype) in the facial area for 6 months or less; facial cosmetic procedure in the glabella area for 6 months or less; treatment with biodegradable filler in the glabella area for 12 months or less; previous insertion of permanent material in the glabella area; or planned facial cosmetic treatment during the study.

Study Treatment

Unblinded personnel used 2.5 mL sterile, unpreserved, physiological 0.9% saline solution to reconstitute one vial (100 U) of IncobotulinumtoxinA or OnabotulinumtoxinA. Blinded syringes were loaded with 20 U (0.5 mL) reconstituted BoNT/A and presented to the treating investigator for injection with a 30G needle in 4 U (0.1 mL) aliquots to five injection points: procerus muscle, medial (inner) part of both corrugator muscles, and middle part of both corrugator muscles.

Efficacy Assessments and Endpoints

At baseline and all postbaseline visits, two photonumeric MAS were used by investigators and subjects to evaluate GFL severity at rest (Glabella Lines – At Rest) and at maximum frown (Glabella Lines – Dynamic) on a five-point scale (0, no lines; 1, mild lines; 2, moderate lines; 3, severe lines; and 4, very severe lines). Both MAS were validated[16,17] and have been used in IncobotulinumtoxinA studies in White[6,18] and Asian (Dynamic only)[9] subjects. For this study, both MAS were adapted slightly for the Chinese population; the GFL severity displayed remained identical to the original MAS.[16] All MAS were translated to Chinese through linguistic validation.

To re-confirm reliability of the adapted MAS in Chinese subjects, a live validation with two rating sessions (14 days apart) was performed in China. In total, 56 Chinese subjects participated [mean (SD) age: 46.5 (15.37) years; range: 21–75 years], representing all GFL severity levels. Three aesthetic clinicians independently evaluated each subject's GFL at rest and maximum frown using the respective MAS. Inter-rater reliability (intraclass correlation and weighted Kappa) for both sessions was 0.87 or more ("almost perfect") for MAS Glabella Lines – At Rest and 0.78 or more ("substantial") for MAS Glabella Lines – Dynamic.[19] Overall intrarater reliability was greater than or equal to 0.89 ("almost perfect") for MAS Glabella Lines – At Rest and 0.91 or more ("almost perfect") for MAS Glabella Lines – Dynamic. Results confirmed both MAS allow for consistent clinical assessments of GFL severity in Chinese subjects.

The primary efficacy endpoint was the percentage of responders at maximum frown (score "none (0)" or "mild (1)" on MAS Glabella Lines – Dynamic) at day 30 per investigator live rating. All investigators were trained and qualified on both MAS before evaluating study subjects. Two secondary efficacy endpoints were defined as

the percentage of responders at maximum frown at day 30 per (1) subject live rating and (2) independent rater panel review of subject photographs. The independent rater panel included three qualified physicians, highly experienced in BoNT/A-GFL treatment. All three raters received prior MAS training and qualification, and treatment response was assumed if two or more raters scored a subject as "none (0)" or "mild (1)."

Severity of GFL at rest was also assessed by the investigator, subject, and independent rater panel. As baseline status was not restricted to a specific severity grade, treatment response was defined as one or more point improvement on the MAS Glabella Lines – At Rest. To evaluate GFL appearance at day 30 compared with baseline status (per subject photograph), the subject and investigator provided Global Impression of Change Scale (GICS) ratings on a seven-point scale, ranging from +3 (very much improved) to –3 (very much worse); a score of 0 indicated no change. Treatment response was defined as a score of at least +2 (much improved) at day 30. Subjects also completed diaries for 14 days postinjection to record onset of treatment effect.

Safety Assessments and Endpoints

Safety assessments included monitoring incidence, causal relationship to treatment, and seriousness of the following: adverse events (AEs) as determined by the investigator, deaths, AEs leading to discontinuation, and AEs of special interest (AESI; AEs indicating potential toxin spread). Incidence of AEs was a secondary safety endpoint.

Statistical Analysis

Efficacy analyses were conducted on the per protocol set (PPS; all treated subjects with MAS score at maximum frown per investigator rating at baseline and day 30, without major protocol deviations) for observed cases (OC). Unless otherwise stated, all efficacy results are reported for the PPS. For confirmatory analysis of the primary efficacy endpoint on the PPS, the adjusted difference in response rates was derived using a generalized linear model for binary data. This model was fitted to treatment response at maximum frown at day 30 with treatment group, site, gender, and BoNT pretreatment status as fixed factors and baseline MAS score and age as covariates. A two-sided 95% confidence interval (CI) for the adjusted difference in response rates was derived using the delta method. Noninferiority of IncobotulinumtoxinA compared with OnabotulinumtoxinA was concluded if this 95% CI lay completely above the predefined noninferiority margin of –15%.

For sensitivity, the analysis was repeated on the full analysis set (FAS; all treated subjects with MAS score at maximum frown per investigator rating at baseline and onre or more postbaseline visit) for OC, with exploratory two-sided 95% CI built for the unadjusted difference in response rates using the Wilson method (Newcombe score, no continuity correction) for the PPS and FAS. Analogous analyses were performed for secondary efficacy endpoints. Other MAS-based efficacy endpoints were analyzed by frequency tables including 95% Wilson CIs for differences in response rates. Time to onset of treatment effect was analyzed using Kaplan-Maier to calculate median duration of effect per treatment group and by log-rank test. For safety endpoints, descriptive analyses were conducted for the safety evaluation set (all treated subjects). All statistical analyses were performed using SAS version 9.4 (Cary, N.C.).

RESULTS

Participants

A total of 503 subjects were randomized, and 500 (99.4%) subjects received treatment with IncobotulinumtoxinA (N = 333) or OnabotulinumtoxinA (N = 167) (Fig. 1) and were included in the safety evaluation set. The PPS included 481 subjects (IncobotulinumtoxinA: N = 319; and OnabotulinumtoxinA: N = 162), with 22 subjects excluded for major protocol violations. PPS-subject demographics were comparable between groups (Table 1). All subjects presented at baseline with moderate or severe GFL at maximum frown, with approximately even score distributions in both groups. Most subjects in both groups presented at baseline with none or mild GFL at rest (IncobotulinumtoxinA: 68.9%; OnabotulinumtoxinA: 75.9%) (Table 1).

Primary Efficacy Analysis

Per investigator live rating, treatment response rates at maximum frown (score of "none (0)" or "mild (1)" on MAS Glabella Lines – Dynamic) at day 30 were comparably high in both groups (IncobotulinumtoxinA: 92.5% [295/319]; OnabotulinumtoxinA: 95.1% [154/162]; Fig. 2), corresponding to an unadjusted difference in response rates of –2.6% (95% CI: [–6.8% to 2.5%]). The decisive primary confirmatory analysis yielded an adjusted difference in response rates of –0.27% (95% CI: [–0.97% to 0.43%]) (Table 2). As the two-sided 95% CI for the adjusted difference in response rates lay completely above –15%, IncobotulinumtoxinA was shown to be noninferior to OnabotulinumtoxinA, successfully demonstrating efficacy of IncobotulinumtoxinA for treatment of moderate to severe GFL at maximum frown. This finding was confirmed by sensitivity analyses on the PPS and FAS.

Secondary Efficacy Analyses

Per independent rater panel review of subject photographs, treatment response rates at maximum frown at day 30 were high and comparable between treatment groups (IncobotulinumtoxinA: 96.9% [309/319]; OnabotulinumtoxinA: 98.1% [159/162]; Fig. 3). A similar relationship was observed for treatment response rates at maximum frown per subject live rating at day 30 (IncobotulinumtoxinA: 85.9% [274/319]; OnabotulinumtoxinA: 88.9% [144/162]; Figure 4). Similar to the primary analysis, the adjusted differences in response rates at maximum frown per independent rater panel review (–0.01%; 95% CI: [–0.04% to 0.02%]) and for subject self-assessment (–0.62%; 95% CI: [–1.75% to 0.51%]) approached zero (Table 2). For the primary endpoint, both 95% CIs for the adjusted difference in

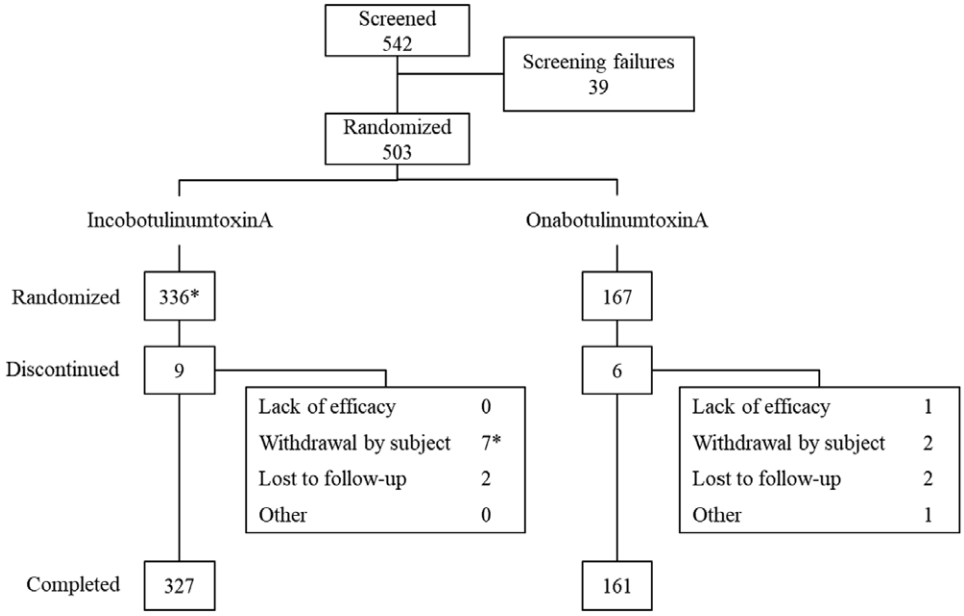

Fig. 1. Subject disposition. Three subjects (*) randomized to IncobotulinumtoxinA withdrew before receiving treatment.

Table 1. Subject Demographics (PPS)

	IncobotulinumtoxinA 20 U(N = 319)	OnabotulinumtoxinA 20 U(N = 162)	Total (N = 481)
Sex, n (%)			
Men	38 (11.9)	19 (11.7)	57 (11.9)
Women	281 (88.1)	147 (88.0)	442 (88.4)
Age (y)*			
Mean (SD)	44.8 (9.37)	45.9 (10.15)	45.2 (9.64)
Median	47.0	47.0	47.0
Min, max	21, 64	22, 65	21,65
Race, n (%)			
Asian	319 (100.0)	162 (100.0)	481 (100.0)
Baseline MAS score, n (%)†			
At maximum frown			
Moderate (2)	156 (48.9)	84 (51.9)	240 (49.9)
Severe (3)	163 (51.1)	78 (48.1)	241 (50.1)
At rest			
None (0)	47 (14.7)	26 (16.0)	73 (15.2)
Mild (1)	173 (54.2)	97 (59.9)	270 (56.1)
Moderate (2)	89 (27.9)	35 (21.6)	124 (25.8)
Severe (3)	10 (3.1)	4 (2.5)	14 (2.9)

Note: % = (n/N)*100.
*Age as documented in the case report form.
†Baseline MAS score determined by screening investigator at the baseline visit.
n, number of subjects; N, number of subjects in the analysis population.

response rates lay completely above −15% (PPS and FAS), supporting efficacy of IncobotulinumtoxinA.

Other Efficacy Endpoint Analyses

Throughout the study, treatment response rates at maximum frown were comparable between groups per investigator live rating (Fig. 2), independent rater panel review (Fig. 3), and by subject live rating (Fig. 4). At day 120, treatment effect remained for 51.9% (164/316) and 51.3% (82/160) of subjects treated with IncobotulinumtoxinA and OnabotulinumtoxinA, respectively (Fig. 2), per investigator live rating.

Overall, GFL status at rest also improved after treatment, with the highest treatment response rates at rest (≥1-point improvement) for both groups observed at day 30. When comparing IncobotulinumtoxinA versus OnabotulinumtoxinA, respectively, at day 30, response rates at rest were comparable between groups per investigator live rating (51.7% [165/319] versus 49.4% [80/162]), per independent rater panel review (25.1%

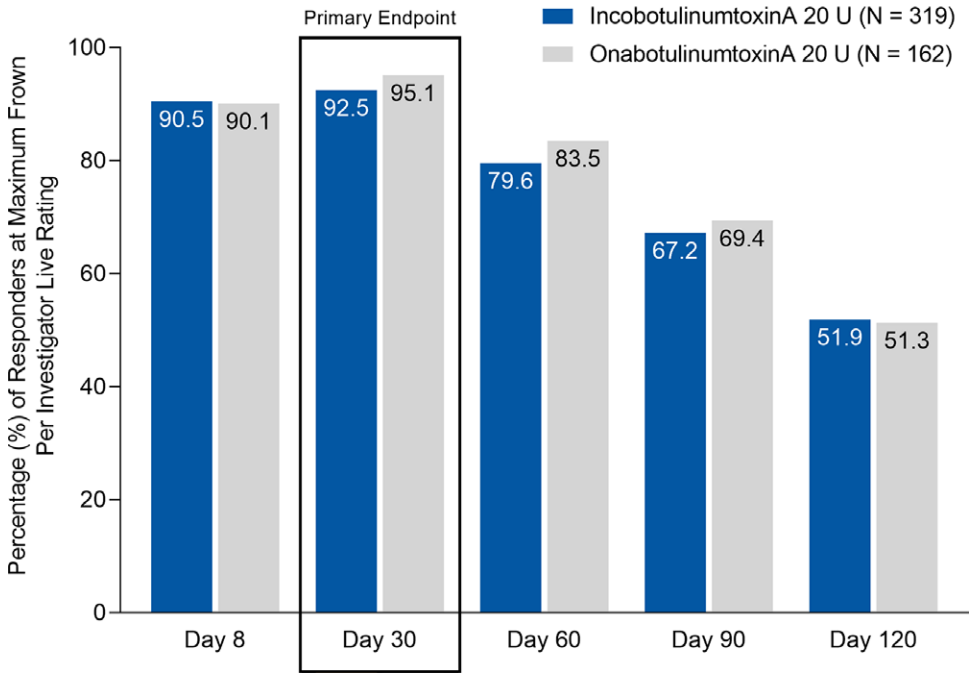

Fig. 2. Percentage of MAS responders at maximum frown, per investigator live rating. Response data are presented for OC in the PPS. Treatment response was defined as a score of "none (0)" or "mild (1)" on the MAS Glabella Lines – Dynamic.

Table 2. Response Rates per MAS at Maximum Frown at Day 30 (PPS, OC)

	IncobotulinumtoxinA 20 U (N = 319)		OnabotulinumtoxinA 20 U (N = 162)		Difference in Response Rates			
					Unadjusted		Adjusted†	
	n	(%)	n	(%)	%	[95% CI] *	%	[95% CI] ‡
Primary efficacy endpoint								
Per investigator	295	(92.5)	154	(95.1%)	– 2.6	[–6.8 to 2.5]	– 0.27	[–0.97 to 0.43]
Secondary efficacy endpoints								
Per independent rater panel	309	(96.9)	159	(98.1%)	– 1.3	[–4.1 to 2.4]	– 0.01	[– 0.04 to 0.02]
Per subject	274	(85.9)	144	(88.9%)	– 3.0	[– 8.8 to 3.7]	– 0.62	[– 1.75 to 0.51]

Note: % = (n/N) *100. Response per investigator and subject: MAS score of "none (0)" or "mild (1)" at day 30. Response per independent rater panel: MAS score of "none (0)" or "mild (1)" for majority of raters at day 30.
*CI based on Wilson's method (Newcombe score).
†Adjusted difference in response rates from a generalized linear model for binary data.
‡CI based on the delta method.
n, number of subjects; N, number of subjects in the analysis population.

[80/319] versus 25.3% [41/162]), and per subject live rating (63.6% [203/319] versus 60.5% [98/162]).

Consistent with MAS response rates, treatment response rates per GICS (defined as a score ≥"much improved") at day 30 were high and comparable for IncobotulinumtoxinA versus OnabotulinumtoxinA, respectively, as assessed by the subject (82.4% [263/319] versus 81.5% [132/162]) and investigator (91.5% [292/319] versus 93.8% [152/162]). This corresponded to differences in GICS response rates of 1.0% (95% CI: [–6.0 to 8.6]) per subject assessment and –2.3% (95% CI: [–6.8 to 3.2]) per investigator assessment.

Per subject diaries, median time to onset of treatment effect was 4.0 days (95% CI: 4.0–5.0) for both groups, and time to onset of treatment effect did not differ between groups (log-rank *P* value = 0.5910).

Safety

AE incidence was 28.5% (95/333) for the IncobotulinumtoxinA group and 34.7% (58/167) for the OnabotulinumtoxinA group; most AEs were mild to moderate in intensity in each group. The AE with the highest incidence rate for both groups was upper respiratory tract infection (IncobotulinumtoxinA: 6.3% [21/333]; OnabotulinumtoxinA: 6.6% [11/167]). (**See table, Supplemental Digital Content 1,** which displays the table reporting AEs at 1% or more incidence by preferred term by treatment group and in total. **http://links.lww.com/PRSGO/C517**.) Further, 1.8% (6/333) of subjects receiving IncobotulinumtoxinA experienced treatment-related AEs, compared with 4.2% (7/167) of subjects receiving OnabotulinumtoxinA. Serious AEs were reported for two subjects receiving IncobotulinumtoxinA (lower limb

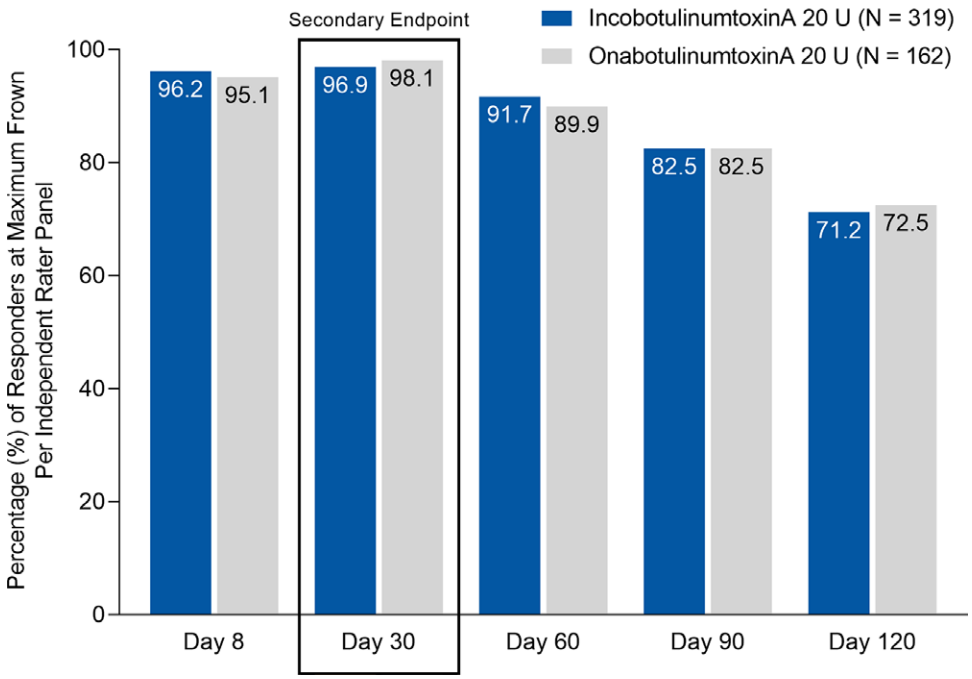

Fig. 3. Percentage of responders at maximum frown, per independent rater panel. Response data are presented for OC in the PPS. Treatment response was defined as a score of "none (0)" or "mild (1)" on the MAS Glabella Lines – Dynamic in the majority of raters.

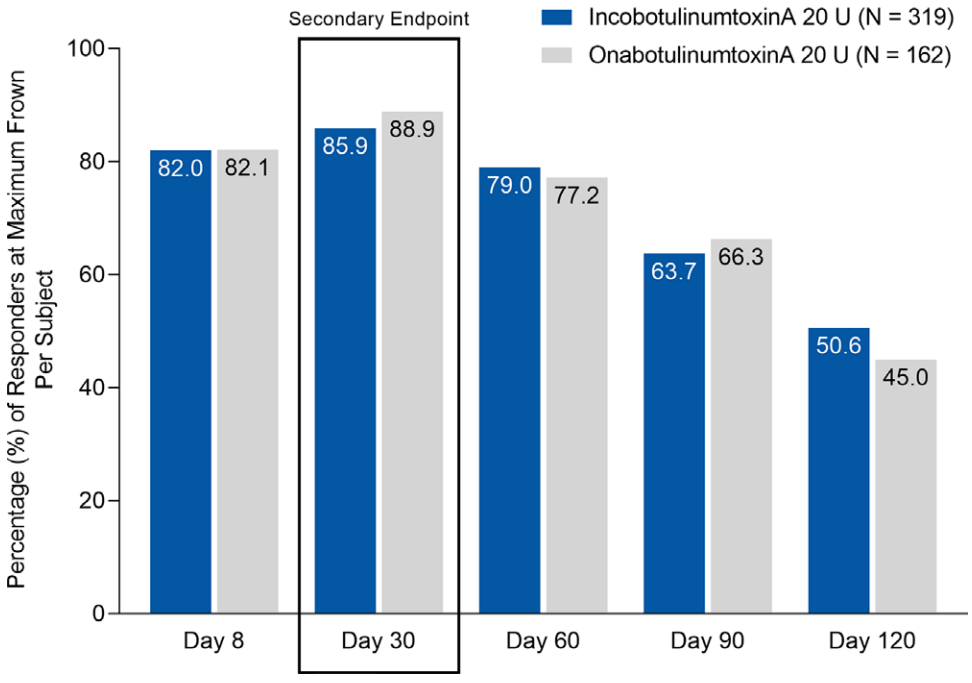

Fig. 4. Percentage of responders at maximum frown, per subject. Response data are presented for OC in the PPS. Treatment response was defined as a score of "none (0)" or "mild (1)" on the MAS Glabella Lines – Dynamic.

fracture; intravertebral disc protrusion). Neither was considered related to treatment, and both resolved or were resolving at study completion. No subject discontinued due to an AE, and no deaths occurred. Four subjects (IncobotulinumtoxinA: N = 1; OnabotulinumtoxinA: N = 3) experienced an AESI, all mild in severity. The only AESI categorized as related by the investigator was eyelid ptosis, occurring in two OnabotulinumtoxinA subjects.

DISCUSSION

BoNT/A use has increased immensely and is considered the most common nonsurgical aesthetic procedure worldwide.[20] Until recently, comparability of different BoNT/A preparations was not well defined due to a lack of head-to-head comparisons in randomized controlled trials, with a prior meta-analysis identifying only limited data to guide treatment selection of BoNT/A preparations.[21] In 2015, Kane et al demonstrated the equivalence of IncobotulinumtoxinA and OnabotulinumtoxinA for GFL treatment in primarily White cohorts;[13] however, limited efficacy and safety data were available for other racial/ethnic groups. This phase-3 study in Chinese subjects successfully demonstrates that IncobotulinumtoxinA 20 U is effective for treatment of moderate to severe GFL at maximum frown, with treatment effects comparable to the OnabotulinumtoxinA 20 U dose approved for GFL in China.[12] For the primary endpoint analysis, treatment response rates at maximum frown at day 30 were high in both groups (IncobotulinumtoxinA: 92.5%; OnabotulinumtoxinA: 95.1%) per investigator's live rating. Further, the adjusted difference in response rates (0.27%) and associated 95% CI [−0.97% to 0.43%] observed in the confirmatory primary analysis indicate IncobotulinumtoxinA 20 U is noninferior to OnabotulinumtoxinA 20 U, clearly demonstrating the efficacy of IncobotulinumtoxinA 20 U for aesthetic GFL treatment in Chinese subjects. Similar results were obtained for secondary endpoint analyses, with high and comparable treatment response rates at maximum frown observed between groups at day 30 per subject (>85% both groups) and independent rater panel (>96% both groups) rating, supporting the findings of the primary analysis.

High response rates observed after treatment are consistent with findings from a large, placebo-controlled, phase-3 study conducted in Europe examining IncobotulinumtoxinA 20 U for GFL treatment.[6] Further, noninferiority of IncobotulinumtoxinA 20 U versus OnabotulinumtoxinA 20 U demonstrated for GFL treatment in Chinese subjects is consistent with results from two large, head-to-head studies indicating noninferiority/equivalence of IncobotulinumtoxinA versus OnabotulinumtoxinA for aesthetic treatment of GFL in mainly White populations. In a European study of 381 subjects, IncobotulinumtoxinA 24 U was noninferior to OnabotulinumtoxinA 24 U for GFL treatment, with comparable response rates between groups 4 weeks postinjection as determined by independent raters (>95% both groups) and by investigator assessment (>95% both groups); response was defined as one or more point improvement on the four-point Facial Wrinkle Scale [range: "none (0)" to "severe (3)"] at maximum frown.[14] Using the same treatment response definition in a US study of 250 subjects, Kane et al demonstrated the clinical equivalence of IncobotulinumtoxinA 20 U and OnabotulinumtoxinA 20 U for GFL treatment; similar response rates at maximum frown were observed between groups at 30 days posttreatment as determined by an independent rater panel (>95% both groups) and by treating physician rating (>93% both groups).[13] Findings of the current study are also consistent with a recent prospective investigation of IncobotulinumtoxinA for GFL treatment in Asian subjects, where response rates (≥1-point improvement on the MAS Glabella Lines – Dynamic) were 100% for both BoNT/A-naïve (N = 23) and BoNT/A-experienced subjects (N = 22) at 14 days posttreatment, and improvement was maintained over at least 4 months.[9]

Altogether, the current study confirms the efficacy of IncobotulinumtoxinA in Chinese subjects and provides further, substantial clinical evidence for a 1:1 dose conversion ratio between IncobotulinumtoxinA and OnabotulinumtoxinA for aesthetic GFL treatment. Although clinical results are comparable across these BoNT/A preparations, clinicians should consider the least immunogenic BoNT/A formulation to minimize potential neutralizing antibody-associated responses, which may lead to reduced efficacy over time. This matter is of particular concern given the increase in younger patients seeking aesthetic toxin treatments.[1]

Time to onset of treatment effect, according to daily assessment by subjects, was identical between groups (4 days; 95% CI: 4.0–5.0) and consistent with previous investigations.[18,22] Additionally, high MAS response rates at maximum frown were observed for both groups up to 120 days posttreatment, as determined by investigator live rating, independent rater panel review, and subject self-assessment. This finding is consistent with previous investigations of IncobotulinumtoxinA in Asian subjects,[9] as well as placebo-controlled studies[6,12] and head-to-head, comparative investigations in mainly White cohorts,[13,14] demonstrating duration of treatment effect beyond 120 days is common for GFL treatment with IncobotulinumtoxinA across ethnic/racial groups. Additionally, IncobotulinumtoxinA treatment improved GFL aesthetic status at rest (ie, ≥1-point improvement) at day 30. Response rates for this parameter were generally lower than those at maximum frown, which is common for BoNTA.[18] Further evidence for meaningful clinical improvement and high satisfaction with treatment results comes from the high GICS response rates (score ≥ "much improved") at day 30 as reported by investigators (≥90% both groups) and subjects (≥80% both groups).

IncobotulinumtoxinA treatment was safe and well tolerated in Chinese subjects, with a slightly lower overall incidence of AEs compared with OnabotulinumtoxinA. No clinically meaningful differences in the type of AEs were observed between groups, with comparable incidence of treatment-related AEs (IncobotulinumtoxinA: 1.8%; OnabotulinumtoxinA: 4.2%). No treatment-related, serious AEs were observed in either group, and only two AESIs were considered related to treatment (eyelid ptosis, OnabotulinumtoxinA: N = 2). Overall, the safety profile for IncobotulinumtoxinA was consistent with current product labeling[2,3,15] and previous reports in the broad population[4,6,13,14,23–25] and in Asian subjects.[9,10,12] Due to exclusion of subjects with a history of facial nerve palsy, facial synkinesis was not observed in this study. Future investigations and treating physicians should be mindful of facial synkinesis as an under-recognized condition, one to potentially incorporate in GFL screening and treatment paradigms.[26,27]

CONCLUSIONS

In this double-blind phase-3 study in Chinese subjects, efficacy was successfully demonstrated as IncobotulinumtoxinA 20 U was noninferior to OnabotulinumtoxinA 20 U in the treatment of moderate to severe GFL at maximum frown. Secondary and further efficacy analyses through 4 months posttreatment consistently confirmed this result. IncobotulinumtoxinA was shown to be safe and well tolerated in Chinese subjects, with reported AEs consistent with the known safety profile for IncobotulinumtoxinA and no new safety concerns identified for Chinese subjects.

DISCLOSURES

Bi Li was a consultant for Merz Aesthetics, Inc. as a member of the Aesthetics China Expert Group, serving on an advisory board for Belotero in China. Susanna Roll, Gudrun Klein, and Thorin Geister are employees of Merz Pharmaceuticals GmbH. Michael Makara is a former employee of Merz North America, Inc. Yan Wu has no conflict of interest to declare in relation to the content of this article. This study was supported by Merz Pharmaceuticals GmbH.

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