HYC-24L Demonstrates Greater Effectiveness With Less Pain Than CPM-22.5 for Treatment of Perioral Lines in a Randomized Controlled Trial

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OBJECTIVE This trial compares the effectiveness and safety of HYC-24L (Juvéderm Ultra XC; Allergan plc, Dublin, Ireland) (24 mg/mL of hyaluronic acid, 0.3% lidocaine) and CPM-22.5 (Belotero Balance; Merz Aesthetics, Raleigh, NC) (22.5 mg/mL of hyaluronic acid) for the treatment of perioral lines.

MATERIALS AND METHODS Men and women aged 35 years or older with moderate-to-severe perioral lines were recruited for this randomized controlled, rater-blinded, 2-arm trial. The primary endpoint was a comparison of rater-assessed responder rates by the validated 4-point Perioral Lines Severity Scale at Month 6; responders were those who showed a ≥1 point improvement. A secondary endpoint was subject-assessed change in perioral lines measured by the Global Assessment of Change Scale.

RESULTS A total of 136 subjects received treatment and 132 completed the trial (mean age: 58 ± 8 years). Total volume injected was 1.18 mL (HYC-24L) and 1.32 mL (CPM-22.5). At Month 6, a significantly greater proportion of HYC-24L subjects responded to treatment (87%) than CPM-22.5 subjects (72%) ($p < .04$). At all time points, HYC-24L subjects reported significantly greater improvement in their perioral lines than CPM-22.5 subjects, with the greatest difference at Month 6. No unexpected adverse events occurred.

CONCLUSION HYC-24L subjects showed a higher response rate and a greater improvement in their perioral lines than CPM-22.5 subjects for up to 6 months.

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Perioral lines are the wrinkles that develop in the skin perpendicular to the direction of contraction of the orbicularis oris muscle, radiating superiorly from the vermilion border of the upper lip or inferiorly from the lower lip. These lines also are referred to as "vertical lip lines" or "bar code lines" and often develop in response to repetitive pursing of the lips. The development of these lines may be accelerated by age-related changes, such as thinning of the skin, degeneration of elastin and collagen, and atrophy of supporting muscles.[1,2]

A recent study found that by age 18 to 29 years, more than 20% of women and men had developed perioral lines, and this percentage increased to 60% by age 50 to 59 years (Data on file, Allergan plc, 2014). Another study found that women aged 50 years or older were increasingly bothered by their lower face features and were inclined to seek treatment of this area.[3] In particular, they selected the perioral area as "the most likely to treat" 54% of the time.[3]

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Perioral lines are frequently treated using soft hyaluronic acid (HA) dermal fillers.[4,5] As the perioral region is a dynamic area subject to a high degree of movement with facial animation, fillers used in this area must integrate well with the tissue to provide a "natural" look and feel both statically and with facial movement. To achieve these results, a filler must have the appropriate rheological properties to provide easy molding and spread within tissue, have minimal projection, and be non-palpable.[6] In addition, an ideal HA filler has low extrusion force, allowing for ease and precise dosing during injection.[6]

HYC-24L (Juvéderm Ultra XC; Allergan plc, Dublin, Ireland) and CPM-22.5 (Belotero Balance; Merz Aesthetics, Raleigh, NC) are HA dermal fillers approved in the United States for injection into the mid to deep dermis for correction of moderate-to-severe facial wrinkles and folds. HYC-24L is produced with 24 mg/mL of HA that is cross-linked using a proprietary manufacturing process called Hylacross, and 0.03% lidocaine is added to enhance patient comfort.[7] CPM-22.5 differs from HYC-24L because it is produced with 22.5 mg/mL of HA that is cross-linked using a different manufacturing process and is not formulated with lidocaine.[8] The different formulation and manufacturing process of HYC-24L provides greater cohesivity and a higher G′ than that of CPM-22.5.[6,9]

Despite widespread use of HYC-24L and CPM-22.5 for correction of perioral lines, these products have not been formally evaluated in this treatment area. Given the significant differences in the formulation and properties of these products, it is conceivable that they will demonstrate different levels of effectiveness. This is the first published head-to-head trial to compare the effectiveness and tolerability of these products for the treatment of moderate-to-severe perioral lines.

Materials and Methods

This was a 6-month, randomized, controlled, 2-arm, multicenter trial to assess the tolerability and effectiveness of HYC-24L versus CPM-22.5 for the treatment of upper and lower perioral lines. Touch-up treatment was given at approximately 2 weeks if needed. Follow-up visits were conducted by a blinded evaluating investigator at 7 and 14 days after the initial and touch-up treatments and at 1, 3, and 6 months after the last treatment. This trial was registered at www.clinicaltrials.gov (NCT #01970397) and approved by applicable institutional review boards. Subjects provided informed consent prior to enrollment.

Subjects

Male and female subjects aged 35 years or older were recruited from 8 North American sites from October 2013 to February 2014. Subjects were eligible for enrollment if they had moderate-to-severe perioral lines as assessed by the investigator using the validated Perioral Lines Severity Scale (POLSS).[10] Key inclusion and exclusion criteria are listed in Table 1.

The sample size calculation assumed a minimum between-arm difference of 0.30 points on the POLSS. With a 2-sided significance level of .05, 58 subjects per arm were needed to attain 80% power. Allowing for 10% attrition, a total 130 subjects (i.e., 65 per arm) were planned for enrollment.

Treatment

Subjects were randomized to receive treatment with either HYC-24L or CPM-22.5. Only the treating investigator and the study coordinator at each site had access to the randomization assignments. All clinical staff, the subjects, and the evaluating investigator remained blinded to the treatment assignment throughout the trial.

The treating investigator administered up to 2 treatments (i.e., the initial treatment and touch-up treatment given at 2 weeks if needed) with the aim of achieving optimum correction in the subjects' upper and lower perioral lines. Use of topical anesthesia, injection volume, needle gauge, technique, and depth of injection were at the investigator's discretion; however, injectors were instructed to inject each product in a similar manner. The maximum total

TABLE 1. Key Inclusion and Exclusion Criteria

Inclusion	*Exclusion*
Male or female ≥35 years	Have lip tattoos, facial hair, scars, or devices that would interfere with visualization of the lip or perioral area
Have moderate-to-severe perioral lines as assessed by the investigator on the POLSS	Have deformities in the perioral area
Agree to refrain from undergoing other facial procedures or treatments during the trial	Have a history of skin cancer
	Be a current smoker
	Have current inflammation, infection, cancerous or precancerous lesions, or unhealed wounds, herpes, or cold sores (within 12 months) in the perioral area
	Have undergone radiation treatment in the perioral area (any time prior to enrollment) or oral surgery (within 1 month prior to enrollment) or plan to undergo these procedures during the trial
	Use anticoagulation, antiplatelet, or thrombolytic medications
	Have undergone any of the following cosmetic procedures or treatments in the perioral area (or areas that may have affected the perioral area) prior to enrollment or plan to undergo any of these procedures during the trial: permanent cosmetic facial procedures (any time prior to enrollment), filler injections below the orbital rim (within 24 months), botulinum toxin for any indication below the infraorbital rims (within 12 months), facial mesotherapy or resurfacing procedures (within 6 months), new antiwrinkle products (within 3 months), or epilation (within 3 months)
	Be pregnant, lactating, or planning to become pregnant during the trial

volume allowed for each subject at the initial and touch-up treatments combined was 3.0 mL, a maximum of 2.0 mL at the initial treatment and 1.0 mL at the touch-up treatment. HYC-24L is supplied with 30-gauge needles, and CPM-22.5 is supplied with 27- and 30-gauge needles. Treatment details regarding topical anesthesia, volume, technique, and needles used were recorded.

Effectiveness Measures

Primary Effectiveness Endpoint

The primary endpoint was perioral line severity as assessed by the blinded evaluating investigator using the validated 4-point POLSS at Month 6. Scores on the POLSS can range from 0 (none) to 3 (severe). Responders were defined as subjects with a ≥1 point improvement on the POLSS.

Subject-Assessed Effectiveness Endpoints

Subjects assessed change in their perioral lines using the 7-point Subjects' Global Assessment of Change Scale (SGA) at all time points. Scores on the SGA can range from 1 (very much improved) to 7 (very much worse). A responder analysis defined responders as those who reported that their perioral lines were *very much improved*[1] or *much improved*.[2] Subjects also assessed natural look and natural feel of the perioral area at Months 1, 3, and 6 using 11-point scales of which 0 = unnatural and 10 = natural.

Pain, Bruising, and Tyndall

Pain was assessed by subjects at the initial visit during the injection and immediately, 15, 30, and 45 minutes after injection on an 11-point scale of which 0 = no pain and 10 = worst pain imaginable. Bruising and Tyndall were assessed by the evaluating investigator at Days 7 and 14 (after both initial and touch-up treatments).

Bruising was measured with the 5-point Bruising Assessment for Perioral Lines scale of which 0 = none and 4 = severe. Tyndall was reported as present or absent.

Ease-of-Injection

The treating investigator assessed the ease-of-injection during the initial treatment. Scores were rated on an 11-point scale of which 0 = difficult and 10 = easy.

Tolerability

All subjects who received treatment were included in the tolerability analyses. Adverse events (AEs) and serious AEs reported by the investigator were categorized as being related to the procedure or related to the device. Injection site reactions were recorded by subjects in a 30-day diary after each treatment. They were asked to document the presence of redness, pain, tenderness to touch, firmness, swelling, lumps/bumps, bruising, itching, discoloration, and/or other reactions. Severity was assessed as 0 = none, 1 = mild, 2 = moderate, or 3 = severe. If injection site reactions were unresolved at 30 days after the final treatment they were included as AEs.

Data Analyses

Primary and secondary effectiveness analyses were performed on a modified intent-to-treat population (i.e., subjects who received treatment) without imputation of missing data. Differences between response rates were calculated using a 2-sided, 2-arm χ^2 test. Differences between mean scores were calculated using a 2-sample *t*-test (or Wilcoxon rank sum test for non-normal data). Analyses were considered statistically significant at $p < .05$.

Results

Subjects

A total of 146 subjects were enrolled and screened in the trial, of whom 138 were randomized (i.e., 69 per arm). Two randomized subjects (i.e., 1 in each arm) were not treated; therefore, there were 68 subjects in each arm (Figure 1). No imputation was performed for missing data. In both arms, subjects were mainly female, Caucasian, and Fitzpatrick Skin Type II and III, and there were no statistically significant demographic differences between the groups (Table 2). Results from the per-protocol population were similar to the results from the modified intent-to-treat population; as such, this manuscript focuses on the modified intent-to-treat population only.

Treatment

Table 3 shows the treatment details for the HYC-24L and CPM-22.5 arms. The total volume injected was lower for the HYC-24L arm than the CPM-22.5 arm, although this difference was not statistically significant. Moreover, touch-up was needed for less than half of the HYC-24L subjects but most of the CPM-22.5 subjects. Topical anesthesia usage was similar

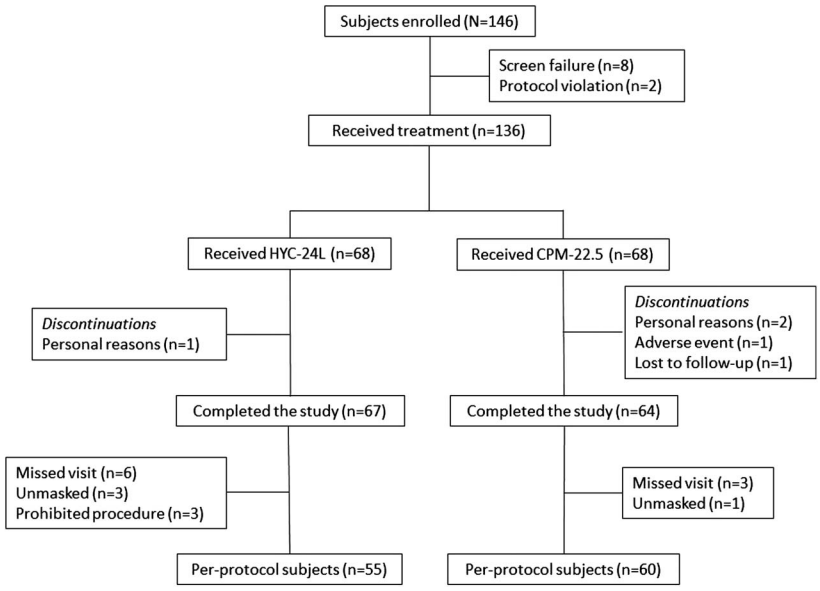

Figure 1. CONSORT diagram.

TABLE 2. Demographics

Characteristic	*HYC-24L (N = 68)*	*CPM-22.5 (N = 68)*	*All Subjects (N = 136)*
Age (years), mean ± SD	58.2 ± 7.5	58.2 ± 9.3	58.2 ± 8.4
Sex, *n* (%)			
Male	1 (1)	0	1 (1)
Female	67 (99)	68 (100)	135 (99)
Race/ethnicity, *n* (%)			
Caucasian	66 (97)	66 (97)	132 (97)
Asian	1 (1)	0	1 (1)
Hispanic	1 (1)	1 (1)	2 (1)
Unknown	0	1 (1)	1 (1)
Fitzpatrick skin type, *n* (%)*			
I	4 (6)	2 (3)	6 (4)
II	38 (56)	34 (50)	72 (53)
III	19 (28)	27 (40)	46 (34)
IV	6 (9)	3 (4)	9 (7)
V	1 (1)	1 (1)	2 (1)
Smoking status, *n* (%)			
Never smoked	35 (51)	37 (54)	72 (53)
Former smoker	33 (49)	31 (46)	64 (47)

*Missing data from 1 CPM-22.5 subject.

between the arms, and no nerve blocks were used. Most of the investigators in both arms used multiple injection techniques: for the initial and touch-up treatment combined, the most frequently used injection technique was linear threading, followed by serial puncture, cross-hatching, and fanning. There were no differences in the technique or depth of injection used to place each filler. All of the HYC-24L injections and most of the CPM-22.5 injections were performed using a 30-gauge needle.

Effectiveness Measures

Primary Effectiveness Endpoint

A significantly greater proportion of HYC-24L subjects (87%, $n = 58/67$) experienced a 1-point improvement in their perioral lines than CPM-22.5 subjects (72%, $n = 46/64$) as assessed by the POLSS at Month 6 ($p < .04$) (Figure 2). A significant difference was also found using data from the per-protocol population with an 87% ($n = 48/55$) responder rate in the HYC-24L arm and 71% ($n = 41/58$) in the CPM-22.5 arm ($p < .04$). In addition, at all time points the HYC-24L arm showed numerically greater mean improvement than the CPM-22.5 arm, with a statistically significant mean difference at Month 6 (Figure 3). Figures 4 and 5 show representative photographs of the subjects' perioral area at baseline, Month 1, and Month 6.

Subject-Assessed Effectiveness Endpoints

Subjects treated with HYC-24L reported significantly greater mean improvement in their perioral lines than CPM-22.5 subjects as assessed by the SGA at all time points evaluated. In addition, more HYC-24L subjects (79%) reported that their perioral lines were *very much improved* or *much improved* than CPM-22.5 subjects (48%) at Month 6 ($p < .001$) (Figure 6). Subjects rated both products as providing a similar natural look and natural feel at all time points. At Month 6, natural look was rated as 9.0 ± 1.5 by HYC-24L subjects and 8.5 ± 2.4 by CPM-22.5 subjects, and natural feel was rated as 9.4 ± 1.1 by HYC-24L subjects and 9.1 ± 2.2 by CPM-22.5 subjects.

Pain, Bruising, and Tyndall

On average, HYC-24L subjects reported significantly less pain (mean pain score: 2.9 ± 2.3) during the injection than CPM-22.5 subjects (4.4 ± 2.4) ($p < .001$). HYC-24L subjects also reported

TABLE 3. Initial and Touch-up Treatment Details

Characteristic	*HYC-24L*	*CPM-22.5*
Treatments		
Initial, *N*	68	68
Touch-up, *n* (%)	31 (46)	43 (63)
Volume (mL), mean ± SD		
Initial	0.96 ± 0.48	0.97 ± 0.43
Touch-up	0.49 ± 0.31	0.55 ± 0.29
Total*	1.18 ± 0.71	1.32 ± 0.63
Used anesthesia, *n* (%)		
Initial	67 (99)	68 (100)
Touch-up	31 (100)	42 (98)
Technique, *n* (%)†		
Linear threading	91 (92)	106 (95)
Serial puncture	54 (55)	55 (50)
Cross-hatching	50 (51)	49 (44)
Fanning	44 (44)	43 (39)
Multiple techniques	80 (81)	85 (77)
Single technique	19 (19)	26 (23)
Needle type, *n* (%)†		
30 gauge	99 (100)	108 (97)
27 gauge	0	3 (3)

*No significant difference between arms.
†Data refer to both initial and touch-up treatments.

significantly less postprocedural pain at all time points than CPM-22.5 subjects, with the exception of the 30-minute time point that approached significance at $p < .059$ (Figure 7). Immediately following the injection, HYC-24L subjects reported a mean pain score of 0.8 ± 1.2, whereas CPM-22.5 subjects reported a significantly greater mean score of 1.8 ± 1.9 ($p < .001$). At Days 7 and 14, numerically fewer HYC-24L subjects experienced bruising (Day 7: $n = 34$, Day 14: $n = 13$)

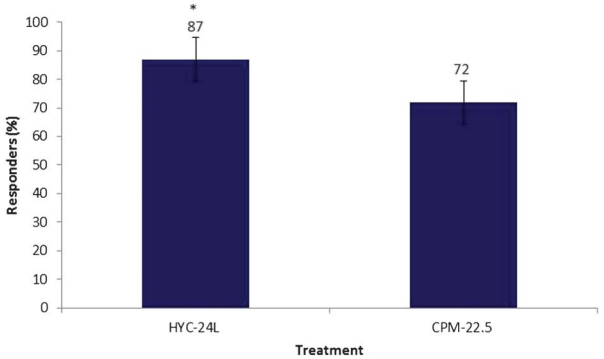

Figure 2. Percentage of HYC-24L and CPM-22.5 subjects who experienced a 1-point improvement in their perioral lines at Month 6 (*$p < .04$).

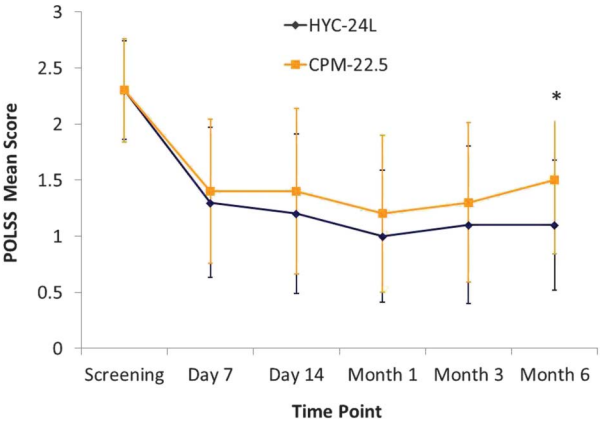

Figure 3. Mean improvement on the 4-point perioral lines severity scale for HYC-24L and CPM-22.5 subjects (*$p < .001$).

than CPM-22.5 subjects (Day 7: $n = 38$, Day 14: $n = 18$), and bruising appeared less severe in the HYC-24L arm. In almost all cases, the intensity of bruising was minimal or mild on both days. In a small number of subjects, there was moderate or severe bruising at Day 7, with a lower incidence of moderate bruising for the HYC-24L arm (3%) than the CPM-22.5 arm (12%). One subject had severe bruising at Day 7 (HYC-24L arm). No Tyndall effect was observed by investigators at the Day 7 or 14 evaluations; however, 1 episode was reported as a spontaneous AE by a CPM-22.5 subject at Month 3 (see the Tolerability section).

Ease-of-Injection

Treating investigators reported similar ease-of-injection scores for both arms. The mean scores were 7.9 ± 2.1 for the HYC-24L arm and 7.8 ± 2.0 for the CPM-22.5 arm.

Tolerability

Adverse Events

The number of subjects who had at least 1 AE were similar in the HYC-24L ($n = 20$, 29%) and CPM-22.5 ($n = 21$, 31%) arms. The majority of AEs were of mild or moderate intensity. One subject in the CPM-22.5 arm discontinued the trial due to an AE that was unrelated to the study product or procedure. No unexpected AEs occurred.

Adverse events related to the procedure were reported for 10 (15%) subjects in each arm (Table 4). The most

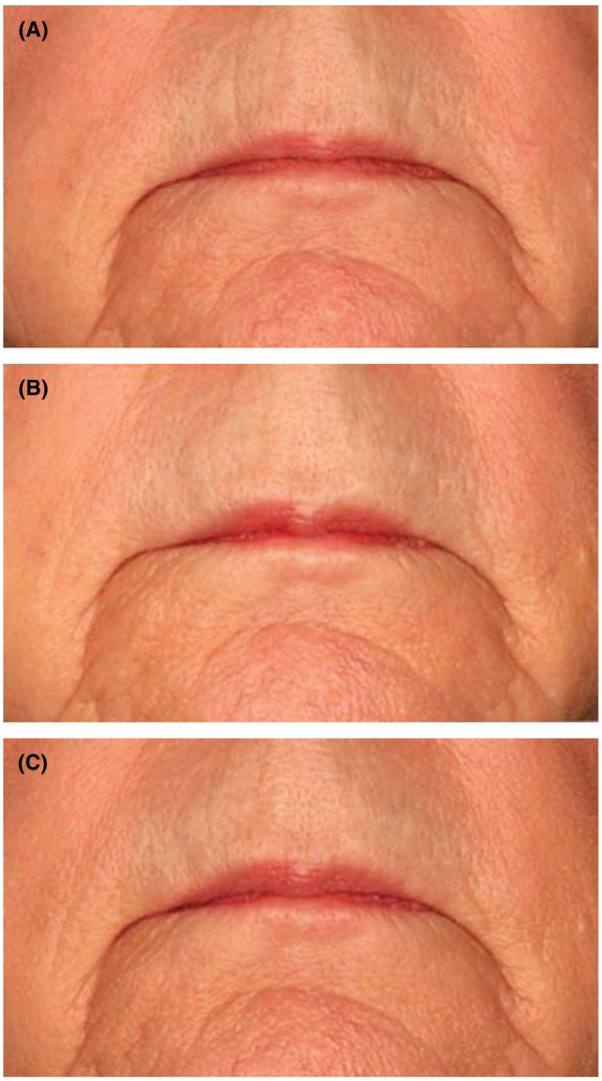

Figure 4. (A) A 79-year-old Caucasian woman who was enrolled in the HYC-24L arm. At Day 1, the subject had severe perioral lines as measured by the POLSS (score = 3). The subject was treated with 0.6 mL of HYC-24L (0.6 mL upper lip, 0 mL lower lip), and no touch-up treatment was needed. (B) At Month 1, the subject had mild perioral lines (POLSS score = 1). (C) At Month 6, the subject had mild perioral lines (POLSS score = 1).

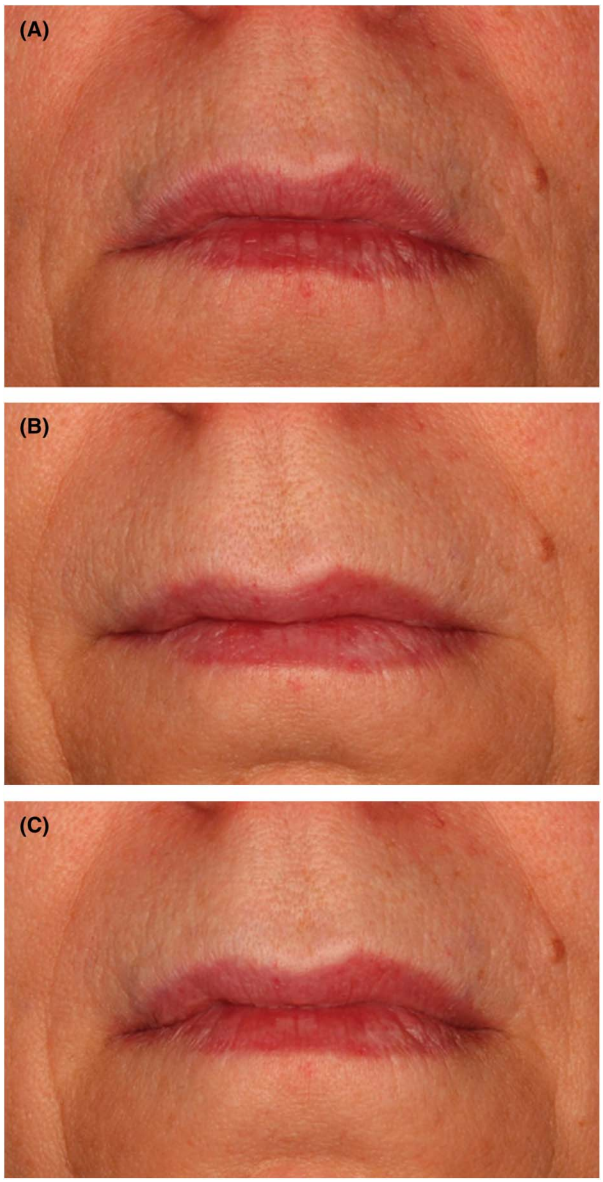

Figure 5. (A) A 56-year-old Caucasian woman who was enrolled in the CPM-22.5 arm. At Day 1, the subject had moderate perioral lines as measured by the POLSS (score = 2). The subject was treated with 0.95 mL of CPM-22.5 (0.9 mL upper lip, 0.05 mL lower lip), and at Day 14, the subject received 0.3 mL of touch-up treatment (upper lip 0.2 mL, lower lip 0.1 mL). (B) At Month 1, the subject had mild perioral lines (POLSS score = 1). (C) At Month 6, the subject had mild perioral lines (POLSS score = 1).

frequently reported AE related to the procedure was injection site bruising. All other procedure-related AEs were reported by no more than 3 subjects in either arm. Severe injection site bruising was reported for 1 (1%) subject in each arm. Adverse events deemed related to the device were reported for 3 (4%) subjects in the HYC-24L arm and 1 (1%) subject in the CPM-22.5 arm (Table 4). Furthermore, there was no indication that the 3 subjects injected using a 27-gauge needle experienced greater number or severity of AEs associated with treatment. There were no severe device-related AEs.

One episode of Tyndall effect of the upper lip was reported as a spontaneous AE by a CPM-22.5 subject on Day 106. This was observed by the blinded evaluating investigator and confirmed with a second site

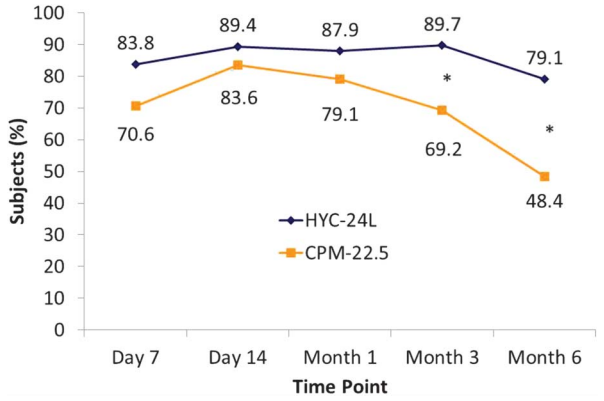

Figure 6. Percentage of subjects who reported that their perioral lines were *Improved* or *Very much improved* on the SGA (*$p < .005$).

staff member. This subject was treated with a total of 0.65 mL of CPM-22.5 (0.5 mL at the initial treatment and 0.15 mL at touch-up). The Tyndall was assessed as nonserious, and mild in intensity, and was resolved 17 days later. It was considered to be unrelated to the trial procedure but related to the device.

Injection Site Reactions

There were no statistically significant differences in incidence or severity of injection site reactions between the HYC-24L and CPM-22.5 arms. The most commonly reported reactions in both arms were bruising, swelling, lumps/bumps, firmness, and tenderness to touch (Table 5). The most frequently reported reactions that subjects rated as *severe* at any time point were bruising (HYC-24L: 26%, CPM-22.5: 34%) followed by swelling (HYC-24L: 16%, CPM-22.5: 12%), lumps/bumps (HYC-24L: 12%, CPM-22.5: 6%), and redness (HYC-24L: 4%, CPM-22.5: 13%).

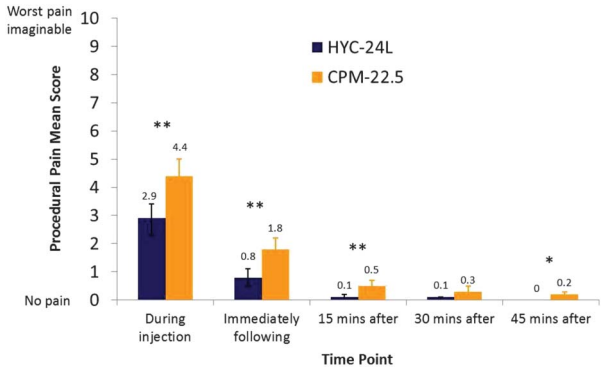

Figure 7. Procedural pain mean score for HYC-24L and CPM-22.5 subjects (*$p < .05$, **$p < .005$).

TABLE 4. Adverse Events Related to Procedure and Device, n *(%)*

AE	*HYC-24L*	*CPM-22.5*
Related to procedure		
Bruising	5 (7)	9 (13)
Induration	3 (4)	0
Swelling	3 (4)	0
Hematoma	1 (1)	0
Nodules	1 (1)	0
Dryness	0	1 (1)
Pain	0	1 (1)
Related to device		
Induration	2 (3)	0
Swelling	2 (3)	0
Nodules	1 (1)	0
Tyndall effect	0	1 (1)

For all other reactions, the incidence of those who reported a *severe* response was <10% in both arms.

Discussion

This is the first published study to compare HYC-24L and CPM-22.5 for the treatment of moderate-to-severe perioral lines. This trial met its primary endpoint and found that the subjects in the HYC-24L arm showed a significantly greater response rate than those in the CPM-22.5 arm as assessed by blinded investigators at Month 6. Secondary endpoints showed that the HYC-24L arm had greater mean improvement in perioral lines than the CPM-22.5 arm as assessed by

TABLE 5. Injection Site Reactions, n *(%)**

Response	*HYC-24L*	*CPM-22.5*
Bruising	59 (87)	62 (91)
Swelling	59 (87)	58 (85)
Lumps/bumps	52 (76)	46 (68)
Firmness	49 (72)	48 (71)
Tenderness to touch	49 (72)	45 (66)
Redness	43 (63)	43 (63)
Pain after injection	28 (41)	36 (53)
Itching	15 (22)	9 (13)
Discoloration	12 (18)	18 (26)
Other	11 (16)	9 (13)

*Subjects reported injection site reactions in a 30-day diary after each treatment (initial and touch-up, as applicable).

investigators and subjects. Both products provided a similar natural look and natural feel of the perioral region and a similar ease-of-injection. It is relevant to note that HYC-24L subjects received lower treatment volumes and fewer touch-up visits than CPM-22.5 subjects.

Despite physicians treating perioral lines to optimal correction, subjects perceived differences in effectiveness between the products at all time points, with the greatest difference at Month 6. This greater persistence of effectiveness at Month 6 suggests that HYC-24L may exhibit a longer duration of clinical benefit than CPM-22.5. Long-lasting correction may increase patient satisfaction, as it would reduce the frequency of repeat treatments.

Both arms had similar tolerability profiles, with some exceptions. First, despite no between-arm differences in the use of anesthesia, HYC-24L subjects experienced significantly less procedural pain than CPM-22.5 subjects at the initial treatment and at most time points thereafter. These lower pain scores most likely can be attributed to the inclusion of lidocaine in the HYC-24L formulation and suggests a more comfortable injection experience with HYC-24L. CPM-22.5 does not include lidocaine in the formulation, and therefore, some physicians will add it to reduce injection pain. However, the addition of lidocaine in the physician's office will dilute the product and may change its rheological properties, likely reducing the G′ and cohesivity. It is important to note that in this trial, CPM-22.5 was not altered. Second, fewer HYC-24L subjects experienced bruising than CPM-22.5 subjects, and bruising was less severe in the HYC-24L arm; however, these differences were not statistically significant. Third, it has been suggested that the Tyndall effect does not occur with CPM-22.5[11,12]; however, 1 case was observed in the CPM-22.5 arm. This result is consistent with post-marketing surveillance reports of the occurrence of the Tyndall effect in patients treated with CPM-22.5[8] and confirms that the Tyndall effect can occur with use of any HA-based dermal filler.

The results found in this trial may be attributable to the formulation and manufacturing process of HYC-24L. The higher concentration of cross-linked HA in the HYC-24L formula may protect the filler from metabolic degradation in the body, allowing for a greater persistence of the product.[13] Moreover, the manufacturing process of HYC-24L produces a gel with the appropriate rheological properties designed for dermal implantation, including the ability to treat dynamic areas of the face such as the perioral region. These specific rheological properties allow HYC-24L to withstand various types of deformation from intrinsic (e.g., motion between bone and overlying tissue) and extrinsic (e.g., motion associated with daily activities) forces when implanted in tissue, while also providing an optimal filling effect.[6]

A limitation of this trial is that the sample was comprised of mainly women and most were Caucasian and Fitzpatrick Skin Type II and III. Future studies could strive to enroll a more diverse population. In addition, a longer trial may provide additional evidence regarding duration of effect.

Blinded investigators and subjects found HYC-24L to be superior to CPM-22.5 for the treatment of moderate-to-severe perioral lines. Both implanted products had a similar natural look and natural feel, but HYC-24L provided more effective correction with less pain than CPM-22.5. These results can be attributed to the unique formula and proprietary manufacturing process of HYC-24L that provides a gel with the appropriate rheological properties needed for the perioral region. Aesthetic clinicians can use the results of this trial to help create tailored treatment algorithms and long-term treatment plans to attain optimal outcomes for their patients.

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