Safety and effectiveness of three new commercially available injectable dermal fillers in moderate to severe nasolabial folds treatment.

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BACKGROUND

Teoxane developed the new line of hyaluronic acid dermal fillers RHA (Resilient Hyaluronic Acid®), specifically dedicated to the dynamic areas of the face, using a patented "preserved network" technology with less BDDE and with higher strength and stretch properties.

OBJECTIVE

The objective of this double-blinded randomized controlled trial was to compare the safety and effectiveness of three new RHA fillers developed to fit the facial dynamics with that of classic competitors, for nasolabial folds (NLF) severity.

MATERIAL AND METHODS

Study design

The is an ongoing, pilot, prospective, double-blinded, split-face (one side injected with the tested product and the other side injected with the comparator), randomized (side and order of injection), controlled trial.

The study was carried out on 3 groups of 30 subjects:

- 30 subjects with moderate NLFs : Teosyal® RHA 2 versus Juvéderm® Volift
- 30 subjects with severe NLFs : Teosyal® RHA 3 versus Juvéderm® Ultra 4
- 30 subjects with severe NLFs : Teosyal® RHA 4 versus Teosyal® PureSense Ultra Deep

If deemed necessary, an optional touch-up injection was performed on Day 14 after initial treatment to achieve optimal cosmetic result, and evaluations were made at Month 1, 6, and 9 after baseline.

Subjects

The study included male and female between 40 and 70 years old, with 2 symmetrical moderate (WSRS=3) to severe (WSRS=4) nasolabial folds, on the 5-grade (1-5) Wrinkle Severity Rating Scale1.

Key exclusion criteria included absorbable filling product injections in the nasolabial folds within 1 year of study entry, Botulinum toxin injection in the face within 6 months of study entry, or a history of permanent or semipermanent filling products in the face.

Assessments

The main efficacy criterion was the WSRS score improvement from pre-injection, at 6 months after last injection session, by a Blinded Live Evaluator (BLE).

Secondary criteria included variation of the NLF volumes, GAIS, FACE-Q, satisfaction assessment.

Safety was assessed with Common Treatment Reactions (CTR), Patient's diaries, and AE collection.

RESULTS

Subject characteristics

The mean age of subjects was 57.9 years (± 8.12, SD), 83.3% were female, and 5.6% were Fitzpatrick skin phototype IV-VI.

WSRS

There were no statistically significant differences between the WSRS scores of the two products in each of the three arms, at any follow-up visit (Wilcoxon signed rank test, p=NS) (Figure 1)**.**

Table 1. WSRS (% of subjects with improvement at 9 months)

	Juvederm Volift	Teosyal RHA 2	Juvederm Ultra 4	Teosyal RHA 3	PureSense Ultra Deep	Teosyal RHA 4
At least 1-grade improvement	83.3	93.3	100.0	100.0	93.3	100.0
At least 2-grades improvement	30.0	13.3	62.1	55.2	60.0	65.5
At least 3-grades improvement	0.0	0.0	10.3	24.1	10.0	13.3

Figure 1. Volume of NLFs filled at 1, 6, and 9 months (fringe projection), in % from pre-treatment

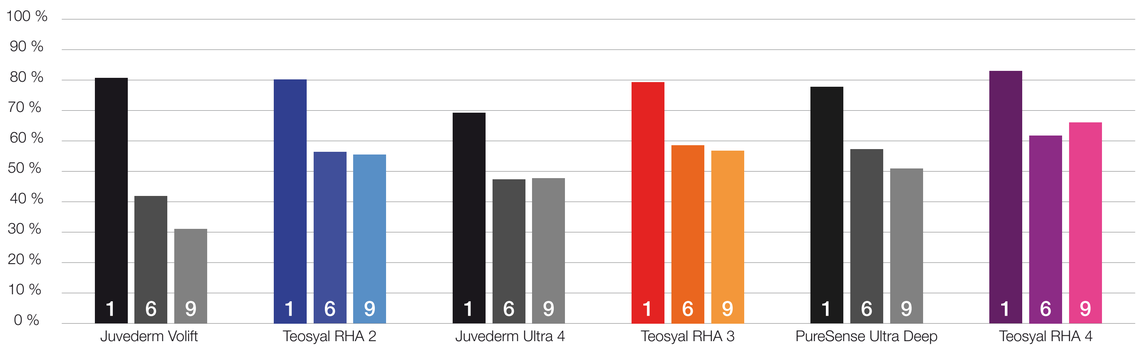
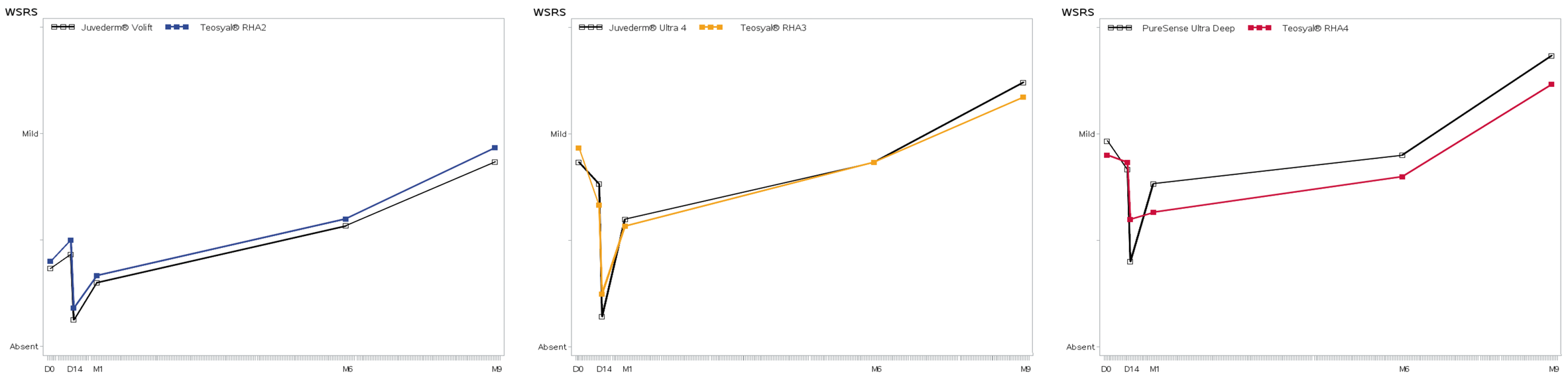


Figure 2. Wrinkle Severity



Physician's evaluation of the product

A touch-up was performed for 26.7% of the NLFs injected with a RHA product, and 35.6% of the NLFs with a control product.

Table 2. Satisfaction of Treating Investigators (% satisfied or very satisfied)

	Juvederm Volift	Teosyal RHA 2	Juvederm Ultra 4	Teosyal RHA 3	PureSense Ultra Deep	Teosyal RHA 4
Easiness of injection	100.0	95.1	95.5	97.4	85.0	97.1
Easiness of product positionning	100.0	95.1	91.0	100.0	92.5	100.0
Immediat aesthetic result	100.0	97.6	97.7	100.0	97.5	97.1
Aesthetic result after massage	100.0	100.0	100.0	100.0	100.0	100.0

GAIS and FACE-Q

All subjects and BLE rated the Global Aesthetic Improvement as improved or much improved, for all products, and there was no difference in appraisal of the NLF, at any follow-up visit.

Table 3. GAIS (% of opinion rated improved or much improved at 9 months)

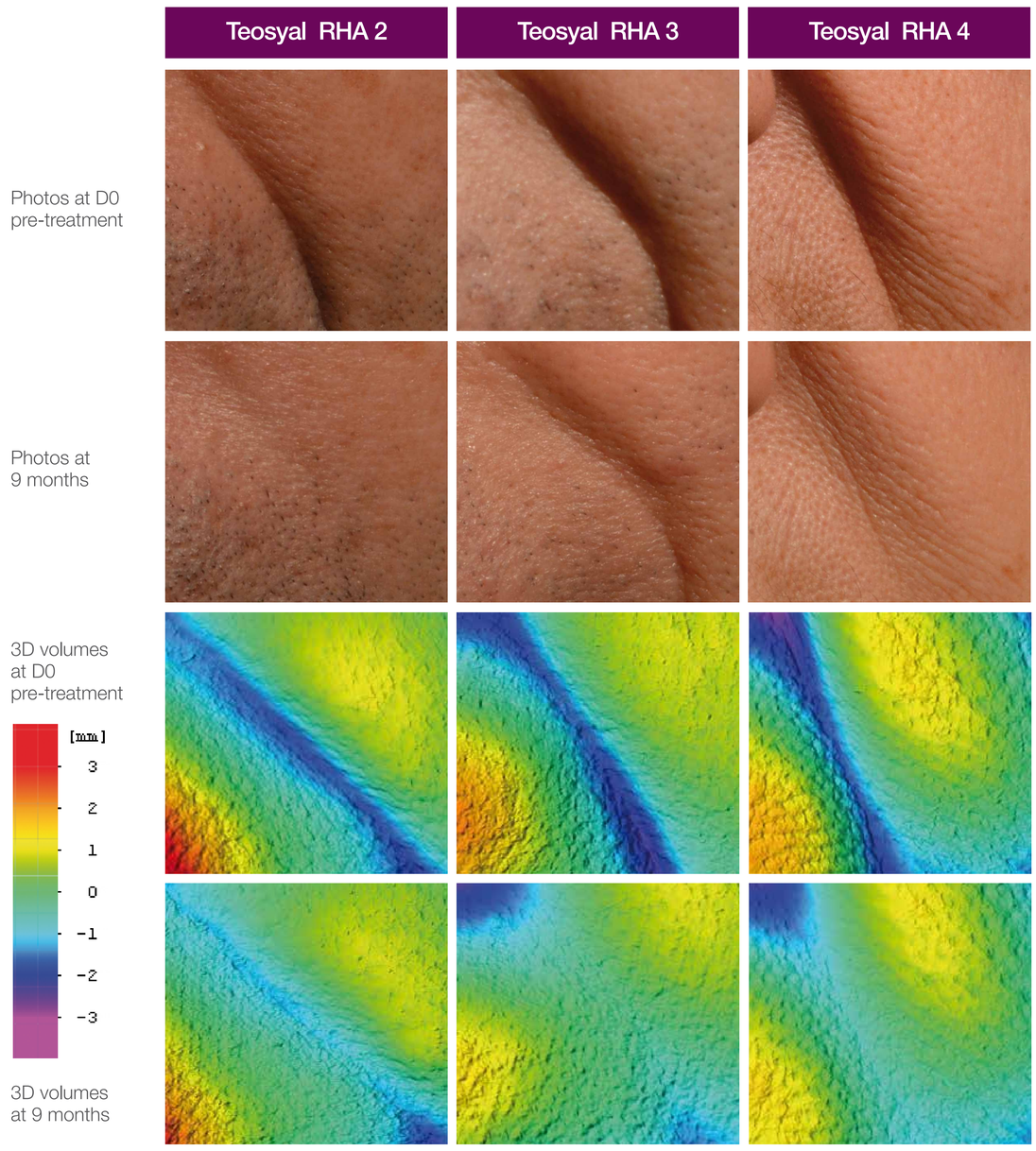
	Juvederm Volift	Teosyal RHA 2	Juvederm Ultra 4	Teosyal RHA 3	PureSense Ultra Deep	Teosyal RHA 4
From the BLE opinion	96.7	97.6	96.6	100.0	93.3	100.0
From the subject opinion	86.7	80.0	93.1	96.6	100.0	93.3

NLF volumes

Fringe projection2,3 provided objective measurements of the volume of the NLF cavities in mm3.

Improvement from pre-treatment is statistically significant for each product (Student t test for paired data, p< 0.001), and **all of the 3 arms demonstrated a trend of long lasting results with RHA products as compared with control products.**

Figure 3. NLF photos and volume using PRIMOS 3D (Phaseshift Rapid In vivo Measurement Of Skin)



Pain during injection

Pain on a 100 mm VAS was below the «no pain» threshold after 5 min., and **there is no statistically significant differences in pain during injections**, even 5, 15, and 30 minutes after, between the two products, in any of the the 3 arms (Wilcoxon signed rank test, p=NS).

Safety

The Common Treatment Reactions (CTR) for injectable acid hyaluronic filling products reported by the subjects and observed by the investigators, were bruising, erythema, induration, pain, lumps/bumps and swelling, were generally mild to moderate, and mainly had a duration of less than 7 days. **No Unexpected Adverse Device Effect (UADE) , nor device related Serious Adverse Event (SAE) was reported.**

CONCLUSION

The three new RHA products induced a good aesthetic improvement in all subjects with equivalent results to the comparators at nine months, and demonstrated better results with objective 3D volume measurements. The subjects and treating investigators were globally very satisfied by the immediate natural aesthetic result obtained with the RHA products. All RHA dermal fillers have a very good safety profile, equivalent to comparators.

ACKNOWLEDGMENTS

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Juvéderm® Volift and Juvéderm® Ultra 4 are manufactured by ALLERGAN (PRINGY, FRANCE)

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