SAFETY AND EFFECTIVENESS OF THREE NEW DYNAMIC FILLERS FOR THE TREATMENT OF MODERATE TO SEVERE NASOLABIAL FOLDS: AN 18-MONTH RANDOMIZED CONTROLLED TRIAL VERSUS COMPETITORS

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BACKGROUND

TEOXANE Laboratories developed a new line of hyaluronic acid dermal fillers, TEOSYAL®RHA (Resilient Hyaluronic Acid®), based on a patented "preserved network" technology using less BDDE[µ] and with higher stretch and strength properties, specifically dedicated to suit the dynamic areas of the face.

OBJECTIVE

The objective of this double-blinded randomized controlled trial was to compare the safety and effectiveness of three new RHA fillers, developed to suit the facial dynamics, with classical competitor products in the treatment of nasolabial folds (NLF).

METHODS

Study design

This is a 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, 9, 12, 15, and 18 after baseline.

Subjects

The study included both genders between 40 and 70 years old, with 2 symmetrical moderate (WSRS=3) to severe (WSRS=4) nasolabial folds, based on the 5-grade (1-5) Wrinkle Severity Rating Scale[1].
Key exclusion criteria included past injections in the NLF with absorbable filling products within 1 year of study entry, past injection with botulinum toxin in the face within 6 months of study entry, or a history of permanent or semi-permanent filling products injected in the face.

Assessments

The main efficacy criterion was the WSRS score improvement from pre-injection, 6 months after the last injection session, by a Blinded Live Evaluator (BLE).
The secondary criteria included variation of the NLF volumes using PRIMOS 3D (Phaseshift Rapid In vivo Measurement Of Skin), Global Aesthetic Improvement Scale (GAIS), FACE-Q, satisfaction assessment.
Safety was assessed through Common Treatment Reactions (CTR), patient's diaries, pain during injection using a 100 mm Visual Analog Scale (VAS) and adverse events (AE) collection.

RESULTS

Subject characteristics

Mean age of the 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 groups, at any follow-up visit (Wilcoxon signed rank test, p=NS) (*Table 1, Figure 1*).

	Juvéderm® Volift	TEOSYAL® RHA 2	Juvéderm® Ultra 4	TEOSYAL® RHA 3	TEOSYAL® PureSense Ultra Deep	TEOSYAL® RHA 4
1-grade improvement						
• at 6 months	100.0	100.0	100.0	100.0	100.0	100.0
• at 9 months	83.3	93.3	100.0	100.0	93.3	100.0
• at 12 months	70.0	50.0	79.3	72.4	73.3	86.7
• at 15 months	56.7	50.0	69.0	62.1	46.7	66.7
• at 18 months	46.7	40.0	55.2	58.6	33.3	56.7

Table 1. WSRS (% of subjects with still 1-grade improvement over time)

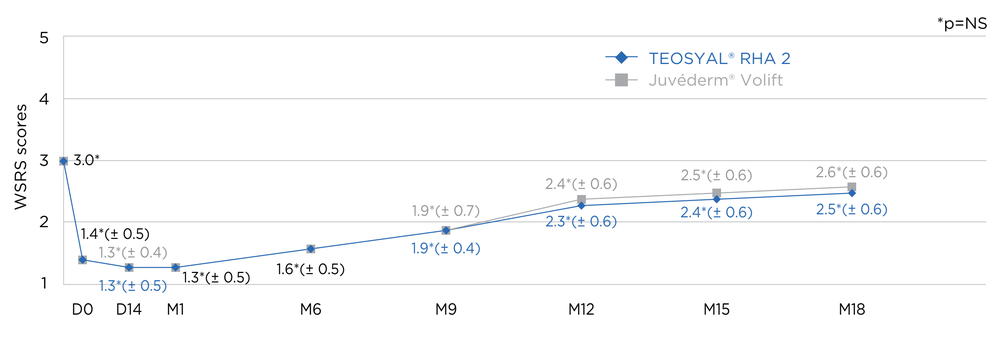

Figure 1. WSRS

Evaluation of the product by the Treating Investigator

Less touch-up was needed with RHA products. Indeed a touch-up was performed for 26.7% of the NLFs injected with a RHA product *versus* 35.6% of the NLFs injected with a control product. Globally the injectors had a preference for the RHA line regarding immediate aesthetic results, easiness of injection and product positioning *(Table 2)*.

	Juvéderm® Volift	TEOSYAL® RHA 2	Juvéderm® Ultra 4	TEOSYAL® RHA 3	TEOSYAL® PureSense Ultra Deep	TEOSYAL® RHA 4
Easiness of injection	100.0	95.1	95.5	97.4	85.0	97.1
Easiness of product positioning	100.0	95.1	91.0	100.0	92.5	100.0
Immediate 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

Table 2. % of Treating Investigators satisfied or very satisfied

GAIS

All subjects and BLE rated the Global Aesthetic Improvement as improved or much improved, for all products *(Table 3)* and there was no difference in appraisal of the NLF according the the FACE-Q scale, at any of the follow-up visit.

	Juvéderm® Volift	TEOSYAL® RHA 2	Juvéderm® Ultra 4	TEOSYAL® RHA 3	TEOSYAL® PureSense Ultra Deep	TEOSYAL® RHA 4
From the BLE opinion	72.2	66.7	60.0	66.7	50.0	77.8
From the Subject opinion	100.0	100.0	93.3	93.3	94.4	94.4

Table 3. GAIS (% of opinion rated improved or much improved) at 18 months

NLF volumes

Fringe projection[2,3] provided objective measurements of the NLF cavities volume in mm³.
Improvement from pre-treatment is statistically significant for each of the products at every follow-up visit (Student t test for paired data, p<0.02), and all of the 3 groups demonstrated a trend of longer lasting results with RHA products as compared with control products *(Figure 2)*.

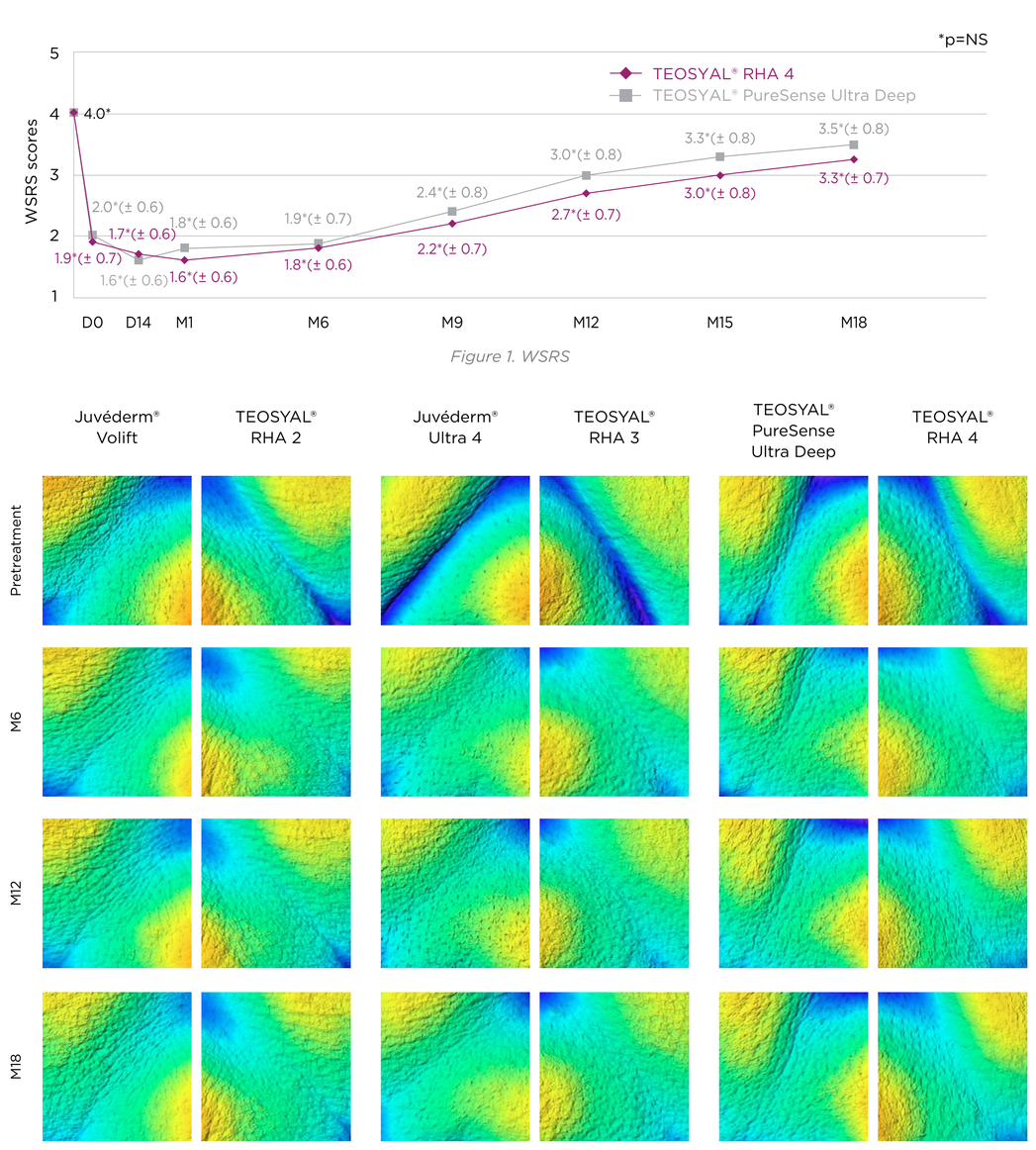

Figure 2. NLF volumes

Pain during injection

Pain on a 100 mm VAS was below the «no pain» threshold after 5 mininutes and there was no statistically significant difference in terms of pain during injections, even at 5, 15 and 30 minutes after injection, between each of the compared products, in any of the 3 groups (Wilcoxon signed rank test, p=NS).

Safety

The Common Treatment Reactions (CTR) reported by the subjects and observed by the investigators (bruising, erythema, induration, pain, lumps/bumps and swelling) were generally classified between mild to moderate and lasted less than 7 days. Neither Unexpected Adverse Device Effects (UADE) nor device related Serious Adverse Events (SAE) were reported with the use of RHA products in this study.

CONCLUSION

The three new TEOSYAL®RHA products induced a good aesthetic improvement in all subjects with equivalent results to the comparators at 18 months, and demonstrated better wrinkle filling using objective 3D volume measurements. Subjects and treating investigators were globally very satisfied by the immediate natural aesthetic result obtained with the TEOSYAL®RHA products. All tested products have a very good safety profile.

µ 1,4-butanediol diglycedyl ether

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