A SPLIT-FACE COMPARISON OF TWO HYALURONIC ACID DERMAL FILLERS IN THE TREATMENT OF SEVERE NASOLABIAL FOLDS: 6-MONTH INTERIM RESULTS OF A RANDOMIZED AND EVALUATOR-BLINDED STUDY

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INTRODUCTION

Hyaluronic acid (HA) dermal fillers are used extensively for facial rejuvenation and correction of soft tissue defections, due to their advantages of high biocompatibility and long duration of effect. Emervel® (Galderma SA) is a new range of HA dermal filler that recently received CE mark in Europe. Emervel® range includes Emervel® Classic, Emervel® Deep, Emervel® Touch, Emervel® Lips and Emervel® Volume, each of which was specifically designed to have the optimal gel texture for its indication, by keeping the same ideal concentration of HA (20mg/ml) and varying the degree of cross-linking and gel calibration. Emervel® Deep was developed to be injected into the deep dermis for the correction of severe facial wrinkles.

In this split-face, randomized and evaluator-blinded study, we aimed to assess the efficacy and safety of Emervel® Deep and compare them to those of Restylane® Perlane (Q-Med), in the treatment of severe nasolabial folds (NLF).

METHODS

Study Design

- Multi-centre, randomized, evaluator-blinded, split-face comparison study.

Subject Selection

- Subjects of 18 years or older, with severe NLF (defined as having a Wrinkle Severity Rating Score [WSRS] of 4 on the scale of 1 to 5) on both sides.
- Subjects who had received HA- or collagen-based soft tissue augmentation in NLF in the previous 18 months were excluded.

Treatments

Group A

- The first 3 subjects enrolled in each centre were included in the open-label Group A.
- All subjects received Emervel® Deep on NLF of both sides in order for the injectors to be familiar with the product and to develop proper injection technique.

Group B

- The subsequently enrolled subjects were randomized into Group B to receive Emervel® Deep and Restylane® Perlane on their left or right NLF.
- Subjects may receive a touch-up injection 3 weeks after baseline, if deemed necessary by a blinded evaluator.
- The injection technique and volume were at the discretion of the injector.
- Study visits: baseline, week 3, weeks 12, 24 and 48 after the initial treatment (after touch-up or after baseline if no touch-up was received).

Assessments

- WSRS was evaluated by blinded investigators at each visit.
- Local tolerability (erythema, oedema/swelling, bruising, pain/tenderness and pruritus) during the first 3 weeks after baseline injection was assessed based on subject diary.
- Adverse events were assessed by blinded investigators at each visit.

RESULTS

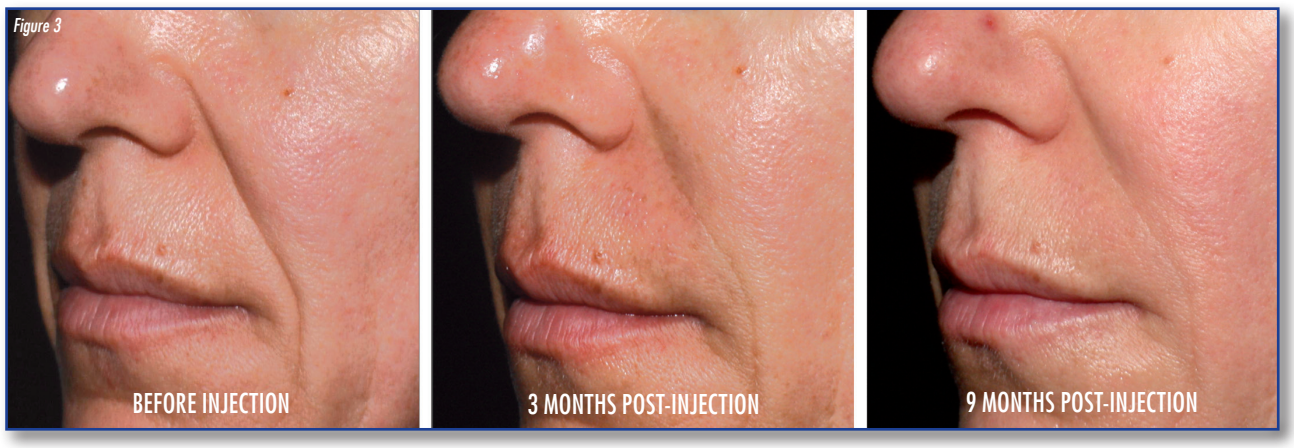
DEMOGRAPHY AND BASELINE CHARACTERISTICS (Group B, ITT population)

Table 1	Emervel® Deep/ Restylane® Perlane (N=60)
Age, year Mean ± SD Min, Max	 52.7 ± 8.7 31, 76
Gender, N (%) Male Female	 7 (11.7) 53 (88.3)
Race, N (%) Caucasian	 60 (100.0)
Evaluator's WSRS, N (%) 4: Severe	 60 (100.0)

STANDARDIZED PHOTOGRAPHS OF A REPRESENTATIVE PATIENT FROM THE OPEN-LABEL GROUP A

Emervel® Deep injected on both sides :

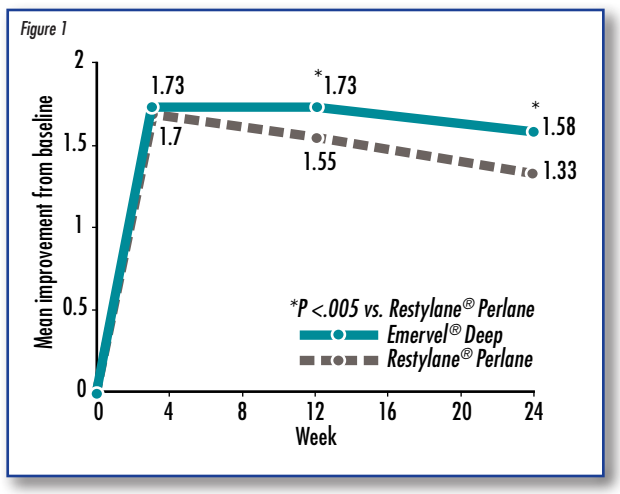
Figure 3



Efficacy

MEAN IMPROVEMENT IN THE INVESTIGATOR-EVALUATED WSRS FROM BASELINE AT WEEKS 3, 12 AND 24 (Group B, ITT population)

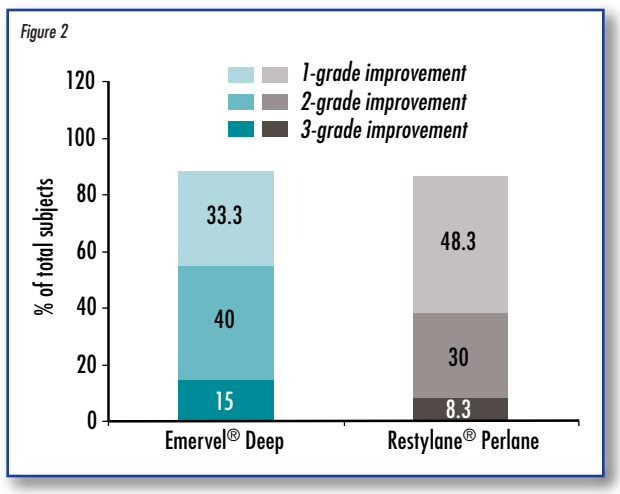
Figure 1



- Emervel® Deep was significantly more efficacious than Restylane® Perlane in terms of improvement in WSRS from baseline at both week 12 and week 24 (*P*<.005).
- The superior efficacy of Emervel® Deep compared to Restylane® Perlane was also confirmed in the PP population.
- The total volume injected for Emervel® Deep and Restylane® Perlane was similar (1.3 ± 0.5 and 1.3 ± 0.6mL per side).

DISTRIBUTION OF IMPROVEMENTS FROM BASELINE ON THE EVALUATOR-ASSESSED WSRS AT WEEK 24 (Group B, ITT population)

Figure 2



Local Tolerability

DISTRIBUTION OF WORST SCORES ON ERYTHEMA, OEDEMA/SWELLING, BRUISING, PAIN/TENDERNESS AND PRURITUS, BASED ON SUBJECT DIARY 3 WEEKS AFTER BASELINE INJECTION (Group B, Safety population)

Table 2		Emervel® Deep (N=67)	Restylane® Perlane (N=66)	*P*-value
Erythema	None - Mild	45 (67.1%)	41 (62.2%)	0.856
	Moderate	17 (25.4%)	22 (33.3%)	
	Severe	5 (7.5%)	3 (4.5%)	
Oedema/ Swelling	None - Mild	40 (59.7%)	32 (48.5%)	0.340
	Moderate	23 (34.3%)	31 (47.0%)	
	Severe	4 (6.0%)	3 (4.5%)	
Bruising	None - Mild	47 (70.2%)	49 (74.3%)	0.066
	Moderate	13 (19.4%)	15 (22.7%)	
	Severe	7 (10.4%)	2 (3.0%)	
Pain/ Tenderness	None - Mild	47 (70.1%)	45 (68.2%)	0.122
	Moderate	18 (26.9%)	18 (27.3%)	
	Severe	2 (3.0%)	3 (4.5%)	
Pruritus	None - Mild	65 (97.0%)	63 (95.5%)	0.688
	Moderate	1 (1.5%)	3 (4.5%)	
	Severe	1 (1.5%)	0 (0.0%)	

- Both Emervel® Deep and Restylane® Perlane were well-tolerated in general, with a majority of subjects reporting none or only mild injection site reactions.

MEAN SCORES (± SD) ON ERYTHEMA, OEDEMA/SWELLING, BRUISING, PAIN/TENDERNESS AND PRURITUS, BASED ON SUBJECT DIARY 3 WEEKS AFTER BASELINE INJECTION (Group B, Safety population)

Table 3	Emervel® Deep (N=67)	Restylane® Perlane (N=66)	*P-value*
Erythema	0.209 ± 0.260	0.207 ± 0.262	0.704
Oedema/Swelling	0.366 ± 0.458	0.393 ± 0.468	0.484
Bruising	0.268 ± 0.362	0.201 ± 0.278	0.152
Pain/Tenderness	0.161 ± 0.224	0.193 ± 0.268	0.044
Pruritus	0.054 ± 0.152	0.062 ± 0.155	0.287

- The local tolerability of Emervel® Deep and Restylane® Perlane was comparable, in terms of mean severity of erythema, oedema/swelling, bruising and pruritus.
- Pain/tenderness associated with Emervel® Deep was significantly less severe than that associated with Restylane® Perlane (*P*<.05).

Safety

- A total of 3 treatment-related adverse events were reported in the study: 3 for Emervel® Deep (1 erythema, 1 injection site pain and 1 telangiectasia) and 1 for Restylane® Perlane (1 injection site pain).
- All adverse events were mild in intensity and resolved spontaneously without additional treatments.

CONCLUSIONS

- Emervel® Deep is one of the few HA fillers whose efficacy and safety have been formally investigated in clinical studies.
- Emervel® Deep was significantly more efficacious than Retylane® Perlane 12 and 24 weeks after injection (P<.005), suggesting that Emervel® Deep has a longer duration of effect.
- Both Emervel® Deep and Restylane® Perlane are safe and similarly well-tolerated.

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