# HYALURONIC ACID PLUS MANNITOL TREATMENT FOR IMPROVED SKIN HYDRATION AND ELASTICITY

Authors: Dr Maryna Taieb, 11 avenue d'Eylau 75116 Paris, France, Dr Christian Gay, 6 place de la Madeleine, 75008 PARIS, Dr P Secnazi, avenue Franklin Roosevelt, 75008 PARIS, Dr S Sebban, 22 Place Georges Pompidou, Levallois-Perret

## BACKGROUND

Juvéderm® HYDRATE is a new un-crosslinked hyaluronic acid (HA) injectable treatment with mannitol comprising 13.5mg/g uncross-linked hyaluronic acid plus 0.9% mannitol. It is indicated for improving skin hydration and elasticity by multi-injection into the dermal/epidermal junction and into the superficial dermis to improve skin tone and reduce fine lines and wrinkles. The addition of mannitol leads to reduced free radical degradation of the hyaluronic acid to extend longevity.

## METHOD

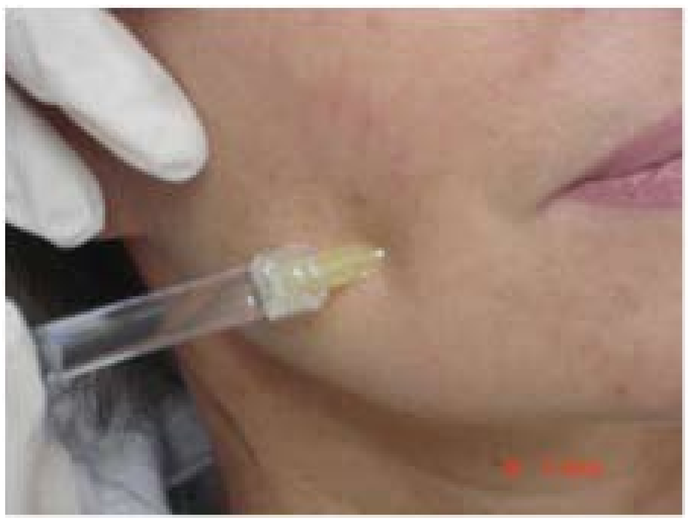
**Objectives:**
**Primary Objective:**
- To evaluate the efficacy of Juvéderm® HYDRATE on skin hydration at day 60

**Secondary Objective:**
- Evaluation of subject and physician satisfaction

**Study Design:**
- Prospective
- Multicentre
- Non-interventional
- Post-marketing surveillance

**Study Centres:**
- 3 study centres in France, each recruiting a maximum of 10 subjects per centre
- All 3 investigators used the 'depot' injection technique comprising small injections into the middle to deep dermis (Figure 1)
- Physicians used Juvéderm® HYDRATE as per their normal clinical practice and in line with the Directions For Use

**Figure 1: Depot Technique**



Juvéderm HYDRATE is injected in 20 to 40 sites; in the mid dermis. The drop is then massaged to spread the gel.

**Subjects:**
- A total of 27 healthy female subjects (mean age: 42.6 years) were enrolled by 3 investigators

**Exclusion Criteria:**
- Breast-feeding or pregnant
- Allergy to hyaluronic acid
- Tendency to keloids
- Treatment with permanent fillers
- Mesotherapy treatment in the last 6 months

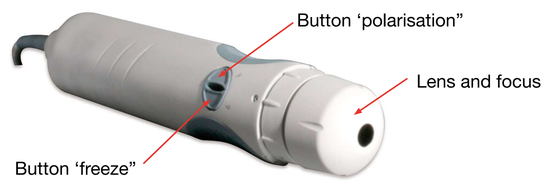
**Study Schedule:**
- Total study duration was 60 days
- On Baseline visit (Day 0), all baseline data were collected and eligible subjects were injected with Juvéderm® HYDRATE according to the injector's usual practice
- Follow-up visits were planned in accordance with the subject's normal clinic schedule (typically on Days 15, 30 and 60)

**Outcome Measures:**
Skin measurements were performed at each of the 4 visits on different areas (i.e. eye, cheek, peri-oral and neck-line areas) using a probe-based system to assess physical and visual skin.

The biophysical and mechanical properties of the skin were measured using the Visio Probe, a high-resolution sensor to capture precise skin images (i.e. wrinkles, sebum, hair distribution, dark spots and clogged pores/bacterial infection) (Figure 2).

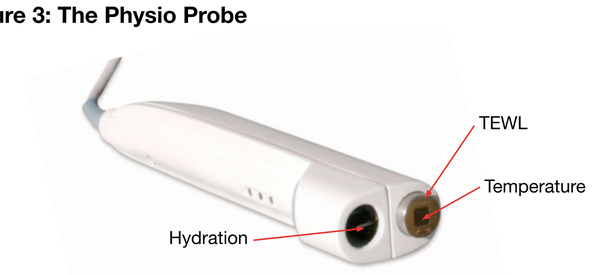
CONFLICT OF INTEREST STATEMENT
This study was sponsored by Allergan and the presenting author received payment for participation in the study, as well as payments for consultancy services.

**Figure 2: The Visio Probe**




The Physio Probe was also used to determine key characteristics of the skin (i.e. hydration, trans-epidermal water loss [TEWL] and skin temperature) (Figure 3).

**Figure 3: The Physio Probe**




**Primary Criterion:**
- Hydration (%) was measured at each visit from Day 0 to Day 60

**Secondary Criteria:**
- Anisotropy (%), roughness and luminance were measured at each visit from Day 0 to Day 60
- Assessment of injection technique (i.e. treatment, needle, ease of injection) was assessed on Days 0, 15 and 30
- Subject discomfort using a Visual Analogue Scale (VAS) (0: No pain to 10: Maximum pain)
- Physician assessment of aesthetic results (Days 15, 30 and 60)
- Subject self-assessment of aesthetic results (Days 15, 30 and 60)
- Adverse events

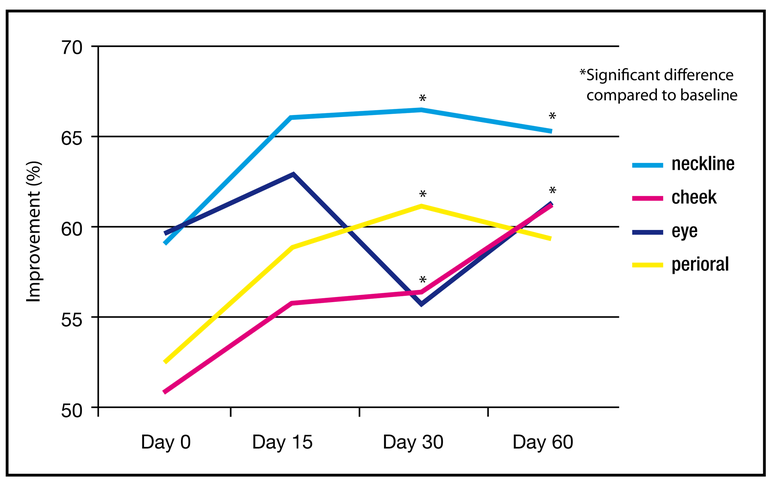
## RESULTS

**Hydration:**
There was a statistically significant improvement in skin hydration for the cheek at Day 30 (mean 56.4%) and Day 60 (mean 59.3%) compared to baseline (p=0.0262 and 0.0021, respectively). (Figure 4)

There was a statistically significant improvement in skin hydration for the peri-oral area at Day 30 (mean 61.2%) and Day 60 (mean 59.3%) compared to baseline (p=0.0041 and 0.0467, respectively). (Figure 4)

There was a statistically significant improvement in skin hydration for the neck-line area at Day 30 (mean 66.5%) and Day 60 (mean 65.3%) compared to baseline (p=0.0022 and 0.0448, respectively). (Figure 4)

**Figure 4: Mean improvement in Hydration over time per area**




**Subject Discomfort:**
At Day 0, mean subject discomfort was 4.1 (range: 0-9).

**Injection Technique:**
All subjects underwent manual injection using a 30 G 1/6" needle. Mean total volume injected into the face was approximately 1mL at each visit, and mean total volume injected in the neck-line area was 0.8mL. The majority of investigators found ease of injection to be 'easy' or 'very easy'.

**Physician Satisfaction:**
Physician satisfaction showed that skin texture, brightness, hydration and appearance were 'improved' or 'very improved' for >90% of subjects at Day 60.

**Table 1: Percentage Skin Improvement (Combined 'Very Improved' and 'Improved')**

| Assessment | Day 15 | Day 30 | Day 60 |
|---|---|---|---|
| Texture | 88.9% | 100% | 95.6% |
| Brightness | 74.1% | 87.5% | 91.3% |
| Hydration | 88.9% | 100% | 95.6% |
| Appearance | 48.1% | 91.7% | 91.3% |

**Subject Satisfaction:**
Subject satisfaction indicated that skin texture, brightness and hydration were 'improved' or 'very improved' for >80% of subjects at Day 60.

**Table 2: Percentage Skin Improvement (Combined 'Very Improved' and 'Improved')**

| Assessment | Day 15 | Day 30 | Day 60 |
|---|---|---|---|
| Texture | 72% | 94.7% | 80.9% |
| Brightness | 84% | 84.3% | 85.7% |
| Hydration | 84% | 94.8% | 95% |
| Colour | 36% | 42.1% | 42.9% |

Further assessment of subject satisfaction at Day 60 revealed that global aesthetic result and skin revitalisation were 'very improved' or 'improved' in 100% of subjects, and face fullness was 'much better' or 'better' in 78.9% of subjects. 95% of subjects were delighted with treatment, with 85% being both happy to undergo repeat treatment and would recommend treatment to a friend.

**Skin aspect:**
Patients are very satisfied with the brightness and texture of the skin after treatment. Although skin brightness is not easy to assess with physical parameter both the patient and the physician observed a clear improvement in the brightness of the skin.
However an improvement of the skin texture is not only observed by both patient an injector but also objectively assessed by the Intuiskin machine that measures anisothropy of the skin .
This improvement is shown in figures 5 and 6.

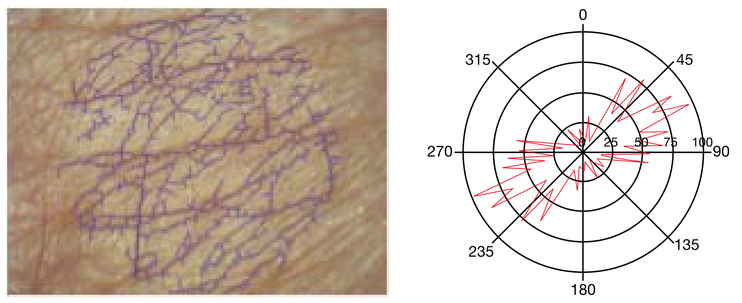



**Figure 5: Right cheek of a patient before Juvéderm® HYDRATE treatment. There is a strong anisotropy**

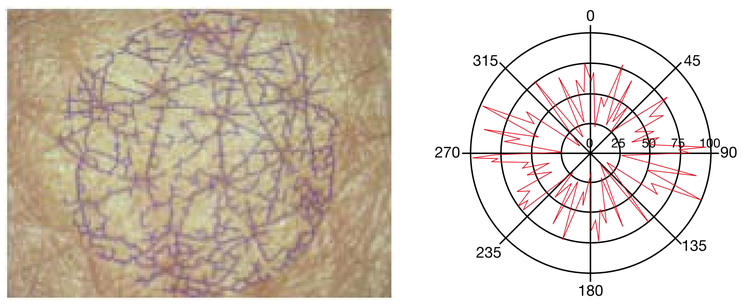



**Figure 6 : After 3 injections of Juvéderm® HYDRATE, the skin has a better isotropy.**

## ADVERSE EFFECTS

ADVERSE EFFECTS
Treatment was well-tolerated with all adverse events related to injection technique rather than to the product. All adverse events were transient with no sequelae.

## CONCLUSIONS

Juvéderm® HYDRATE delivered significant improvements in skin hydration at Day 60 in the cheek, neck-line and peri-oral areas compared to Baseline.

Physician and subject satisfaction of aesthetic results showed that skin texture, brightness, hydration and appearance were 'improved' or 'very improved' for >90% and >80% of subjects at Day 60, respectively.

Subject assessment of overall global aesthetic effect and skin revitalisation was 'very improved' or 'improved' in 100% of subjects and in almost 80% of subjects with respect to face fullness. Most subjects were delighted with treatment and 85% would undergo repeat treatment and would recommend treatment to a friend.

## REFERENCES

1. Rittes PG, Rittes JC, Carriel Amary MF. Injection of phosphatidylcholine in fat tissue: experimental study of local action in rabbits. *Aesthetic Plast Surg* 2006;**30**(4):474-478

8th Anti-Aging Medicine World Congress, 8-10 April 2010, Monaco

EU/0143/2010 Date of preparation: March 2010