

## **Transplantation 2020: Assessment of the efficacy and tolerance of a new combination of retinoids and de-pigmenting agents in the treatment of melasma- Maria Vitale- Madrid, Spain**

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### **Abstract:**

Melasma may be a common hyperpigmentation disorder which mainly affects women with a high prototype and sometimes remains active for several years, being related to a substantial psychological impact. The management of melasma is often challenging, because it is very resistant to treatments and requires long-term therapeutic protocols. Conventional treatment includes de-pigmenting products, like hydroquinone (HQ), retinoid, equinox, atelic acid, arbutin, kojic acid, etc., which exert their action at different stages of melanogenesis. In addition, avoidance of aggravating factors is strongly indicated. Combination therapy is typically prescribed, with a typical association of HQ and retinoic acid. However, HQ's safety has been questioned in certain cases, and prolonged use may lead to adverse effects such as depigmentation and ochronosis, so it cannot be considered as a golden standard. In the look for safer alternatives, a replacement product supported RetinSphere technology has been designed. It incorporates two topical retinoids: Retinol glycospheres and hydroxypinacoloneretinoate, which directly interacts with the retinoic acid receptor but doesn't induce irritation. Additionally, the product includes other DE pigmenting active ingredients. The objective has been creating a product which may reduce or even substitute the use of HQ in the management of melasma patients. We will show the results of clinical assays on several skin types and thus the efficacy and safety of the new combination of retinoids within the

improvement of melasma will be discussed.

### **Patients/Methods**

Prospective, double-blind, vehicle-controlled, and randomized study in 30 patients with melasma. The product was applied on one side of the face and the vehicle on the other, twice daily during 3 months. Standardized photographs were taken using RBX technology on the three visits (basal, at one and a half months and at 3 months). The main variable to work out the efficacy was the development of the hemi facial Melasma Area Severity Index (MASI). Other variables were determined like improvement perceived by the investigator, improvement perceived by the patient, impact on quality of life or side effects. Results The MASI improvement at 3 months of treatment was significant on the treated side vs. the vehicle side, reaching an improvement of 70%, which is like the share of improvement described with hydroquinone. No notable side effects were detected, in spite of an enormous percentage of patients included within the study citing a history that might be compatible with sensitive skin.

### **Conclusions:**

This new combination of retinoids and DE pigmenting agents proved to be effective and safe within the treatment of melasma.

### **Introduction**

Melasma could also be a hyperpigmentation condition distributed generally symmetrically within the facial area, which can have a very negative impact on patients' quality of life. It mainly affects women with a high prototype. It often persists indefinitely,

remaining active for several years. The exact etiology is unknown, but certain trigger factors are suggested like genetics, ultraviolet, light, hormone alterations (pregnancy, oral contraceptives), and increase of the melanocyte-stimulating hormone (MSH).<sup>2</sup> Melasma is usually immune to treatments, and therefore, it's a frustrating dermatosis for both patients and dermatologists. The results are variable, often imperceptible. Conventional treatment includes avoiding possible trigger factors, daily application of suitable photo protection also as DE pigmented products. The efficacy of sun protection is backed by the study of Ennes et al. <sup>7</sup> where 8.3% of the patients showed total disappearance of the melasma and 58% partial improvement when treated exclusively with photo protection cream. Lakhdar observed an incidence of melasma of two .7% in pregnant women who used photo protection <sup>8</sup> compared to 53% in pregnant women of that exact same population who didn't use it as demonstrated by Khadir.<sup>9</sup> DE pigmented agents exert their action through different mechanisms: elimination of excess melanin, regulation of the activity of melanocytes, control of the dispersion of melanin granules, or inhibition of the transfer of melanin to keratinocytes. Most commonly used DE pigmented agents include hydroquinone, retinoids, mequinol, azelaic acid, arbutin, kojic acid, oleosin, liquorice extract, ascorbic acid, n-acetyl-glucosamine, niacin amide, etc.<sup>10–16</sup> A new product has been designed recently, supported RetinSphere Technology, which encompasses the association of two topical retinoids: retinol glycospheres and hydroxypinacolone retinoate. Retinol encapsulated in glycospheres has been used previously in patients with acne. The retinoic acid ester, hydroxypinacolone retinoate, has similar action to tretinoin, but doesn't cause the irritation observed with this retinoid. Recently, Veraldi demonstrated that use at 0.1% during 2 weeks in patients with acne can improve

skin roughness by 50% and scaling by 40%. <sup>14</sup> Unlike retinol and other derivatives that has got to be converted into the biologically active sort of retinoic acid, hydroxypinacolone retinoate binds on to retinoic acid receptors (RAR).<sup>17</sup> RetinSphere technology has combined with other DE pigmented active ingredients like N-acetyl glucosamine (inhibits glycosylation of tyrosinase), kojic acid, Cromabright and Antiques (they uptake the copper and iron ions needed by tyrosinase for its activation), albatin & alistin (they act synergistically inhibiting melanin synthesis), and niacin amide (vitamin B3 that forestalls the transfer of melanosomes to keratinocytes). Furthermore, the formulation contains 10% of hydrating active ingredients and 3% anti-irritant, anti-inflammatory active ingredients. This study aimed to determine the efficacy of the protocol with the study products vs. a vehicle within the treatment of patients with melasma. A secondary objective was to determine the safety of the product vs. the vehicle.

#### **Materials and methods**

A prospective, randomized, double-blind, vehicle-controlled study was carried out. 30 patients were selected. Inclusion criteria were as follows:

- Aged over 18 years.
- Absence of treatment for melasma in the last 3 months.
- No desire to get pregnant in the forthcoming months and use of contraceptives.
- No concomitant diseases.
- No administration of another topical or systemic product that may interfere or affect the process.
- No allergy to the product ingredients

#### **Treatment**

The treatment protocol included the application of the active cream with sun protection factor SPF 50 (Neoretin discrom control gelcream—IFC Pharmaceuticals) during the day and active serum (Neoretin discrom control serum booster fluid—IFC Pharmaceuticals) at

night on one side of the face vs. vehicle gelcream with SPF 50 during the day and vehicle serum during the night on the opposite side of the face; thus, the patient was also the control group. The vehicle had the same photo protector as the study product.

### **Clinical assessment**

The observation period was 3 months, organized into visits at baseline (T0), at one and a half months (T1) and at 3 months (T2). Classical clinical photography was administered and with polarized light via Reveal System with RBX technology (Red/Brown/X identified). To determine the efficacy, the share of improvement within the Melasma Area Severity Index (MASI) after treatment was deemed as principle variable.

The MASI is calculated supported the share of relative surface of involvement (A), the intensity of darkness (D) of melasma, and therefore the homogeneity (H) of the hyperpigmentation. The area of involvement is given a numerical value of 0–6 (0 indicates no involvement; 1, 0–9%; 2, 10–29%; 3, 30–49%; 4, 50–69%; 5, 70–89%; and 6, 90–100%). The intensity of darkness (D) and therefore the homogeneity of melasma (H) were rated on a scale from 1–4 (0 indicates absent; 1, slight; 2, mild; 3, marked; and 4, maximum).

The global MASI (0–48) and the MASI on each side of the face (0–24) were calculated. A coefficient of correlation was applied consistent with location: Each cheek corresponds to 30% of the entire face, the forehead corresponds to 30%, and therefore the chin corresponds to 10%. On the unilateral MASI, the forehead corresponds to 15% and the chin to 5%, and only one cheek is taken into account (30%). The higher the score, the more intense the melisma.

### **Biography**

Maria Vitale is currently working as a Medical Director for IFC Group [Industrial Farmaceutica Cantabria], at Madrid, Spain. She is an active speaker and has delivered presentations in different conferences. Her principle expertized topics are Acne, Herpes, Photoprotection, Photo aging, and Phototherapy. She is member of various scientific societies- American Academy of Dermatology (AAD), Dermatology Society of Argentina (SAD), and many more.

**Note:** This work is partly presented at 4th International Conference and Expo on Cosmetology & Trichology June 22-24, 2015 held at Philadelphia, USA.