Evaluation of malon-di-aldehyde in localized and generalized vitiligo and its correlation with the duration and disease activity.

Sinu Rose Mathachan\*1

<sup>1</sup>ABVIMS & Dr RML Hospital, Dermatology, New Delhi, India

**Introduction & Objectives:** There are several ways by which oxidative stress is generated and is involved in the development of vitiligo. This study evaluated the role of malon-di-aldehyde (MDA) related to the oxidative stress pathway in patients with active and stable vitiligo with either localized or generalized disease. Aim of this study was to evaluate the serum levels of the oxidative stress parameter Malon-di-aldehyde (MDA) in patients of localized and generalized vitiligo and to correlate with the duration and activity of the disease

**Materials & Methods:** 60 clinically diagnosed vitiligo patients were categorized into generalized (n = 30) or localized vitiligo (n = 30) and were further grouped according to their disease activity in to active and stable groups. Thirty healthy volunteers were included in the control group. ELISA was used for the evaluation of MDA.

**Results:** Patient group demonstrated significantly raised levels of MDA compared to the control group. Further, MDA was significantly more deranged in patients with the generalized vitiligo ( $157.23\pm212.197$ ) than in those with localized ( $49.93\pm40.82$ ) vitiligo (Figure 1). Also MDA was significantly more deranged in patients with disease activity ( $60.85\pm54.44$  in localised vitiligo/ $179.25\pm242.89$  in generalised vitiligo) than in those with stable disease ( $42.65\pm27.99$  in localised/ $96.68\pm61.88$  in generalised) (Figure 2,3). No significant association was noted in relation to the duration of the disease.

#### Localized

# Generalized

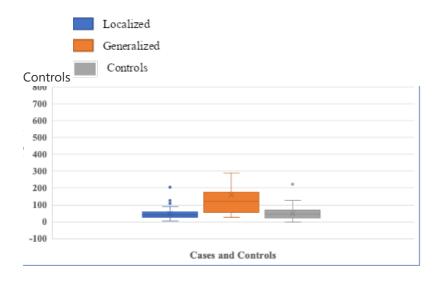
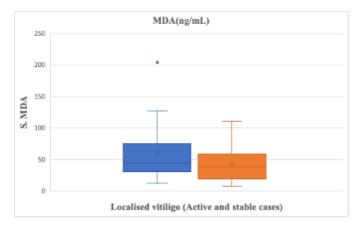


Figure 1: Comparison of serum MDA levels between groups

Active





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Figure 2: Serum level of MDA in patients with active and stable disease in localized vitiligo

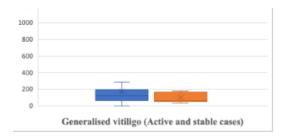


Figure 3: Serum level of MDA in patients with active and stable disease in generalized vitiligo

**Conclusion:** Our findings suggest an essential role of free radical damage and oxidative stress in localized and generalized vitiligo. Further, this study also highlights that uncontrolled oxidative damage may be a contributory factor in causing progression to generalized disease. We noted the key role of MDA in the progression and activity of the disease process.

Methotrexate Gel Either Alone or Combined with Narrow Band Ultraviolet B or Excimer Light for the Treatment of Vitiligo

Khaled Gharib<sup>1</sup>

<sup>1</sup>zagazig university, dermatology, zagazig, Egypt

Methotrexate Gel Either Alone or Combined with Narrow Band Ultraviolet B or Excimer Light for the Treatment of Vitiligo

Introduction & Objectives: Methotrexate has been used successfully in the treatment of vitiligo. It leads to decrease in the number of TNF-α secreting T cells in association with increase in the number of interleukin (IL)-10 producing T cells. Topical forms of methotrexate do not have significant hematologic or hepatotoxic side effects unlike the systemic forms of the drug. OBJECTIVE: We sought to evaluate the efficacy and safety of methotrexate gel for the treatment of vitiligo, either alone or combined with narrowband (NB) ultraviolet B (UVB) or with excimer light.

**Materials & Methods:** Forty-eight patients with vitiligo were randomized into three treatment groups. Group I was treated with methotrexate gel twice daily. Group II was treated with methotrexate gel twice daily plus NB-UVB twice weekly. Group III was treated with methotrexate gel twice daily combined with excimer light twice weekly. Treatment was continued for three months followed by a one-month follow-up period.

Results: there was a statistically significant difference between groups regarding the therapeutic response. The highest response was recorded in the group treated with methotrexate gel and NB- UVB. More patients in Group II showed good or excellent response than in the other groups.

Conclusion: Methotrexate gel could increase the therapeutic effect of NB- UVB and excimer laser and shorten the treatment period of vitiligo. However, it was not effective enough to induce repigmentation when used alone.

## Ethnic and cultural background may influence feeling of stigmatisation in vitiligo patients

Khaled Ezzedine<sup>1</sup>, Marketa Saint Aroman<sup>2</sup>, Nuria Perez Cullell<sup>2</sup>, Catherine Baissac<sup>2</sup>, Charles Taieb<sup>3</sup>, Bruno Halioua\*<sup>4</sup>

<sup>1</sup>CHU Creteil, <sup>2</sup>Pierre Fabre, <sup>3</sup>EMMA, <sup>4</sup>Dermatologist

### **Introduction & Objectives:**

Vitiligo is a relatively common condition, affecting around 0.5-2% of people in the world. Vitiligo causes isolation, stigmatization, loss of self-esteem, depression, and self-consciousness. Dark-skinned people are thought to have a higher burden of vitiligo in their daily life and decreased quality of life have been reported in those darker skinned individuals as compared to fair-skinned patients. The objective of this study was to investigate and to compare the prevalence of stigmatization associated with vitiligo among different ethnic population.

#### **Materials & Methods:**

Patients with vitiligo were selected from All project, an international online conducted int the general population (50552 individuals over 16)) across 20 countries from 5 continents.

Vitiligo (confirmed by a physician) was self-reported by the patients. Patients with vitiligo who agreed to specify their ethnic origin [EADV STUDY] and to rate their skin as one of the six Fitzpatrick skin phototypes (FSP) were selected. Four groups were distinguished: African descent, with FSP V-VI] (AD), Caucasian descent with FSP type 1-3 (C), East-Asian cohort from South Korea and Japan (EA) and Indian Cohort (I). Patients were further divided in two groups, those who acknowledge vitiligo on at least one visible area (head, face, neck, arms or hands) and those who report involvement of non-visible area (abdomen, legs, feet, genitals).

# Results:

From the 764 vitiligo respondents (VR), a population of 488 reported both their FSP and their ethnicity. Of these, 246 (50.4%) were males and 242 (49.6%) were females with a mean age of respectively 38.22+/-12.64.

There were 40 (13.9%) patients with AD 230 (79.9%) withCaucasian, 86 (29.9%) with EA and respondents and 132 I (45.8%) with Indian descent. Of the 364 (74.9%) patients who declared vitiligo on visible areas, 268 (54.9%) felt ostracized or rejected by others, 271 (55.5%) felt looked at with disgust, 270 (55.3%) reported that people avoided touching them, and 267 (54.7%) reported that people avoided approaching them because of their vitiligo. One hundred twenty-four VR were considered to have no feelings of stigmatization (FS). The prevalence of FS was not significantly different among the four ethnic patient groups of VR, with the exception of Indian respondents who were more likely to experience feelings of stigma than Caucasian descendants (89.4% versus 63.5% in the non FS population; P = 3.55E-05).

The prevalence of FS in patients with lesions on visible areas and those without lesions on visible areas was not significantly different (71.2% VS 77.3%; P 0,68)

Indian respondents were more likely to experience feelings of stigma than Caucasian descendants.

Indian patients were more likely to report denial to take a selfie due to vitiligo than East Asian (87.1% vs 65.1%, p0,011) and Caucasian (87.1% vs 53.5%, p7,18E-08). A total of 217/474 (45.8%) VR reported using

corrective makeup to avoid stigma linked with vitiligo. Accordingly, prevalence of FS was significantly higher in VS using corrective makeup (187/217= 86.2% vs 171/256=66.8%, p 0,0002)

# **Conclusion:**

In conclusion, feeling of stigmatizing in individuals with vitiligo is highly prevalent among people throughout the world with a marked higher prevalence in the Indian Subcontinent. Educational campaigns targeting the general population and aiming at deciphering beliefs and behaviors linked to vitiligo is of most importance and may help reducing stigma toward persons with vitiligo.

Histopathological analysis of remnant nevus cells after 84 times of 1064nm Q-switched Nd:YAG treatment in a patient with a congenital melanocytic nevus: a case report

Hyunjoon Chang\*1, Yoon Seob Kim1, Kyung Ho Lee1, Chul Jong Park1

<sup>1</sup>Bucheon St. Mary's Hospital, Department of Dermatology, Bucheon-si, Korea, Rep. of South

# **Introduction & Objectives:**

Congenital melanocytic nevi are skin lesions that can penetrate deeper than the dermis, so complete excision is considered the treatment of choice; however, lasers have been used as an alternative treatment modality. The objective of this case report is to present a rare case of a congenital melanocytic nevus treated with 1,064nm Q-switched Nd:YAG laser and to determine the depth of penetration of the laser.

#### Materials & Methods:

We reviewed the treatment records of a 26-year-old woman who underwent multiple sessions of 1,064nm Q-switched Nd:YAG laser treatment for a congenital melanocytic nevus. Histological examinations were performed to determine the depth of penetration of 1,064nm Q-switched Nd:Yag laser.

## **Results:**

The patient presented with a solitary, skin-colored plaque (6×4 cm) surrounded by whitish patches on her right calf. She recalled that the lesion had originally been a blackish mass since birth. She was diagnosed with a congenital melanocytic nevus at a private dermatology clinic and underwent 84 laser treatment sessions over 7 years using a 1,064 nm Q-switched Nd:YAG laser (2.6  $\sim$  3.0 cm², 7 mm spot size). Histopathological examination of the whitish plaque lesion revealed small foci of nevus cells at a depth of more than 1,260  $\mu$ m from the epidermis.

## **Conclusion:**

Our findings suggest that 1,064nm Q-switched Nd:YAG laser may not be effective in completely treating congenital melanocytic nevi due to its limited depth of penetration. This case report highlights the need for further studies to determine the effectiveness of this treatment modality.

The effect of narrowband ultraviolet B on tissue level of Interleukin 15 and interleukin 15 receptor alpha subunit in active non-segmental vitiligo cases: An interventional cohort study.

Rania Mogawer\*1, Nourhan Emad1, Olfat Shaker1, Randa Youssef1

<sup>1</sup>Kasr Al Ainy medical school, Dermatology, Egypt

# **Introduction & Objectives:**

Vitiligo is an acquired depigmenting skin disorder in which CD8 effector and memory T-cells contribute to its pathogenesis and recurrence. Interleukin (IL)-15 contributes to CD8 effector T-cell cytotoxicity and CD8 memory T-cell survival and maturation. Recently, IL-15 and its related receptor has evolved as a potential therapeutic target that is hoped to meet the previously unmet need for a therapy that prevents recurrence of vitiligo. This study aimed at evaluating the tissue levels of IL-15 and IL-15 receptor alpha (IL-15Ra) in patients with active nonsegmental vitiligo (NSV) and the potential effect of narrowband ultraviolet B (NB-UVB) on their expression.

### **Materials & Methods:**

Thirty active NSV patients were recruited. The patients were assessed clinically for vitiligo extent and activity using vitiligo extent plus (VES) and vitiligo signs of activity (VSAS) scores respectively. Perilesional skin biopsies were taken at baseline. Patients were given 48 sessions of total body NB-UVB, after which follow up skin biopsies were taken. Skin biopsies were taken from 30 healthy matched controls, to assess for the normal expression of IL-15 and IL-15Ra.

### **Results:**

Before NB-UVB treatment, the tissue levels of both IL-15 and IL-15Ra were significantly higher in vitiligo patients than controls; moreover, they were significantly higher than their levels after NB-UVB treatment. In contrast, after NB-UVB treatment, no statistically significant difference was detected between the patients and controls. The levels of IL-15 and IL-15Ra were significantly correlated, whereas they were not correlated with either vitiligo activity or extent.

#### **Conclusion:**

IL-15 and IL-15Ra were higher in vitiligo patients than controls before NB-UVB treatment. However, their tissue levels were normalized after treatment with NB-UVB, emphasizing its therapeutic potential. Further studies are due to assess the normalizing effect of total body NB-UVB on IL-15 and IL-15Ra and its potential utility as an adjuvant modality with the newly emerging biologic therapy targeting IL-15 and its receptor.

The value of adding platelet rich plasma (PRP) to non-cultured epidermal cell suspension (NCECS) in surgical treatment of stable resistant vitiligo: A self-controlled randomized double blinded study

Rania Mogawer\*<sup>1</sup>, Ahmad Fekry<sup>2</sup>, Dalia Abdel-Halim<sup>3</sup>

<sup>1</sup>Kasr Al Ainy medical school, Giza, Egypt, <sup>2</sup>Al-Ayyat Central Hospital (Emergency), Egypt, <sup>3</sup>Kasr Al Ainy medical school, Egypt

# **Introduction & Objectives:**

Non-cultured epidermal cell suspension (NCECS) is a commonly used surgical treatment for resistant stable acral vitiligo as well as vitiligo overlying joints. Platelet-rich plasma (PRP) has been reported to enhance the repigmentation response of different therapeutic modalities for vitiligo, including vitiligo surgery.

The aim of the study is to assess the value of adding of PRP to NCECS in the surgical treatment of acral vitiligo as well as vitiligo overlying joints, which has not been evaluated solely in surgical treatment of resistant acral vitiligo and vitiligo overlying joints.

#### **Materials & Methods:**

This self-controlled randomized trial included 15 patients with 30 lesions in which NCECS suspended in PRP was done for one lesion and NCECS in Ringer's lactate for another comparable lesion using a low expansion ratio of 1:3 to enhance outcome. Furthermore, following NCECS, patients underwent thrice weekly excimer light sessions for 3 months. After 8 weeks, patients underwent preliminary assessment. By the end of the 3 months, both lesions were compared as regards improvement in surface area as per point counting technique and pigmentation as per Vitiligo Extent Score for Target Area (VESTA). Additionally, physician global assessment was done by a blinded investigator.

## **Results:**

Significant improvement was reported in both lesional extent and pigmentation (after PRP and lactated ringer NCECS) with no statistical difference between them. Different disease characteristics as well as baseline platelet count were not found to influence the outcome as per improvement in pigmentation and reduction in surface area.

# **Conclusion:**

Despite previous promising results, based on this work, optimized surgical technique using a low expansion ratio of 1 donor to 3 recipient surface area and its combination with thrice weekly excimer light sessions, yielded comparable results to what stated in the literature in surgical treatment of such resistant areas with no difference between PRP suspended NCECS and lactated ringer suspended NCECS. Thus, PRP proved not to be a valuable adjunctive tool to non-cultured epidermal cellular suspension (NCECS) when treating acral vitiligo and vitiligo overlying joints.

In vitro and clinical efficacy of a new skin-lightening cream containing a combination of azelaic acid, hesperidin methyl chalcone and glycolic acid on hyperpigmentation disorders.

Bogdanowicz Patrick<sup>1</sup>, Marie-Dominique Thouvenin<sup>1</sup>, Séréno Jérémy<sup>1</sup>, André Karine<sup>1</sup>, Valérie Mengeaud<sup>2</sup>, Layral Fanny<sup>1</sup>, Noharet Julie<sup>1</sup>, Ribet Virginie<sup>1</sup>, Ferret Pierre-Jacques<sup>1</sup>, Sandrine Bessou-Touya<sup>1</sup>, Helene Duplan\*<sup>1</sup>

<sup>1</sup>Pierre Fabre Dermo-Cosmétique and Personal Care, R&D, Toulouse, France, <sup>2</sup>Laboratoires dermatologiques Ducray, Medical Department, LAVAUR

# **Introduction & Objectives:**

Hyperpigmentation disorders are common and can have a significant impact on the patient's quality of life. The physiopathology depends on the etiology and can involve complex interaction of several actors as epidermal melanocytes, keratinocytes, dermal fibroblasts, mast cells. A vascular component and an overproduction of nitric oxide (NO) have been identified in melasma. A new skin-lightening cream dedicated to hyperpigmentation disorders, containing a combination of azelaic acid, hesperidin methyl chalcone (HMC) and glycolic acid has been developed. A complete *in vitro* and *in vivo* assessment program has been done to evaluate its efficacy and tolerance.

#### Materials & Methods:

Different studies were conducted to evaluate: 1/ HMC efficacy on the modulation of vascular responses after substance P (SP) stimulation in human skin explants *in vitro*, 2/ the effect of HMC on NO-induced melanin synthesis *in vitro*, 3/ the effect of HMC and the combination of HMC with azelaic acid (AZA) on reconstructed human pigmented epidermis (RHPE) pigmentation and 4/ the clinical efficacy of the product through a clinical study and a comparative **H**ome **U**se **T**est (HUT) on subjects with hyperpigmentation disorders.

## Results:

In human skin explants, SP stimulation induced significant vasodilation and an increase in the vessel surface. In this model, HMC (0.2 mg/mL) significantly decreased the proportion of dilated vessels (-48%) and total vessel area (-72%). Our results also showed that the color difference (DE) between RHPE control and ethyl ascorbic acid treated RHPE (1mg/ml) reached 3.77 and HMC (0.5 mg/mL) induced a DE = 4.42. In a second set of experiments, our data also showed that AZA (1 mg/ml) strongly reduced RHPE pigmentation (DE = 12.8) and HMC (0.5mg/ml) reduced RHPE pigmentation by 5.21 (DE = 5.21). Moreover, combination of HMC (0.5mg/ml) with AZA (1 mg/ml) strongly reduced RHPE pigmentation since DE reached 15.05, which was statistically stronger than KA (DE=12.80). Our result also showed that HMC\*\* (0.01%) significantly reduced NO-induced melanin synthesis (-69%) in melanocytes. The results from a clinical study on 54 subjects with hyperpigmentation disorders (melasma, lentigos, acne Post-Inflammatory Hyperpigmentation) has demonstrated an improvement of skin pigmentation from baseline including a significant increase of Individual Typological Angle parameter (+ 31 %, lesional / non lesional areas, p <0,001) and a significant improvement of skin homogeneity (p < 0.001) assessed clinically after 8 weeks of use. The tolerance assessed by the investigator was good. The results from a comparative, parallel groups HUT on 132 consumers showed a good perceived efficacy with an improvement of their dark spots and the maintenance of the effects after 12 weeks.

# **Conclusion:**

In vitro and in vivo studies of a new skin-lightening cream containing a combination of azelaic acid, hesperidin

methyl chalcone and glycolic acid has demonstrated its interest in hyperpigmentation disorders. *In vitro* studies showed that HMC reduced vasodilatation and that the combination of HMC and AZA reduced RHPE pigmentation with a stronger efficacy than kojic acid. Moreover, HMC reduced NO-induced melanin synthesis in melanocytes. *In vivo* studies confirmed the good efficacy and tolerance of the product.

# Combination of two plant flavonoids - magnolol and honokiol as a tyrosinase inhibitor for sensitive and uneven skin care

Bozena Tyszczuk<sup>1</sup>, Dawid Dębowski<sup>2</sup>, Krzysztof Cal<sup>3</sup>, Anna Załuska<sup>1</sup>, Iwona Zyglińska<sup>1</sup>, Monika Pasikowska-Piwko\*<sup>1</sup>, Renata Debowska<sup>1</sup>, Katarzyna Rogiewicz<sup>1</sup>, Irena Eris<sup>1</sup>

<sup>1</sup>Dr Irena Eris S.A., Department of Research and Innovations, Piaseczno, Poland,<sup>2</sup>University of Gdansk, Department of Molecular Biochemistry, Gdansk, Poland, <sup>3</sup>Laboratory of Molecule Engineering, Gdańsk, Poland

# **Introduction & Objectives:**

Tyrosinase is a key enzyme in melanin formation. Its inhibition is a crucial step for hyperpigmentation reduction. Magnolol and honokiol (extracted from the bark of *Magnolia officinalis*) are known from strong antioxidant and anti-inflammatory activity. The aim of this study was to evaluate the efficacy of magnolol and honokiol complex in novel delivery system (MaHo) on tyrosinase inhibition as well as their whitening and anty-aging properties in group of panelist with sensitive skin.

#### **Materials & Methods:**

Tyrosinase inhibitory activity was conducted spectrophotometrically *in vitro*. Substances, in several concentrations, were tested: MaHo (powder), MaHo in delivery system, placebo (delivery system).

Preliminary *in vivo* test were performed on emulsion with 1% MaHo in the delivery system in group of 14 female volunteers with sensitive skin (aged 41-70 y. o.). All the participants applied product on face area, twice a day for 4 weeks. Measurements were taken at the baseline and after 4 weeks of product application. Instrumental skin evaluation of melanin content and erythema (Mexameter), intensity of discolorations and UV spots (VISIA) were performed. In addition, a self-evaluation questionnaire was conducted.

Next stage was conducted on serum containing 1% MaHo in delivery system supplemented by squalane, bioceramides, probiotics and heptapeptide on another group of 25 women with sensitive skin (aged 28-69 y. o.). Serum was applied on face area for 3 weeks. All participants completed a satisfaction questionnaire after that time. Among this group, in 13 females, instrumental analysis of skin condition was performed before and after 3 weeks of product usage. In this group, changes in melanin content, elasticity, skin smoothness (Visioscan), number and size of wrinkles and UV spots (Visia) were evaluated.

#### **Results:**

MaHo in delivery system displayed high tyrosinase inhibitory potential and it showed approx. 40% better results compared to control and approx. 25% compared to placebo.

In the preliminary *in vivo* tests, after 4 weeks of emulsion use reduction in melanin concentration (-19%) were proved. All volunteers confirmed, that their skin become soft and more elastic with soothing and calming effect.

In group of participants using serum objective measurements showed improvement in skin elasticity (+6%), reduction of melanin content (-10%), skin roughness (-12%) and number of wrinkles (-17%). Moreover after 3 weeks of serum usage all volunteers self-reported soothing, calming and nourishing effect and improvement in skin tone, moisturization and skin elasticity.

#### Conclusion:

Novel combination of active ingredients (magnolol and honokiol in delivery system) used in tested cosmetic formulations showed very good properties in case of whitening, anty-aging as well as calming effect on sensitive skin with uneven skin tone.

## Efficacy and safety of the 5% cysteamine cream leftin overnight for facial melasma: a pilot study

Paula Basso Lima\*<sup>1, 2</sup>, Daniel Cassiano<sup>3</sup>, Joana Alexandria Ferreira Dias<sup>1</sup>, Ana Cláudia Cavalcante Espósito Lemos<sup>4</sup>, Helio Miot<sup>1</sup>

<sup>1</sup>UNESP, <sup>2</sup>UNIFRAN, <sup>3</sup>UNIFESP, <sup>4</sup>UNOESTE

**Introduction & Objectives:** Melasma is a common, acquired chronic hyperpigmentation of the skin photoexposed areas. The standard therapy of melasma relies on photoprotection based on broad-spectrum sunscreen associated with topical bleaching agents. Among the bleachers available on the market, L-cysteamine (mercaptoethylamine hydrochloride) is an aminothiol compound with antioxidant and depigmenting properties. The recommendation for cysteamine is as a rapid contact therapy, for up to three hours, due to its irritating potential. Nevertheless, it has been suggested that leaving it in overnight was safe and well-tolerated to treat melasma, what was not yet been investigated.

Materials & Methods: We performed a prospective open intervention pilot study between October and December 2021, aiming to assess the safety profile and the efficacy gain of cysteamine left in overnight. Ten women with facial melasma, without treatment for at least one month, were oriented to apply 5% cysteamine cream on their face after the facial moisturizer, leaving it overnight for two months. The daily applications should be tailored according to individual tolerability. All the participants received the same sunscreen (SPF50, PPD19) to be applied during the day. Subjects were assessed at the inclusion and after 60 days of treatment. We evaluated the safety by the report of adverse events, such as facial erythema, scaling, and burning sensation (primary outcomes). Other parameters used were modified Melasma Area and Severity Index (mMASI), Melasma Quality of Life Scale (MELASQoL), and the difference in colorimetric luminosity (Dif\*L) between skin affected by melasma and the adjacent unaffected skin (<2 cm distance). The Global Aesthetic Improvement Scale (GAIS) was used to assess the difference (T0 versus T60) in the skin appearance through standardized photographs.

**Results:** Only four patients (40%) tolerated cysteamine overnight for seven days a week. Albeit, the main obstacle to daily use was the discomfort generated by the sulfur odor. One patient reported worsening of migraine episodes due to the bad smell. Two other patients reported nausea also caused by the odor, and one did not tolerate overnight use on any day for the same reason. Three patients (30%) reported transient mild facial erythema, scaling, and burning at the beginning of the treatment, which faded over the eight weeks.

Five patients (50%) showed a consistent lightening of the melasma through the GAIS assessment (Table 1) Table 1 presents the other clinimetric parameters. The mMASI decreased by 13.5% (CI 95%: 4% to 27%) in eight weeks. There was no difference in colorimetric parameters between D0 and D60. Also, no improvement in the quality of life score at the end of the study was observed.

**Conclusion:** Topical 5% cysteamine left in overnight proved to be safe and well tolerated. However, in a similar study conducted in the same population, 5% cysteamine left in for three hours overnight, provided an mMASI reduction of 15–33% after two months. The study suggests that overnight use may not add efficacy over short contact therapy. Interestingly, in this series, the frequency of use was limited by the sulfur odor and not by skin irritation. In conclusion, 5% cysteamine cream left in overnight is a safe option to treat facial melasma for patients who prefer not to wash it out at bedtime. New cysteamine formulations aiming at minimizing the sulfur odor can increase adherence to the treatment and improve clinical outcomes.

## Clinicopathological and Dermoscopic study of longitudinal melanonychia among Egyptian population.

Mohamed El-Khalawany<sup>1</sup>, Azza Mostafa<sup>2</sup>

<sup>1</sup>Al-Azhar University, Egypt, <sup>2</sup>Ain Shams University, Egypt

## **Introduction & Objectives:**

Longitudinal melanonychia (LM) is a challenging condition that may affect quality of life and lead to psychogenic stress due to its close relation to malignant melanoma (MM). The underlying causes of LM are variable and could be serious in adult age group. The objectives of this study were to identify the underlying causes of LM in Egyptian population and record the incidence of MM among those patients.

#### **Materials & Methods:**

A cross sectional study was performed along 5 years duration during the period from 2017 to 2022, collecting a total of 82 patients with LM. Full history and examination in addition to onychoscopy and nail biopsy was performed for each patient. immunostaining with S100 and MART-1 was performed if melanocytic nests were observed. Special staining with PAS and GMS was performed if fungal infection was suspected. The results were recorded and patients were asked to follow up for one year.

#### **Results:**

The study included 49 males (59.8%) and 33 females (40.2%) ranged from 18 to 54 years (mean 36 +/- 11.7 years). The duration of lesions ranged from 3 weeks to 2 years (avreage 5+/- 2.4months). The majority of patients (90.2%) were presented with single nail affection while only 8 patients (9.8%) were presented with multiple nail affection. The most common nail affected was thumbs (39%) followed by big toe (24.4%) and middle finger (20.7%). Benign underlying causes were recorded in 78 patients (95.1%) while malignnat melanoma was observed in only 4 patients (4.9%). Benign causes included lentigo simplex (31.7%), racial (30.5%), junctional nevi (17.1%), post traumatic hemorrhage (13.4%) and fungal infection (2.4%). Cases of MM were observed in big toe (two cases) while one case was observed in thumb and middle finger. All cases were males with solitary nail affecion and average age of 38 years. Hutchinson's sign was observed in two cases while nail dystrophy was observed in one case.

## **Conclusion:**

To the best of our knowledge, this is the first study to investigate LM among Egyptian population. The outcome of this study proposed that LM is almost due to a benign condition and the incidence of MM is less than reported in other countries. Middle age male patients with solitary nail affection in big toe or thumb and show Hutchinson's sign is considered a high risk group. The collaboration of dermoscopy and biopsy is highly recommended for early detection of nail melanoma. Although it seems that awaerness of such condition is increased among Egyption population, a multicenter large scale study is recommended to fullty evaluate the magnitude of this condition in this ethenic group.

Effect of Ruxolitinib Cream on VASI50 Achievement by Body Region Through Week 104 in Patients With Vitiligo: Analysis of the TRuE-V Long-Term Extension Phase 3 Study

Thierry Passeron\*<sup>1, 2</sup>, John E. Harris<sup>3</sup>, Kim A. Papp<sup>4, 5</sup>, Amit G. Pandya<sup>6, 7</sup>, Julien Seneschal<sup>8</sup>, Andrew Blauvelt<sup>9</sup>, Mark Amster<sup>10</sup>, Shaoceng Wei<sup>11</sup>, Deanna Kornacki<sup>11</sup>, Khaled Ezzedine<sup>12</sup>, David Rosmarin<sup>13</sup>

<sup>1</sup>Centre Hospitalier Universitaire de Nice, Université Côte d'Azur, Nice, France, <sup>2</sup>INSERM U1065, C3M, Université Côte d'Azur, Nice, France, <sup>3</sup>University of Massachusetts Chan Medical School, Worcester, MA, United States, <sup>4</sup>Alliance Clinical Trials and Probity Medical Research, Waterloo, ON, Canada, <sup>5</sup>Division of Dermatology, Department of Medicine, University of Toronto, Toronto, ON, Canada, <sup>6</sup>Palo Alto Foundation Medical Group, Sunnyvale, CA, United States, <sup>7</sup>University of Texas Southwestern Medical Center, Dallas, TX, United States, <sup>8</sup>Department of Dermatology and Pediatric Dermatology, National Reference Center for Rare Skin Disorders, Hôpital Saint André, CNRS, UMR-5164, ImmunoConcEpT, F-33000, Bordeaux, France, <sup>9</sup>Oregon Medical Research Center, Portland, OR, United States, <sup>10</sup>MetroBoston Clinical Partners, Brighton, MA, United States, <sup>11</sup>Incyte Corporation, Wilmington, DE, United States, <sup>12</sup>Henri Mondor University Hospital and Université Paris-Est Créteil Val de Marne, Paris, France, <sup>13</sup>Indiana University School of Medicine, Indianapolis, IN, United States

# **Introduction & Objectives:**

Vitiligo is a chronic autoimmune disease characterized by melanocyte destruction, leading to skin depigmentation. In 2 randomized, double-blinded, vehicle-controlled phase 3 studies in adults and adolescents (aged ≥12 y) with nonsegmental vitiligo (TRuE-V1 [NCT04052425]; TRuE-V2 [NCT04057573]), ruxolitinib cream application resulted in statistically superior improvements in repigmentation versus vehicle in the primary and all key secondary efficacy endpoints at Week 24; continued improvement was observed through Week 52. In the TRuE-V long-term extension (LTE) study (NCT04530344), further improvements in facial and total body repigmentation (as assessed by Vitiligo Area Scoring Index [VASI] responses) were observed through Week 104 among patients who did not achieve ≥90% facial repigmentation by the end of TRuE-V1/TRuE-V2 (Week 52). Here, we report results from a post hoc analysis on the achievement of ≥50% improvement in VASI (VASI50) by body region in patients who continued to apply ruxolitinib cream through Week 104 of the TRuE-V LTE study.

# **Materials & Methods:**

Patients who completed the parent studies (TRuE-V1/TRuE-V2) were eligible to enroll in the TRuE-V LTE. Patients who did not achieve ≥90% improvement in facial VASI at Week 52 (LTE baseline) continued to apply open-label 1.5% ruxolitinib cream twice daily until Week 104. The proportion of patients achieving VASI50 through Week 104 was determined for each body region (head and neck [excluding face], hands, upper extremities, trunk [including genitals], lower extremities, and feet) as well as total body (excluding face). Only patients with non-zero baseline VASIs for each body region were included in respective body region analyses.

#### **Results:**

A total of 222 patients who were initially randomized to ruxolitinib cream in TRuE-V1/TRuE-V2 continued to apply ruxolitinib cream in the TRuE-V LTE and were included in this analysis (head and neck, n=144; hands, n=193; upper extremities, n=205; trunk, n=182; lower extremities, n=179; feet, n=136). Total body VASI50 (excluding face) was achieved by 40.3% of patients at Week 52 and 60.5% at Week 104. Proportions of patients who achieved VASI50 increased from Weeks 52 to 104 in each body region, including head and neck (57.3% to 78.2%),

upper extremities (48.5% to 65.2%), trunk (42.0% to 63.1%), and lower extremities (49.4% to 67.8%). Improvements were also observed from Weeks 52 to 104 in difficult-to-repigment body regions, such as the hands (31.8% to 50.3%) and feet (24.4% to 33.9%). Similarly, proportions of patients who crossed over from vehicle in the parent studies (n=118; i.e., those who applied ruxolitinib cream after Week 24 in TRuE-V1/TRuE-V2 [total 80 weeks of active treatment]) who achieved VASI50 also increased from Weeks 52 to 104, regardless of body region.

**Conclusion:** # Adolescents and adults with nonsegmental vitiligo who applied ruxolitinib cream for an additional 52 weeks after completion of TRuE-V1/TRuE-V2 achieved continuous improvements in repigmentation (assessed by VASI50) through Week 104 of the TRuE-V LTE across all body regions, including in difficult-to-repigment areas (e.g., hands and feet).

# Efficacy and Safety of Ruxolitinib Cream Through Week 104 in Patients With Vitiligo: Subgroup Analysis of the TRuE-V Long-Term Extension Phase 3 Study

Julien Seneschal\*<sup>1</sup>, Albert Wolkerstorfer<sup>2</sup>, Khaled Ezzedine<sup>3</sup>, Amit G. Pandya<sup>4, 5</sup>, Charles Lynde<sup>6</sup>, Anthony Nuara<sup>7</sup>, Shaoceng Wei<sup>8</sup>, Deanna Kornacki<sup>8</sup>, David Rosmarin<sup>9</sup>

<sup>1</sup>Department of Dermatology and Pediatric Dermatology, National Reference Center for Rare Skin Disorders, Hôpital Saint André, CNRS, UMR-5164, ImmunoConcEpT, F-33000, Bordeaux, France, <sup>2</sup>Amsterdam University Medical Center, Amsterdam, Netherlands, <sup>3</sup>Henri Mondor University Hospital and Université Paris-Est Créteil Val de Marne, Paris, France, <sup>4</sup>Palo Alto Foundation Medical Group, Sunnyvale, CA, United States, <sup>5</sup>University of Texas Southwestern Medical Center, Dallas, TX, United States, <sup>6</sup>Lynde Institute for Dermatology, Markham, ON, Canada, <sup>7</sup>Center for Dermatology & Plastic Surgery, Scottsdale, AZ, United States, <sup>8</sup>Incyte Corporation, Wilmington, DE, United States, <sup>9</sup>Indiana University School of Medicine, Indianapolis, IN, United States

# **Introduction & Objectives:**

Vitiligo is a chronic autoimmune disease characterized by melanocyte destruction, leading to skin depigmentation. In 2 randomized, double-blind, vehicle-controlled phase 3 studies in adults and adolescents (aged ≥12 y) with nonsegmental vitiligo (TRuE-V1 [NCT04052425]; TRuE-V2 [NCT04057573]), ruxolitinib cream application resulted in statistically superior improvements in repigmentation versus vehicle in the primary and all key secondary efficacy endpoints at Week 24; continued improvement was observed through Week 52. In the TRuE-V long-term extension (LTE) study (NCT04530344), further improvements in facial and total body repigmentation (as assessed by Vitiligo Area Scoring Index [VASI] responses) were observed through Week 104 among patients who did not achieve ≥90% facial repigmentation by the end of TRuE-V1/TRuE-V2 (Week 52). In this analysis, efficacy and safety data from TRuE-V LTE were evaluated based on baseline demographic and clinical characteristic subgroups.

#### **Materials & Methods:**

Patients who completed the parent studies (TRuE-V1/TRuE-V2) were eligible to enroll in the TRuE-V LTE. Patients who did not achieve ≥90% improvement in facial VASI at Week 52 continued to apply open-label 1.5% ruxolitinib cream twice daily until Week 104. The proportion of patients achieving ≥75% improvement from baseline in facial VASI (F-VASI75) and ≥50% improvement from baseline in total VASI (T-VASI50) were assessed across key baseline clinical and demographic subgroups (sex, age group, Fitzpatrick skin type, affected facial body surface area [F-BSA], baseline disease status [stable or progressive], and previous therapy). Safety and tolerability were also assessed.

# Results:

A total of 222 patients who were initially randomized to ruxolitinib cream in TRuE-V1/TRuE-V2 continued to apply ruxolitinib cream in TRuE-V LTE and were included in the efficacy analysis. F-VASI75 and T-VASI50 responses were achieved by 66.1% and 63.8% of patients, respectively, at Week 104. Substantive F-VASI75 responses were seen for men (n=73, 56.2%) and women (n=104, 73.1%) at Week 104. F-VASI75 responses at Week 104 were consistent across adolescents (12–17 years [n=31], 54.8%) and adults (18–64 years [n=131], 66.4%;  $\geq$ 65 years [n=15], 86.7%). F-VASI75 responses at Week 104 were also generally consistent based on Fitzpatrick skin type (I–III [n=130], 66.9%; IV–VI [n=47], 63.8%), affected F-BSA (<1.5% [n=141], 61.7%;  $\geq$ 1.5% [n=36], 83.3%), baseline

disease status (stable [n=139], 64.7%; progressive [n=38], 71.1%) and previous therapy (topical corticosteroids [n=57], 64.9%; topical calcineurin inhibitors [n=64], 62.5%; phototherapy [n=53], 71.7%). Similarly, there were no substantive differences in T-VASI50 responses across all subgroups. Treatment-emergent adverse events (AEs) occurred in 50.9% of 224 patients who applied ruxolitinib cream throughout the LTE. Treatment-related AEs occurred in 6.3% of patients, all of which were mild or moderate in severity, and rates were generally similar across demographic subgroups.

**Conclusion:** # Adolescents and adults with nonsegmental vitiligo who applied ruxolitinib cream achieved F-VASI75 and T-VASI50 responses at Week 104 regardless of baseline demographics or clinical characteristics. Ruxolitinib cream was well tolerated, and the incidence of treatment-related AEs was similar across demographic subgroups.

## Vitiligo: a retrospective 10- year single institutional study of 86 patients

Dubravka Zivanovic<sup>1</sup>

<sup>1</sup>School of Medicine, University of Belgrade, University Clinical Center of Serbia, Clinic of Dermatology and Venereology, Belgrade

# **Introduction & Objectives:**

Vitiligo (V) is a chronic acquired pigmentation disorder of an unclear etiopathogenesis, characterized by well circumscribed, sharply demarcated, depigmented confluent macules and patches that can affect the entire skin. Clinically, V is classified into three major categories: segmental vitiligo (SV), non-segmental vitiligo (NSV) and mixed vitiligo. The prevalence is about 0.5–2%; females and males are almost equally affected. The disease can occur at any age; usually it begins between the ages of 10-30 years. Previous research has shown an association between V and various autoimmune diseases and an increased incidence of autoimmune diseases in relatives.

The aim of this study was to analyze clinical forms of vitiligo and to investigate the association between vitiligo and other diseases.

### **Materials & Methods:**

A total of 86 inpatients with vitiligo from 2010-2019, were included in this retrospective study. Data on sex, age of onset, clinical presentation, medical and family history were collected and analyzed using descriptive and analytic statistics.

## **Results:**

Men and women were equally affected (40.7% men and 59.3% women). Vitiligo mostly occurred in the first and second decade of life, the average of the onset of the disease was 28.97 years. NSV was the most frequent form (67.5%). Associated diseases were observed in 87.2% of patients; most common were thyroid gland diseases in 29.1% of patients (women being more frequently affected, p= 0.014) and arterial hypertension in 31.4%. Among relatives, vitiligo was noticed in 12.8%. Other diseases recorded in relatives were cardiovascular diseases (36.0%), different malignancies (30.2%), diabetes mellitus (20.9%), thyroid gland disorders (14%).

#### **Conclusion:**

We have shown that the frequency of vitiligo was equal between sexes, we recorded a high percentage of patients with associated autoimmune disorders, especially thyroid gland diseases and a higher percentage of autoimmune diseases among relatives.

# Role of Erythroid differentiation regulator 1 (Erdr1) cytokine in vitiligo: a case control study

Maha Fathy Elmasry\*1

<sup>1</sup>Faculty of Medicine, Cairo University, Dermatology, Cairo, Egypt

**Introduction & Objectives:** Erythroid differentiation regulator 1 (Erdr1) cytokine is a stress-related survival factor. It has been well-established by several researches that there is a potential relationship between stress and vitiligo, proposing a possible positive association between Erdr1 and induction of vitiligo. This study's objective is to measure the levels of Erdr1 in lesional skin of vitiligo patients and to compare it to that of controls in a trial to study and verify the hypothesis of the role of Erdr1 in the pathogenesis of vitiligo.

**Materials & Methods:** This case-control study was conducted on 50 patients with generalized nonsegmental vitiligo and 50 healthy controls fulfilling the inclusion criteria over a period of 6 months. Patients underwent complete medical history and detailed assessment of vitiligo. Skin biopsies were taken from sun-covered site from both patients' vitiliginous skin and from normal skin of controls for which Erdr1 tissue expression levels were measured using quantitative real-time polymerase chain reaction technique.

**Results:** There was a statistically significant difference upon comparing the Erdr1 levels in vitiligo patients and controls (P<0.001) with lower levels of Erdr1 in vitiligo patients than in controls.

**Conclusion:** As far as we know, this is the first study comparing Erdr1 tissue level in vitiligo patients versus healthy controls. Tissue levels of Erdr1 cytokine were significantly lower in vitiligo patients than healthy controls thus, verifying the important role of Erdr1 in vitiligo pathogenesis. In addition, procedures that can increase Erdr1 level could be a promising treatment option for this disease.

Patient-Reported Outcomes Following 24 Weeks of Treatment With Upadacitinib in Adults With Non-Segmental Vitiligo: Results From a Phase 2, Randomized, Double-Blind, Dose-Ranging Study

Khaled Ezzedine $^{*1, 2}$ , Ahmed M Soliman<sup>3</sup>, David Rosmarin<sup>4</sup>, Amit G Pandya<sup>5, 6</sup>, Bethanee J Schlosser<sup>3</sup>, Nanja Van Geel<sup>7</sup>

<sup>1</sup>AP-HP, Henri Mondor University Hospital, UPEC, Department of Dermatology, Créteil, France, <sup>2</sup>Université Paris-Est Créteil, UPEC, EA 7379 EpidermE, Créteil, France, <sup>3</sup>AbbVie Inc, North Chicago, United States, <sup>4</sup>Indiana University School of Medicine, Department of Dermatology, Indianapolis, United States, <sup>5</sup>Palo Alto Foundation Medical Group, Sunnyvale, United States, <sup>6</sup>University of Texas Southwestern Medical Center, Department of Dermatology, Dallas, United States, <sup>7</sup>Ghent University Hospital, Department of Dermatology, Ghent, Belgium

## **Introduction & Objectives:**

Vitiligo has a considerable negative impact on patients' health-related quality of life (HRQoL). Patients often experience social stigma, low self-esteem, anxiety, and depression. Assessment of HRQoL is therefore recommended as part of the evaluation of disease severity and treatment benefits. Accordingly, the impacts of treatment with upadacitinib (UPA), an oral Janus kinase inhibitor, on a range of patient-reported HRQoL outcomes were evaluated as part of a phase 2, multicenter, randomized, double-blind, placebo-controlled, doseranging study in adults with non-segmental vitiligo.

## **Materials & Methods:**

Adults aged 18–65 years with non-segmental vitiligo with a Facial Vitiligo Area Scoring Index score ≥0.5 and a Total Vitiligo Area Scoring Index score ≥5 at baseline were included in this 52-week study (NCT04927975). During a 24-week, double-blind, placebo-controlled treatment period (period 1), patients were randomly assigned to receive UPA 6 mg (UPA6), UPA 11 mg (UPA11), UPA 22 mg (UPA22), or placebo once daily (QD). Patientreported HRQoL outcomes assessed at the week 24 primary analysis timepoint (ie, end of period 1) included change from baseline in vitiligo QoL (VitiQoL) total score (lower scores reflect better HRQoL), achievement of a Vitiligo Noticeability Scale (VNS) response of 4 ("a lot less noticeable") or 5 ("no longer noticeable"), change from baseline in Dermatology Life Quality Index (DLQI; lower scores reflect better HRQoL), change from baseline in Hospital Anxiety and Depression Scale (HADS) anxiety and depression scores (where lower scores reflect less anxiety and/or depression), and achievement of a Patient's Global Impression of Change-Vitiligo (PaGIC-V) response of 1 ("much better") or 2 ("a little better").

## **Results:**

A total of 185 patients were enrolled in the study (UPA6 n=49; UPA11, n=47; UPA22, n=43; placebo n=46). Mean reductions in VitiQoL scores from baseline to week 24 with UPA22 (-6.6) and UPA6 (-7.5) were numerically larger than with placebo (-5.5), although not statistically significant (**Table**). At week 24, more patients treated with UPA22 reported a VNS response of "a lot less noticeable" or "no longer noticeable" than with placebo (11.6% vs 0%, respectively; P < .05; **Table**). Mean reductions in DLQI scores from baseline to week 24 were significantly larger with UPA22 than with placebo (-2.2 vs -0.6; P < .05). HADS anxiety scores decreased from baseline to week 24 in the UPA6 and UPA22 groups, with similar reductions in HADS depression scores observed for the UPA11 and UPA22 groups; changes in HADS scores were not significantly different vs placebo (**Table**). A significantly greater proportion of patients achieved a PaGIC-V response of "much better" or "a little better" with any UPA dose vs placebo: UPA6 (34.7%), UPA11 (55.3%), and UPA22 (60.5%) vs placebo (19.6%; P < .05 vs

placebo for all UPA doses; Table).

### **Conclusion:**

Among adults with non-segmental vitiligo, 24 weeks of treatment with UPA at all doses resulted in improvements compared to placebo in patient impressions of disease improvement based on PaGIC results. These initial findings suggest that UPA22 may improve patient HRQoL and perceptions of vitiligo noticeability; longer term data from the extension phase of this study will further clarify the impact of UPA treatment on QoL.

Table. Patient-Reported Outcomes Evaluated at Week 24

|  | UPA                | UPA                |                    |               |
|--|--------------------|--------------------|--------------------|---------------|
|  | 6 mg QD<br>(n=49)  | 11 mg QD<br>(n=47) | 22 mg QD<br>(n=43) | PBO<br>(n=46) |
| VitiQoL <sup>a</sup>                         | (11-40)            | (11-47)            | (11-40)            | (11-40)       |
| LS mean change, % (SE)  P value <sup>b</sup> | -7.5 (2.3)<br>.545 | -3.7 (2.3)<br>.565 | -6.6 (2.6)<br>.754 | -5.5 (2.4)    |
| VNS score of 4 or 5c                         |                    |                    |                    |               |
| Responders, n (%)                            | 0                  | 0                  | 5 (11.6)           | 0             |
| P value <sup>b</sup>                         |                    |                    | .005               |               |
| DLQId  |                    |                    |                    |               |
| LS mean change, % (SE)                       | -1.4 (0.5)         | -1.2 (0.5)         | -2.2 (0.5)         | -0.6 (0.5)    |
| P value <sup>b</sup>                         | .212               | .361               | .027               |               |
| PaGIC-V score of 1 or 2°                     |                    |                    |                    |               |
| Responders, n (%)                            | 17 (34.7)          | 26 (55.3)          | 26 (60.5)          | 9 (19.6)      |
| P value <sup>b</sup>                         | .081               | <.001              | <.001              |               |
| HADS Anxiety <sup>f</sup>                    |                    |                    |                    |               |
| LS mean change, % (SE)                       | -0.7 (0.4)         | 0.0 (0.4)          | -0.3 (0.4)         | 0.3 (0.4)     |
| P value <sup>b</sup>                         | .063               | .670               | .343               |               |
| HADS Depression <sup>f</sup>                 |                    |                    |                    |               |
| LS mean change, % (SE)                       | 0.2 (0.3)          | -0.3 (0.3)         | -0.1(0.4)          | 0.4(0.3)      |
| P value <sup>b</sup>                         | .638               | .150               | .352               |               |

DLQI, Dermatology Life Quality Index; HADS, Hospital Anxiety and Depression Scale; PaGIC-V, Patient's Global Impression of Change-Vitiligo; PBO, placebo; UPA, upadacitinib; VitiQoL, Vitiligo Quality of Life; VNS, Vitiligo Noticeability Scale.

aVitiQoL change from baseline. Number of patients: UPA 6 mg, 44; UPA 11 mg 44; UPA 22 mg, 34; placebo 40.

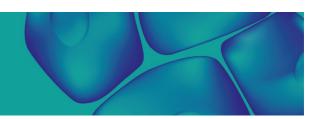
<sup>&</sup>lt;sup>b</sup>P values are vs PBO and are nominal and not multiplicity adjusted.

<sup>&</sup>quot;VNS response was defined as a score of 4 ("a lot less noticeable") or 5 ("no longer noticeable").

<sup>&</sup>lt;sup>d</sup>DLQI change from baseline. Number of patients: UPA 6 mg, 43; UPA 11 mg 42; UPA 22 mg, 35; placebo 38.

ePaGiC-V response was defined as a score of 1 ("much better") or 2 ("a little better").

HADS Anxiety score and HADS Depression score changes from baseline. Number of patients: UPA 6 mg, 44; UPA 11 mg 45; UPA 22 mg, 34; placebo 40.



Effectiveness and benefits of broad-spectrum UVB-UVA-BL sunscreens SPF50+ in preventing lentigines UV-induced in photo-ageing and pigmentary disorders

Priscilla Lapalud<sup>1</sup>, Noizet Maite<sup>1</sup>, Laur Lucie<sup>1</sup>, Cécile Delsol<sup>2</sup>, Gautier Doat\*<sup>2</sup>, Giovanni Pellacani<sup>3</sup>, Nathalie Castex-Rizzi<sup>1</sup>, Ribet Virginie<sup>1</sup>

<sup>1</sup>Pierre Fabre Dermo-Cosmétique et Personal care, R&D Department, Toulouse, France, <sup>2</sup>AVENE, Medical Department, Lavaur, France, <sup>3</sup>Sapienza University of Rome, Dermatology Clinic, Department of Clinical Internal, Anesthesiological and Cardiovascular Sciences, Rome, Italy

**Introduction & Objectives:** Sun exposure including blue light (BL) radiation is well described in skin hyperpigmentation. Photoprotection is therefore essential to prevent brown spots appearance and worsening. We developed a SPF50+ broad-spectrum UVB-UVA-BL sunscreen, containing a very high photoprotective system with TriAsorBTM. The aim of this work was to demonstrate its efficacy in hyperpigmentation and photoaging prevention and benefit for subjects suffering from melasma and lentigo.

**Materials & Methods:** Efficacy in preventing UV-induced hyperpigmentation and UV-induced dermal collagen degradation was measured through in vitro studies. Dermatological and ophthalmological tolerance and efficacy (clinical and instrumental evaluations) study was performed on 66 adults (mean age = 57 years old; from 39 to 70 years old) with sensitive skin and dark spots (53 with lentigo; 13 with melasma) after 56 days of use under sun exposure.

**Results:** The product applications increased in vitro the lightness L\* parameter (+8% (p<0.0001) vs UV control) associated with color modification markedly detectable by human eye ( $\Delta E$ =4) on UV-pigmented epidermis. Moreover, repeated preventive application on photo-exposed skin explants showed significant prevention of dermal collagen alteration. Clinical evaluations concluded that the product was efficient in 100% of the subjects (no aggravation of dark spots) with +17% on average in skin radiance. No decrease in the ITA° (average: +10.6 on a pre-selected dark spot, +9 on surrounding skin), and -15% in intensity of spots (p<0.0001) were observed indicating a natural loss of tan over 2 months of study course while subjects were exposed every day to UV in a country with strong sunlight (Mauritius). Improvement of the skin with a perceived protective anti-dark spot efficacy (the product prevents darkening of existing spots) was observed in 98% of subjects. They reported their skin elasticity was preserved. Skin sensations (i.e.: comfort, skin revitalised) were very good perceived with an excellent acceptability (overall liking: 100%).

**Conclusion:** This work demonstrates the benefit of daily application of broad-spectrum UVB-UVA-BL sunscreen in preventing lentigines UV-induced in photo-ageing and pigmentary disorders.

Eye-opening: combining an effective tyrosinase inhibitor with Oligopeptides and Hyaluronic Acid to tackle brown and blue under-eye circles

Katja Warnke<sup>1</sup>, Uta Meiring<sup>1</sup>, Nadeshda Kurz<sup>1</sup>, Gesa-Meike Muhr<sup>1</sup>, Philip Drescher<sup>1</sup>, Dylan Griffiths<sup>2</sup>

<sup>1</sup>Beiersdorf AG, Research and Development, Hamburg, Germany, <sup>2</sup>Beiersdorf AG, Medical Management, Hamburg, Germany

# **Introduction & Objectives:**

Dark under-eye circles (periorbital hyperpigmentation) are a visible cosmetic concern. Various causes can contribute, such as excessive pigmentation, shadows due to skin laxity and wrinkles, as well thin, translucent skin (Park, 2018). Dark under-eye circles are manifested as brown pigmented and blue vascular types. Most common is the mixed type combining vascular and pigmented (Park, 2016). Thus, to broadly counteract dark under-eye circles, a combined strategy is also needed.

In our in vivo studies, we investigated the new approach combining the skin strengthening actives Oligopeptides and Hyaluronic Acid with the efficacious tyrosinase inhibitor Thiamidol (Isobutylamido Thiazolyl Resorcinol) to reduce all types of dark under-eye circles for a fresh and awake look. For instant effects, using a cooling metal applicator and light reflecting pigments completes the innovative formula

#### Materials & Methods:

To assess dark under-eye circles, skin evenness, healthy looking and radiance, we tested the product split-face applied twice daily for 12 weeks with volunteers covering all types of dark under eye circles (vascular, pigmented and mixed). Clinical grading, self-grading and clinical photography were performed after 2, 4, 8 and 12 weeks in comparison to the control site and baseline. Additionally, questionnaires for self-assessment were applied.

The test product's tolerability was determined in a study with 33 volunteers over 2 weeks applying the product twice daily. Dermatological and ophthalmological assessments were conducted at the beginning and the end of the study. A user survey was conducted with 120 volunteers over 4 weeks to assess product performance using a questionnaire.

#### **Results:**

All types of dark circles (vascular, pigmented and mixed) showed a significant improvement after 12 weeks in clinical grading. Severity of dark circles significantly lessened. The results were further supported by self-grading of dark circles, evenness, lines and wrinkles, radiance and healthy looking. First significant results were visible after 2 weeks with further improvement up to 12 weeks.

Very good tolerability was proven by dermatological and ophthalmological assessment. The formula is very well suitable for all skin types even for sensitive skin and additionally suitable for wearers of contact lenses.

In the survey with consumers having dark under-eye circles, after 4 weeks usage, 98 % confirmed that the product reduces dark circles long-lastingly, reduces wrinkles and lines and provides radiant skin. 97 % confirmed the product brightens the under-eye area. Instant effects were confirmed with 95 % that the product immediately provides a fresh look. In addition, 88 % saw an immediate reduction in puffiness around the eyes.

#### **Conclusion:**

A new formula combining the skin strengthening actives Oligopeptides and Hyaluronic Acid with the efficacious tyrosinase inhibitor Thiamidol (Isobutylamido Thiazolyl Resorcinol) significantly reduced all types of dark undereye circles (vascular, pigmented and mixed). The very well tolerated formula is enriched with light reflecting pigments and delivered by a cooling metal applicator resulting in an instantly fresh and awake look.

Treatment of Benign Epidermal Pigmentations with Dual-wavelength Picosecond Neodymium-Doped Yttrium Aluminium Garnet Laser: A retrospective study

Bo Bin Cha<sup>1</sup>, Sang Yeon Kim<sup>1</sup>, Ji Soo Park<sup>1</sup>, Kyu Yeon Kim<sup>1</sup>, Jin Seop Kim<sup>1</sup>, Young-Jun Choi<sup>1</sup>, Won-Serk Kim<sup>1</sup>, Ga-Young Lee<sup>1</sup>

<sup>1</sup>Kangbuk Samsung Hospital, Samsung Medical Center, Department of Dermatology, Seoul, Korea, Rep. of South

**Introduction & Objectives:** Picosecond neodymium–doped yttrium aluminium garnet laser (PSNY) has emerged as a new alternative in the treatment of pigmentary disorders. The study aimed to evaluate the clinical outcome of dual-wavelength PSNY on the treatment of benign epidermal pigmentations (BEPs).

**Materials & Methods:** A retrospective chart review was performed on patients diagnosed as BEPs (freckles, lentigines and lentigo), and treated with either 532nm, 1064nm PSNY laser or both. Improvement was assessed by three blind dermatologists by evaluating clinical photographs using quartile grading scale.

**Results:** A total of 13 Korean patients (1 male and 12 females; mean age of  $56.15 \pm 13.98$  years) with Fitzpatrick skin types II to IV were included. Laser pulse duration was fixed at 250 picosecond, and a 1064nm PSNY with a mean fluence of 1.67 J/cm2 and a 532nm PSNY with a mean fluence of 0.70 J/cm2 were used. Total number of treatment sessions ranged from 1 to 4. On the quartile grading scale, the final improvement score was 2.67 for freckles,  $2.78 \pm 0.69$  for lentigines and  $3.17 \pm 0.69$  for lentigo. None reported adverse effects such as post-inflammatory hyperpigmentation and persistent erythema.

**Conclusion:** The dual 532nm and 1064nm PSNY can be a treatment modality of BEPs in Koreans.

Management of vitiligo at a tertiary centre for Dermatology, against British Association of Dermatology guidelines 2021.

Smrithi Santhosh\*1, Daniel Shaw1, Firas Kreeshan1

<sup>1</sup>Salford Royal, United Kingdom

# **Introduction & Objectives:**

Updated guidelines for management of patients with vitiligo were published by the British Association of Dermatologists in 2021. We addressed these recommendations and audited current clinical practice, at our tertiary centre for Dermatology, against the guidelines.

#### **Materials & Methods:**

Patients with vitiligo accessing the service were obtained from the analytics department. Multiple searches were required to generate sufficient patients. Patients who were reviewed from 2021 onwards were selected, following on from when the guideline was published. 20 patients were included in the final data collection.

### **Results:**

In all cases (n = 20) the type of vitiligo was documented. Fitzpatrick skin type was recorded in 35% (n = 7) of cases. Extent of disease was documented in 90% (n= 18) of cases, using a descriptive process but no scoring systems were utilised. Quality of life was documented in 15% (n= 3), with the use of DLQI. Disease stability was described by 94.4 % (n = 17) of cases and this was only documented in 18 cases, as 2 patients were discharged following the first clinic visit. 30% (n = 6) of cases documented impact on mental wellbeing of which one patient was referred for formal psychological assessment. 30% (n = 6) of cases performed thyroid antibody screen, 60% (n = 12) of cases documented previous potent topical steroid use and 75% (n = 15) cases had clinical photography performed.

#### **Conclusion:**

Overall, there was good documentation of type of vitiligo, distribution and disease stability. Clinical photography was not mandated in the guidelines but is a useful tool to monitor disease stability. Areas for improvement include more frequent objective measurement of quality of life (e.g. DLQI), thyroid antibody testing on all patients, either in secondary or primary care, and consideration of formal referral to clinical psychology.

Adipose Derived Stem Cells Enhanced with Platelet Rich Plasma as a Novel Treatment of Vitiligo Patients: A Prospective Comparative Controlled Trial.

Dina Hassan Fahmy\*<sup>1</sup>, Nashwa Naeem Elfar<sup>1</sup>, Amira Yousef Ahmed Yousef Ahmed<sup>2</sup>, Walid Ahmed Moustafa<sup>3</sup>, Zeinab Abdelsamad Ibrahim<sup>1</sup>

<sup>1</sup>Faculty of medicine Tanta University, Dermatology and Venereology, Tanta, Egypt, <sup>2</sup>Faculty of medicine Tanta University, Clinical Pathology, Tanta, Egypt, <sup>3</sup>Faculty of medicine Tanta University, Plastic surgery, Tanta, Egypt

**Introduction & Objectives:** Despite\*\* vitiligo has several treatment modalities, it is still challenging for dermatologists to find a proper option for re-pigmentation in many resistant cases. Adipose-derived stem cells (ADSCs) are used widely in the field of regenerative medicine as they can prevent cells from apoptosis and encourage the neighboring cells to develop, producing specialized cells and melanocyte precursors under the influence of certain growth factors.

The aim of our work was to assess the safety and efficacy of ADSCs alone and ADSCs combined with PRP in the vitiligo treatment as a novel treatment option in resistant cases.

**Materials & Methods:** After the approval of ethical committee we recruited 30 patients in this study; each patient had 3 vitiligo patches (two more or less similar patches on both sides of the body and a third patch as a control), the patches were divided into 3 groups, group I injected with autologous ADSCs, group II injected with autologous ADSCs enriched with PRP, and group III (control group) with no injection. The injection was done once then followed by narrow band-UVB sessions twice weekly for three months, and the patients were evaluated at the end of the treatment.

**Results:** Regarding the degree of improvement, there was statistically significant improvement in groups I & II as compared to group III. The median percentage of re-pigmentation in group I was 60%, in group II was 45%, and in group III was 10%. The best response was observed on extremities while the acral patches showed no response. 46.7% of patients did not have any side effects while other patients experienced minimal side effects.

Conclusion: ADSCs could be an encouraging alternative in vitiligo treatment either alone or enriched with PRP.

Topical Methotrexate Loaded Nanoparticles for The Treatment of Vitiligo: a clinical trial.

Rana Gheith\*1

<sup>1</sup>alahrar teaching hospital, dermatology, SHARQIA, Egypt

**Introduction & Objectives:** The objectives of vitiligo treatment is always regimentation as well as disease stabilization. Systemic methotrexate was used in vitiligo treatment with a therapeutic success achieving treatment objectives. Nano-sized carriers are widely used as topical vehicles to accentuate drug delivery to the diseased skin. Topical methotrexate (MTX) loaded nano biopolymer is a new therapeutic option for vitiligo. The Objective of this study\*\* was to evaluate the therapeutic efficacy and safety of topical gel of MTX loaded nano biopolymer in vitiligo treatment.

**Materials & Methods:** The study was performed on 60 vitiligo patients. They were divided in 2 groups .Group I included 30 vitiligo patients and they were applied a topical gel of MTX loaded nano biopolymer on a single vitiligo patch for 6 weeks.Group II included 30 vitiligo patients and they received a topical placebo gel.Clinical responses with digital photographs and dermoscopy for the treated vitiligo patch were evaluated at 3 follow up visits (3 weeks, 6 weeks after start of treatment, and 6 months after the end of the treatment). Two cases in each group were lost during the follow up visits .

**Results:** Six patients of group I showed excellent clinical improvement and four patients of the same group experienced marked clinical improvement. There was a statistically significant relation between vitiligo activity and the clinical response to topical MTX nano gel. Regardind the follow up by dermoscopic signs, there was a statistically highly significant decrease in microkoebner and the ill defined border and a statistically highly significant increase in well defined border, marginal and intralesional pigmentation after treatment with topical MTX nano gel. A statistically significant increase in perifollicular pigmentation was also demonstrated after treatment in MTX group.

Conclusion: Topical MTX nano gel is a new effective treatment option of active Vitiligo

Autologous Non-Cultured Follicular cell suspension with and without phototherapy in The Treatment of Egyptian patients with Stable Vitiligo

Mohamed Elghareeb\*1

<sup>1</sup>zagazig university faculty of human medicine, dermatology, zagazig

**Introduction & Objectives:** Non-Cultured Follicular cell suspension (NC-FCS) is a new surgical treatment of stable vitiligo. The idea of this surgical method is to transfer hair follicle melanocytes and melanocytes stem cells (MelSCs) from uninvolved skin to the vitiligionous patch where they can repopulate the depigmented skin. The objective of the work was to determine therapeutic and adverse effects of non-cultured follicular cell suspension with and without phototherapy in patients with stable vitiligo.

**Materials & Methods:** Thirty patients with stable vitiligo were involved in this study. They were divided into two groups. Group A:15 patients were treated with NC-FCS followed by twice weekly NB-UVB sessions for 6 months . Group B:15 patients were treated with NC-FCS without phototherapy. The repigmentation achieved in each individual vitiliginous lesion was assessed at 1, 3 and 6 months.

**Results:** There was statistically significant difference between the studied cases with better repigmentation response\*\* in Group A.

**Conclusion:** NC-FCS is a novel effective therapeutic method in the treatment of stable vitiligo with better results when combined with NB-UVB.

## Vitiligo and the impact on quality of life utilising K10 and patient survey

Lauren Kennedy\*<sup>1, 2</sup>, Nisal Punchihewa<sup>3</sup>, Zhao Feng Liu<sup>4</sup>, Lawrence Lin<sup>5</sup>, Chris Chew<sup>2, 6</sup>

<sup>1</sup>Peninsula Health, Department of medicine, <sup>2</sup>Skin Health Institute, <sup>3</sup>Eastern Health, Medicine, <sup>4</sup>Alfred Health, Melbourne, Australia, <sup>5</sup>Monash University, Medicine, Melbourne, Australia, <sup>6</sup>Alfred Health, Victoria Melanoma Service, melbourne, Australia

Vitiligo and the impact on quality of life utilising K10 and patient survey

#### **Authors**

Lauren Kennedy, MD1,2, Nisal Punchihewa MD3, Zhao Feng Liu MD4, Lawrence Lim5, Chris Chew, MBBS2,4,6

#### Affiliations

- 1 Department of Medicine, Peninsula Health, Frankston, Victoria 3199, Australia
- 2 Skin Health Institute, Carlton, Victoria 3054, Australia
- 3 Department of Medicine, Eastern Health, Box Hill, Victoria, 3128, Australia
- 4 Alfred Health, Melbourne, Victoria, 3004, Australia
- 5 Monash University, Clayton, Victoria, 3168 Australia
- 6 Victorian Melanoma Service, Alfred Health, Melbourne, Victoria 3004, Australia

# **Introduction & Objectives:**

Skin disease can significantly affect quality of life owing to the visible nature and difficulty to treat. Vitiligo is a condition characterised by depigmented patches of skin. To date Its impacts on quality of life on Australian patients remain poorly understood.

Our study aims to describe and compare the quality of life impacts of vitiligo and the association to clinical parameters in an Australian cohort. This was completed through qualitative analysis of Kessler Psychological Distress Scale (K10) scores and a quality of life survey which were compared against identified factors thought to influence the quality of life of patients with vitiligo.

# **Materials & Methods:**

All surveys from the Victorian Skin Health Institute, a single, private dermatology, centre completed between 1 Jan 2019 to 31 Dec 2022 were reviewed and, from those that met the inclusion criteria, data was collected and recorded. K10 scores were obtained at first visit from patients and evaluated against a vitiligo-specific quality of life survey developed at the centre. Other parameters investigated were demographics, disease related and treatment related. Statistical analysis of the K10 score was conducted using multivariable linear regression while the Mann-Whitney U Test was used for comparison of groups.

#### Results:

The study included 79 patients with a mean age of 42 at the time of survey completion and 53% of participants

were males. The mean age of onset was 32.5 years with participants having vitiligo for an average of 8.7 years. Approximately 56% reported disease progression in the 6 months prior to their initial visit.

After adjustment for age and gender, K10 scores were positively associated with the presence of treatment side effects and higher scores for the centre specific survey item of wanting "to be less depressed" while a negative association was found for the item of wanting "to be less UV sensitive". In group comparisons, females had higher total K10 scores and scored higher for wanting "to be less depressed", "to participate in normal leisure activities" and "to have more contact to other people"

### **Conclusion:**

Our study demonstrates that vitiligo significantly impacts patient quality of life. Females and patients who experienced side effects have been revealed as groups that may be more affected any may benefit from early support pathways.

# Depression and Depressive Symptoms Among Persons Living With Vitiligo: Findings From the Global VALIANT Survey

Khaled Ezzedine\*<sup>1</sup>, Davinder Parsad<sup>2</sup>, John E. Harris<sup>3</sup>, Pearl Grimes<sup>4</sup>, Nanja Van Geel<sup>5</sup>, Jackie Gardner<sup>6</sup>, Kristen Bibeau<sup>7</sup>, Jessy Gao<sup>7</sup>, Haobo Ren<sup>7</sup>, Iltefat Hamzavi<sup>8</sup>

<sup>1</sup>Henri Mondor University Hospital and Université Paris-Est Créteil Val de Marne, Dermatology, Paris, France, <sup>2</sup>Post Graduate Institute of Medical Education and Research, Chandigarth, India, <sup>3</sup>University of Massachusetts Chan Medical School, Dermatology, Worcester, United States, <sup>4</sup>Vitiligo & Pigmentation Institute of Southern California, Los Angeles, United States, <sup>5</sup>Ghent University Hospital, Gent, Belgium, <sup>6</sup>Vitiligo Support International, Lynchburg, United States, <sup>7</sup>Incyte Corporation, Wilmington, United States, <sup>8</sup>Henry Ford Medical Center, Dermatology, Detroit, United States

## **Introduction & Objectives:**

Vitiligo is a chronic autoimmune disease characterized by melanocyte destruction, resulting in pale or white patches of skin. The population-based global Vitiligo and Life Impact Among International Communities (VALIANT) study sought to understand the impact and burden of vitiligo on depression and depressive symptoms from the patient perspective.

## **Materials & Methods:**

Participants aged ≥18 y self-reporting a vitiligo diagnosis by a healthcare professional were recruited to the online survey from 17 countries and answered questions regarding mental health diagnoses and symptoms. The validated Patient Health Questionnaire-Depression screener (PHQ-9) was used to assess depressive symptoms. PHQ-9 scores range from 0 to 27, with scores ≥10 indicating moderate to severe depression. Formal diagnoses of depression and depressive symptoms per the PHQ-9 were compared across demographic and clinical characteristic subgroups as well as with regard to mental illness care.

# **Results:**

Of 3541 patients, 54.6% were male, and 59.2% had Fitzpatrick skin types I-III (ie, fairer skin). Median (range) age was 38 (18–95) y, and disease duration was 9 (1–82) y. Nearly half (49.1%) of patients reported currently receiving mental health care. A diagnosis of depression was reported by 24.5% of patients. Patients with the highest rates of depression diagnoses were younger (27.0% for ages 18-34 y and 26.2% for 35-54 y vs 16.2% for ≥55 y; both P<0.0001), had skin types IV-VI (ie, darker skin; 29.1% vs 21.3% for fairer skin; P<0.0001), >5% body surface area (BSA) affected (30.1% vs 22.0% for 1%-5% BSA and 17.6% for <1% BSA; both P<0.0001), and hand or face involvement (26.3% vs 19.1% for no hand or face involvement; P<0.0001). Depression rates were also higher among those currently vs not currently receiving mental health care (38.6% vs 10.8%; P<0.0001). There was no significant difference in rates of depression diagnoses based on disease duration. Most (78.1%) patients with depression reported receiving treatment for their depression at the time of the survey. Over half (55.0%) reported moderate to severe symptoms of depression per the PHQ-9; highest rates were among those who were younger (62.7% for ages 18-34 y and 59.5% for 35-54 y vs 31.6% for ≥55 y; both P<0.0001) and had darker skin (68.3% vs 45.8% for fairer skin; P<0.0001), disease duration ≤2 y (62.4% vs 55.6% for 3–9 y vs 51.4% for ≥10 y; P<0.01/P<0.0001), >5% BSA (72.0% vs 47.6% for 1%-5% BSA and 34.5% for <1% BSA; bothP<0.0001), and hand or face involvement (59.3% vs 37.9% for no hand or face involvement; P<0.0001). Rates of moderate to severe depressive symptoms were also higher among those currently vs not currently receiving mental health care (75.5% vs 35.2%; *P*<0.0001). An exploratory factor analysis based on all available PHQ-9 data identified only 1 factor that verified empirically that 9 questions can fit into a unified construct.

### **Conclusion:**

Patients with vitiligo reported considerable depression and depressive symptoms, at rates substantially higher than the global rates of 3.8% and 28.2%, respectively. Depression in patients with vitiligo may be underdiagnosed based on the rates of moderate to severe depressive symptoms. Younger patients, those with darker skin, disease duration  $\leq$ 2 y, >5% affected BSA, and hand or face involvement, and those receiving mental health care, experience higher burden than their counterparts.

# Treatment Satisfaction, Breaks, and Cessation Among Patients Living With Vitiligo: Findings From the Global VALIANT Survey

Nanja Van Geel\*<sup>1</sup>, John E. Harris<sup>2</sup>, Iltefat Hamzavi<sup>3</sup>, Pearl Grimes<sup>4</sup>, Mukta Tulpule<sup>5</sup>, Davinder Parsad<sup>6</sup>, Kristen Bibeau<sup>7</sup>, Jessy Gao<sup>7</sup>, Haobo Ren<sup>7</sup>, Khaled Ezzedine<sup>8</sup>

<sup>1</sup>Ghent University Hospital, Dermatology, Gent, Belgium, <sup>2</sup>University of Massachusetts Chan Medical School, Dermatology, Worcester, United States, <sup>3</sup>Henry Ford Medical Center, Dermatology, Detroit, United States, <sup>4</sup>Vitiligo & Pigmentation Institute of Southern California, Los Angeles, United States, <sup>5</sup>Shweta Association, Pune, India, <sup>6</sup>Post Graduate Institute of Medical Education and Research, Chandigarh, India, <sup>7</sup>Incyte Corporation, Wilmington, United States, <sup>8</sup>Henri Mondor University Hospital and Université Paris-Est Créteil Val de Marne, Dermatology, Paris, France

## **Introduction & Objectives:**

Vitiligo is a chronic autoimmune disease characterized by melanocyte destruction, resulting in pale or white patches of skin. The population-based global Vitiligo and Life Impact Among International Communities (VALIANT) study explored vitiligo treatment from the patient perspective, including why they discontinue treatment.

## **Materials & Methods:**

Participants aged ≥18 y who self-reported a vitiligo diagnosis by a healthcare professional were recruited to the online survey and answered questions regarding opinions on treatment and treatment cessation. Participants from 17 countries grouped into geographic regions including: Africa/Middle East, Asia, Australia, Brazil, Canada, Europe, and the United States.

# Results:

Of 3541 patients, 54.6% were male, 59.2% had Fitzpatrick skin types I-III (ie, fairer skin), and 45.2% had >5% affected body surface area (BSA). Median (range) age was 38 (18-95) y, and disease duration was 9 (1-82) y. Most patients who ever used topical treatments (78.8%; n=2172), oral treatments (84.3%; n=1464), phototherapy (83.1%; n=1705), or surgery/other procedures (86.4%; n=1472) were "satisfied," "highly satisfied," or "extremely satisfied" with treatment. Patients who had >5% affected BSA (based on Self Assessment Vitiligo Extent Score), extensive disease (based on Patient Global Assessment), or disease that had severe influence on daily life reported significantly (P<0.05) higher rates of treatment satisfaction than their counterparts. Patients aged <55 y reported significantly higher satisfaction with topical and oral treatments and phototherapy than those aged ≥55 y. Patients with skin types IV-VI (ie, darker skin) and severe disease reported significantly higher satisfaction with topical and oral treatments than their counterparts. Patients with vitiligo for ≤2 y and 3-9 y reported significantly higher satisfaction with oral treatment than those with vitiligo for ≥10 y. Among patients who discontinued topical treatment, oral treatment, and phototherapy, the most common reason reported for discontinuation was lack of response (topical treatment, 30.3%; oral treatment, 33.2%; phototherapy, 29.8%); 25.9% of patients who had surgery/other procedures discontinued treatment to give their skin a rest to prompt a more favorable response. Of 3242 patients who had used any prescription and other management strategies, 56.1% intentionally took a treatment "break"; the most common reasons being to give their skin a rest to prompt a more favorable response (34.9%), being tired of treating their vitiligo (31.5%), and lack of response (29.3%). For 1152 patients who never used a prescription treatment, 31.7% reported they had never had one prescribed, and 23.6% reported concern

about potential side effects. The most common reasons among 595 patients who ceased previous treatment were concern about side effects (33.1%), lack of meaningful response (28.9%), and concern about treatment safety (26.9%). Although 68.7% of patients were hopeful that a new treatment will help their vitiligo someday and 68.5% reported celebrating even small improvements, 60.9% had grown to accept their vitiligo, and 44.6% had given up on finding an effective treatment.

#### **Conclusion:**

Patients with vitiligo were largely satisfied with current treatments but also expressed concerns about treatment safety and efficacy, which influenced treatment breaks or cessation. Patients, however, remain hopeful for new therapies.

# Efficacy and Safety of Upadacitinib in a Phase 2 Randomized, Double-Blind, Dose-Ranging Study of Adults With Extensive Non-Segmental Vitiligo

Thierry Passeron\*<sup>1, 2</sup>, Khaled Ezzedine<sup>3, 4</sup>, Iltefat Hamzavi<sup>5</sup>, Nanja Van Geel<sup>6</sup>, Bethanee J Schlosser<sup>7</sup>, Xiaofei Hu<sup>7</sup>, Xiaohong Huang<sup>7</sup>, David Rosmarin<sup>8</sup>, John E. Harris<sup>9</sup>, Heidi Camp<sup>7</sup>, Amit G Pandya<sup>10, 11</sup>

<sup>1</sup>INSERM U1065, Centre Méditerranéen de Médecine Moléculaire (C3M), Côte d'Azur University, Nice, France, <sup>2</sup>Centre Hospitalier Universitaire de Nice, Côte d'Azur University, Department of Dermatology, Nice, France, <sup>3</sup>AP-HP, Henri Mondor University Hospital, UPEC, Department of Dermatology, Créteil, France, <sup>4</sup>EA 7379 EpidermE, Université Paris-Est Créteil, UPEC, Créteil, France, <sup>5</sup>Henry Ford Hospital, Department of Dermatology, Photomedicine and Photobiology Unit, Detroit, United States, <sup>6</sup>Gent University Hospital, Department of Dermatology, Gent, Belgium, <sup>7</sup>AbbVie Inc, North Chicago, United States, <sup>8</sup>Tufts Medical Center, Boston, United States, <sup>9</sup>University of Massachusetts Medical School, Department of Dermatology, Worcester, United States, <sup>10</sup>Palo Alto Foundation Medical Group, Sunnyvale, United States, <sup>11</sup>University of Texas Southwestern Medical Center, Department of Dermatology, Dallas, United States

## **Introduction & Objectives:**

Janus kinase (JAK) inhibition is a promising approach for the treatment of vitiligo. Here, we report the clinical efficacy and safety of upadacitinib (UPA), an oral JAK inhibitor, in a phase 2b multicenter, randomized, double-blind, placebo-controlled study of adults with extensive non-segmental vitiligo (NSV).

#### **Materials & Methods:**

Eligible patients were aged 18–65 years with NSV, a Facial Vitiligo Area Scoring Index (F-VASI) of ≥0.5, and a Total Vitiligo Area Scoring Index (T-VASI) of ≥5 at baseline. This 52-week study (NCT04927975) comprised 2 periods. In period 1, patients were randomly assigned to once daily UPA 22 mg (UPA22), UPA 11 mg (UPA11), UPA 6 mg (UPA6), or placebo (PBO) for 24 weeks of treatment. In a 28-week blinded extension (period 2), patients receiving UPA during period 1 continued their respective regimens; patients who received PBO in period 1 were pre-assigned to either UPA11 or UPA22. Clinical efficacy endpoints evaluated through week 36 included percent change from baseline (%CFB) in F-VASI (week 24, primary endpoint), reductions from baseline in F-VASI of ≥50% (F-VASI 50) and ≥75% (F-VASI 75), %CFB in T-VASI, and reduction from baseline in T-VASI of ≥50% (T-VASI 50). Safety data as of January 13, 2023 (data cutoff date) are presented.

#### **Results:**

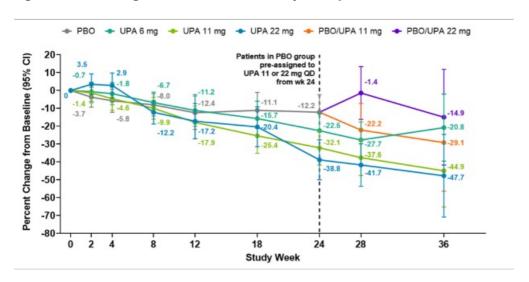
Of the 185 patients enrolled in period 1, 165 (89.2%) continued to period 2. At baseline, 68% of patients had extensive vitiligo (T-VASI > 10), and 71% had active vitiligo. At week 24, the %CFB in F-VASI was greater with UPA11 (-35.6%) and UPA22 (-34.0%) vs PBO (-14.4%; nominal P = .005 and P = .013, respectively; **Figure**; **Table 1**). A greater proportion of patients achieved F-VASI 50 and F-VASI 75 with UPA11 (38.3%, 19.1%) and UPA22 (39.5%, 14.0%) vs PBO (10.9%, 2.2%; nominal P < .05 for both doses and for both endpoints; **Table 1**). Likewise, the %CFB in T-VASI was greater with UPA11 (-17.3%) and UPA22 (-20.7%) vs PBO (-6.4%; nominal P = .026 and P = .005, respectively; **Table 1**). A higher percentage of patients achieved T-VASI 50 with UPA22 (11.6%) than with PBO (2.2%; nominal P = .027; **Table 1**). UPA efficacy continued to improve through week 36, with %CFB in F-VASI for UPA6, UPA11, and UPA22 of -20.8%, -44.9% and -47.7%, respectively (**Figure**; **Table 2**). At week 36, F-VASI 50 was achieved with UPA6, UPA11, and UPA22 by 34.2%, 54.3% and 61.5% of patients and

F-VASI 75 by 15.8%, 40.0%, and 30.8%, respectively (**Table 2**). At week 36, %CFB in T-VASI for UPA6, UPA11 and UPA22 were -24.3%, -32.0% and -37.6%, with 10.5%, 20.0% and 19.2% of patients, respectively, achieving T-VASI 50 (**Table 2**). Treatment-emergent adverse event (TEAE) rates were generally similar with UPA and PBO in period 1 (most common TEAEs: COVID 19, acne, fatigue, and headache) and were similar across treatment arms in period 2. One death adjudicated as undetermined/unknown cause and deemed by the investigator to have no reasonable possibility of being related to study drug occurred in the UPA22 group (period 1). One adjudicated event of nonfatal ischemic stroke occurred with UPA11 (period 2). There were no adjudicated events of venous thromboembolism, gastrointestinal perforation, or events of opportunistic infection, active tuberculosis, or malignancy.

#### **Conclusion:**

Treatment with UPA for 24 weeks resulted in greater improvements vs PBO in the clinical outcomes of adults with extensive NSV. Observed clinical efficacy continued to improve through week 36 with UPA treatment. UPA was generally well tolerated, with no new safety signals identified.

Figure. Percent Change in F-VASI from Baseline by Visit up to Week 368-C



aValues are within-group LS mean with 95% CI.

bAs observed, with a data cutoff date of January 13, 2023.

Patients who received PBO in period 1 were pre-assigned to receive UPA 11 mg or 22 mg QD in period 2.

F-VASI, Facial Vitiligo Area Scoring Index; LS, least squares; PBO, placebo; QD, once daily; UPA, upadacitinib

Table 1. Efficacy at Week 24 (End of Period 1)a,b

| Parameter                              | UPA 6 mg<br>(N = 49)          | UPA 11 mg<br>(N = 47)           | UPA 22 mg<br>(N = 43)           | PBO<br>(N = 46) |
|--|-------------------------------|---------------------------------|---------------------------------|-----------------|
| %CFB F-VASI                            | n = 45                        | n = 43                          | n = 33                          | n = 43          |
| LS mean (SE)                           | -22.0 (5.2)                   | -35.6 (5.3)                     | -34.0 (5.8)                     | -14.4 (5.3)     |
| Difference vs PBO<br>(95% CI)<br>pb    | -7.6<br>(-22.2, 7.0)<br>0.304 | -21.3<br>(-36.0, -6.5)<br>0.005 | -19.6<br>(-35.0, -4.2)<br>0.013 | _               |
| F-VASI 75                              | 0.001                         | 0.000                           | 0.010                           |                 |
| n (%)                                  | 4 (8.2)                       | 9 (19.1)                        | 6 (14.0)                        | 1 (2.2)         |
| Adjusted difference vs PBO, % (95% CI) | 6.9<br>(-1.3, 15.2)<br>0.100  | 17.8<br>(6.5, 29.0)<br>0.002    | 11.7<br>(1.4, 21.9)<br>0.026    | -               |
| F-VASI 50                              |                               |                                 |                                 |                 |
| n (%)                                  | 8 (16.3)                      | 18 (38.3)                       | 17 (39.5)                       | 5 (10.9)        |
| Adjusted difference vs PBO, % (95% CI) | 6.6<br>(-6.6, 19.7)<br>0.327  | 29.3<br>(13.8, 44.9)<br><0.001  | 28.7<br>(12.6, 44.7)<br><0.001  | _               |
| %CFB T-VASI                            | n = 45                        | n = 43                          | n = 33                          | n = 43          |
| LS mean (SE)                           | -13.9 (3.3)                   | -17.3 (3.4)                     | -20.7 (3.7)                     | -6.4 (3.4)      |
| Difference vs PBO<br>(95% CI)          | -7.5<br>(-16.9, 2.0)<br>0.120 | -10.8<br>(-20.4, -1.3)<br>0.026 | -14.3<br>(24.2, -4.3)<br>0.005  | _               |
| T-VASI 50                              |                               |                                 |                                 |                 |
| n (%)                                  | 3 (6.1)                       | 3 (6.4)                         | 5 (11.6)                        | 1 (2.2)         |
| Adjusted difference vs PBO, % (95% CI) | 3.7<br>(-3.9, 11.2)           | 3.8<br>(-4.3, 11.8)             | 9.1<br>(1.0, 17.2)              | _               |
| ₽ <sup>b</sup>                         | 0.340                         | 0.358                           | 0.027                           |                 |

<sup>&</sup>lt;sup>a</sup>Results for binary endpoints are based Cochrane-Mantel-Haenszel test adjusted for strata. Missing data are handled by non-responder imputation [NRI] incorporating multiple imputation [MI] (NRI-MI). Results for continuous endpoints are based on a mixed-effects model for repeated measures (MMRM).

Table 2. Efficacy at Week 36<sup>a</sup>

| Parameter                      | UPA 6 mg<br>(n = 38) | UPA 11 mg<br>(n = 35) | UPA 22 mg<br>(n = 26) | PBO/<br>UPA <sup>b</sup> 11 mg<br>(n = 19) | PBO/<br>UPA <sup>b</sup> 22 mg<br>(n = 19) |
|--------------------------------|----------------------|-----------------------|-----------------------|--|--|
| LS mean change in F-VASI, (SE) | -20.8<br>(9.5)       | -44.9<br>(10.3)       | -47.7<br>(11.7)       | -29.1<br>(13.7)                            | -14.9<br>(13.6)                            |
| F-VASI 75, n (%)               | 6 (15.8)             | 14 (40.0)             | 8 (30.8)              | 3 (15.8)                                   | 2 (10.5)                                   |
| F-VASI 50, n (%)               | 13 (34.2)            | 19 (54.3)             | 16 (61.5)             | 7 (36.8)                                   | 4 (21.1)                                   |
| LS mean change in T-VASI, (SE) | -24.3<br>(3.9)       | -32.0<br>(4.2)        | -37.6<br>(4.8)        | -25.5<br>(5.6)                             | -12.0<br>(5.6)                             |
| T-VASI 50, n (%)               | 4 (10.5)             | 7 (20.0)              | 5 (19.2)              | 3 (15.8)                                   | 0  |

<sup>&</sup>lt;sup>a</sup>Data cutoff date of January 13, 2023. Summaries were based on as observed data. Continuous endpoints were analyzed using analysis of covariance (ANCOVA).

<sup>&</sup>lt;sup>b</sup>All P values for UPA vs PBO are nominal.

<sup>%</sup>CFB, percent change from baseline; F-VASI, Facial Vitiligo Area Scoring Index; LS, least squares; PBO, placebo; T-VASI, Total Vitiligo Area Scoring Index; UPA, upadacitinib

<sup>&</sup>lt;sup>b</sup>Patients who received PBO in period 1 were pre-assigned to receive UPA 11 mg or 22 mg QD in period 2.

F-VASI, Facial Vitiligo Area Scoring Index; LS, least squares; PBO, placebo; QD, once daily; T-VASI, Total Vitiligo Area Scoring Index; UPA, upadacitinib.

## Evaluation of the Utility of 3D Imaging for Facial Vitiligo Area Assessments in a Phase 2 Study of Upadacitinib

Anand K Ganesan\*<sup>1</sup>, Khaled Ezzedine<sup>2, 3</sup>, Sameh Hanna<sup>4, 5</sup>, Mehdi Rashighi<sup>6</sup>, Julien Seneschal<sup>7, 8</sup>, Sandra L Goss<sup>9</sup>, Bethanee J Schlosser<sup>9</sup>, Xiaofei Hu<sup>9</sup>, Tiancheng Ted He<sup>9</sup>, Michelle Crouthamel<sup>9</sup>, Heidi Camp<sup>9</sup>, Thierry Passeron<sup>10</sup>

<sup>1</sup>Skin Biology Resource Center, UC Irvine, Department of Dermatology, Irvine, United States, <sup>2</sup>AP-HP, Henri Mondor University Hospital, UPEC, Department of Dermatology, Créteil, France, <sup>3</sup>EA 7379 EpidermE, Université Paris-Est Créteil, UPEC, Créteil, France, <sup>4</sup>Dermatology on Bloor, Toronto, Canada, <sup>5</sup>University of Toronto, Toronto, Canada, <sup>6</sup>University of Massachusetts Medical School, Department of Dermatology, Worcester, United States, <sup>7</sup>National Reference Center for Rare Skin disorders, Hôpital Saint-André, Department of Dermatology and Pediatric Dermatology, Bordeaux, France, <sup>8</sup>University of Bordeaux, CNRS, Immuno ConcEpT, UMR 5164, Bordeaux, France, <sup>9</sup>AbbVie Inc., North Chicago, United States, <sup>10</sup>Centre Hospitalier Universitaire de Nice, Côte d'Azur University, Department of Dermatology, Nice, France

## **Introduction & Objectives:**

Validated measures such as the Vitiligo Area Scoring Index (VASI) are used to evaluate skin pigmentation change in vitiligo; however, these methods are semi-objective and may lack sensitivity and reproducibility. This study explored a novel 3D imaging platform to objectively determine changes in vitiligo following treatment with upadacitinib (UPA), an oral Janus kinase inhibitor, vs placebo (PBO).

#### **Materials & Methods:**

This was a nested study within a phase 2b multicenter, randomized, double-blind, PBO-controlled, dose-ranging trial (NCT04927975) conducted in adults with non-segmental vitiligo. Eligible patients had a Facial (F)-VASI score of  $\geq 0.5$  and a Total VASI score of  $\geq 5$  at baseline (BL). Patients were randomized to UPA 22 mg (UPA22), UPA 11 mg (UPA11), UPA 6 mg (UPA6), or PBO once daily for 24 weeks (period 1). Following period 1, patients on UPA continued their initial dosages and those on PBO pre-assigned to blinded UPA11 or UPA22 through week 52. A proprietary 3D imaging platform was used to objectively measure the extent of facial vitiligo lesions at a subset of 6 study sites. The platform, a handheld stereoscopic optical scanner and proprietary imaging software (Trace of 5 study sites) images per scan to build an accurate 3D model of skin pigmentation. At each visit, the entire face of each patient was scanned and, independently, F-VASI clinical assessment was performed by the investigator. While examining each patient in-person at BL, investigators independently determined and manually set 3D vitiligo intensity thresholds to distinguish vitiligo from non-vitiligo skin for 10 predefined facial anatomic regions. All facial regions for each scan were analyzed, and area measurements were summed to give a composite facial vitiligo area (cm2) for each patient at each study timepoint. Here we present BL and 24-week data.

#### **Results:**

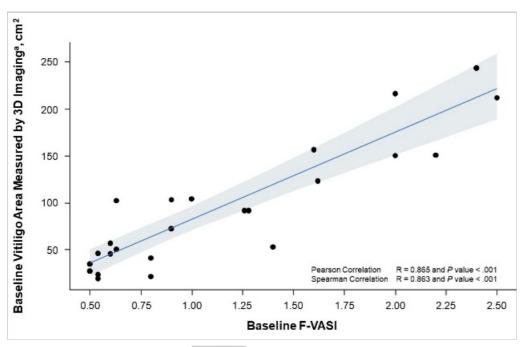
Of the 185 patients enrolled in the main study, 27 patients (UPA6, n=9; UPA11, n=7; UPA22, n=7; PBO, n=4) participated in this substudy; at the time of this analysis, week 24 data were available for 21 patients. Patients had Fitzpatrick skin phototypes II (40.7%), III (25.9%), IV (25.9%), or V (7.4%). There was a significantly high correlation between 3D imaging and FVASI measurements of vitiligo area at BL (Pearson R = 0.87; P < .001; **Figure 1**) and a moderate and significant correlation between percent change in facial vitiligo area determined by 3D imaging and F-VASI, respectively, from BL to week 24 (Pearson R = 0.56; P = .007). Using 3D imaging, a greater decrease in

facial vitiligo area from BL was observed at 24 weeks with UPA than with PBO (UPA6, -15.2%; UPA11, -35.0%, UPA22, -23.0% vs PBO 5.1%; **Figure 2A**). The treatment effect of UPA at week 24 as measured by F-VASI (UPA6, -27.6%; UPA11, -51.0%; UPA22, -38.3% vs PBO -48.5% [n = 3]) was less pronounced than by 3D imaging as greater changes in the PBO group were recorded with FVASI than with 3D imaging. (**Figure 2B**).

#### **Conclusion:**

This study showed a moderate-to-high correlation between facial vitiligo area determined by using a 3D imaging technology and F-VASI. This 3D imaging technology enables objective measurement of facial vitiligo area, detects changes in facial vitiligo area over time, and provides visual confirmation of vitiligo changes. Preliminary data support further evaluation of this technology in more patients and across all Fitzpatrick skin phototypes. Future assessments of intra- and inter-class variability are necessary to validate reproducibility.

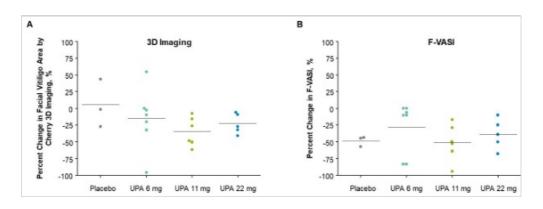
Figure 1. Baseline Vitiligo Area Correlation Between 3D Imaging and F-VASI.



F-VASI, Facial Vitiligo Scoring Index; UPA, upadacitinib.

<sup>a</sup>3D imaging was performed before randomization.

Figure 2. Percent Change From Baseline to Week 24 in Vitiligo Area With Once Daily Upadacitinib and Placebo Using 3D Imaging (A) and F-VASI (B).



Five out of 27 patients did not have a 3D imaging scan at week 24, and 1 patient's data could not be used due to their facial hair

F-VASI, Facial Vitiligo Scoring Index; UPA, upadacitinib.

#### Retrospective Database Analysis of Treatment Patterns in Patients With Vitiligo in Quebec, Canada

Julien Ringuet\*<sup>1</sup>, Grace Wong<sup>2</sup>, Véronique Baribeau<sup>3</sup>, Sunil Kalia<sup>4</sup>, Josée Brisebois<sup>2</sup>, Jean Lachaine<sup>3</sup>

<sup>1</sup>Centre de Recherche Dermatologique du Québec (CRDQ), Dermatology, Québec City, Canada, <sup>2</sup>Incyte Biosciences Canada Corporation, Pointe Claire, Canada, <sup>3</sup>PeriPharm Inc, Montreal, Canada, <sup>4</sup>University of British Columbia, Department of Dermatology and Skin Science, Vancouver, Canada

## **Introduction & Objectives:**

Vitiligo is an autoimmune disease that results in melanocyte destruction and patches of skin depigmentation. There is a lack of effective treatment options, and Health Canada has not yet approved any treatments for repigmentation of vitiligo. This retrospective claims database study sought to address knowledge gaps around the Canadian vitiligo treatment landscape.

#### **Materials & Methods:**

Data were obtained from the Quebec administrative database (*Régie de l'Assurance Maladie du Québec* a public drug plan covering all people aged  $\geq$ 65 y, beneficiaries of the social assistance program, and people without access to a private drug plan) for a subgroup of 125,000 random individuals between 01/2010 and 12/2019 from which patients with vitiligo were selected. Eligible patients were identified as being diagnosed with vitiligo according to a validated algorithm (Bell et al., *Arch Dermatol Res* 2019;315:541-550), combining International Classification of Diseases (ICD)-9 diagnostic code 709 with use of vitiligo-related treatments topical calcineurin inhibitors (TCI) and phototherapy, or the ICD-10 diagnostic code L80. Index date was defined as the date of first diagnosis recorded in the database. Prevalence and incidence of vitiligo were estimated from the selected population and extrapolated to the Quebec population. The percentage of patients using each vitiligo-related treatment (ie, topical corticosteroids [TCS], TCI, phototherapy, topical calcipotriene, oral corticosteroids [OCS], and oral immunosuppressives) during follow-up ( $\geq$ 1 claim;  $\geq$ 3 mo coverage from index date to end of coverage or study period) was reported. Characteristics of patients with vitiligo and treatment patterns were evaluated. A course of treatment was defined as a period of treatment without discontinuation (ie,  $\geq$ 90 d without treatment), and patients could have  $\geq$ 1 course for the same type of treatment if they restarted the treatment after discontinuation.

#### **Results:**

The cohort of patients with vitiligo (N=113) had a mean (SD) age of 50 (25) y; 68% were female. Prevalence of treated patients with vitiligo was evaluated at 0.065% in 2019. Incidence increased over 2-fold from 2011 to 2019 (0.006% vs 0.014%). The most frequently prescribed treatment was TCS (69%), followed by TCI (43%), phototherapy (34%), and OCS (26%). Dermatologists prescribed most claims for TCS (52%), TCI (84%), and phototherapy (100%). During follow-up, 27 patients (24%) had only 1 course of treatment, and 41 (36%) had  $\geq$ 4 courses. In addition, treatment sequence varied among patients, with 43 sequences reported. Treatment usage did not meaningfully differ seasonally for phototherapy.

## **Conclusion:**

The prevalence of patients with vitiligo with treatment claims (0.065%) in Quebec is much lower than the reported rates in the general population (0.5%–2.0%). This may be due to i) barrier of accessing the healthcare system; ii) undertreatment of vitiligo by primary healthcare providers; iii) lack of effective treatment options for vitiligo; or iv)

limitation of administrative healthcare databases for identifying patients with vitiligo. Further research is needed to determine which factors are more likely to account for the undertreatment observed in patients with vitiligo. However, with over a third of patients with vitiligo having ≥4 lines of treatment and 43 treatment sequences identified, a lack of effective treatment options is a major barrier identified in our study that needs further evaluation.

## Characterization and Treatment of Acne That Occurred Among Individuals With Vitiligo Who Applied Ruxolitinib Cream in Two Randomized Phase 3 Trials

David Rosmarin\*<sup>1</sup>, Jennifer Lofland<sup>2</sup>, Haobo Ren<sup>2</sup>, Deanna Kornacki<sup>2</sup>, Thierry Passeron<sup>3</sup>

<sup>1</sup>Indiana University School of Medicine, Dermatology, Indianapolis, United States, <sup>2</sup>Incyte Corporation, Wilmington, United States, <sup>3</sup>Centre Hospitalier Universitaire de Nice/INSERM U1065, Dermatology, Nice, France

## **Introduction & Objectives:**

Vitiligo is a chronic autoimmune disease that targets melanocytes, causing skin depigmentation. A cream formulation of ruxolitinib, a Janus kinase (JAK) 1/JAK2 inhibitor, was approved by the US Food and Drug Administration for the topical treatment of nonsegmental vitiligo in patients aged ≥12 years. In 2 randomized, double-blind, vehicle-controlled phase 3 studies of adults and adolescents with vitiligo (TRuE-V1 [NCT04052425] and TRuE-V2 [NCT04057573]), ~50% of patients applying ruxolitinib cream throughout had ≥75% improvement in facial Vitiligo Area Scoring Index (VASI) at Week 52. Ruxolitinib cream was generally well tolerated over 52 weeks, with application site acne being the most common adverse event. Characteristics of individuals who reported acne in the TRuE-V studies are reported here.

#### Materials & Methods:

TRuE-V1 and TRuE-V2 were conducted in North America and Europe. Patients ≥12 years old diagnosed with nonsegmental vitiligo with depigmentation covering ≤10% total body surface area, including facial and total Vitiligo Area Scoring Index (F-VASI and T-VASI) scores ≥0.5 and ≥3, respectively, were eligible for enrollment. Patients were randomized 2:1 to twice-daily 1.5% ruxolitinib cream or vehicle for 24 weeks, after which all patients could apply 1.5% ruxolitinib cream through Week 52 (open-label extension).

## **Results:**

Among 637 patients who applied ruxolitinib cream at any time during the 52-week TRuE-V studies, 46 (7.2%) patients (n=4 while applying vehicle) reported 51 events of any acne. These 51 events included 10 events of acne (n=1 while applying vehicle) and 41 events of application site acne (n=3 while applying vehicle). Median (range) age in the 46 patients with acne events was 37.5 (12–69) years, with the majority (n=36, 78.3%) in adults aged 18–65 years. Most patients were female (n=34, 73.9%) and White (n=35, 76.1%); 80.4% (n=37) of patients had Fitzpatrick skin types I–III. Most patients had no history of acne vulgaris (n=32, 69.6%) and did not have facial acne vulgaris at baseline (n=41, 89.1%). All acne events were mild or moderate (grade 1, n=37 [72.5%]; grade 2, n=14 [27.5%]), and none were considered serious. Acne was considered possibly related to treatment in 63.0% (n=29) of patients and involved worsening of acne in 17.4% (n=8). Among the 17 patients with a reported location for the acne, the acne was reported as facial in 15 (88.2%). No patients required treatment discontinuation as a result of their acne; only 1 patient had acne that required dose interruption. Acne resolved in 45.0% (n=23) of events and was resolving in 9.8% (n=5). Patients received concomitant medication or a procedure/nondrug therapy for 37.3% (n=19) of acne events. Concomitant medications included retinoids, tetracyclines, and other anti-infectives, all typical for treating acne.

#### **Conclusion:**

All acne events that occurred during ruxolitinib cream treatment for vitiligo were mild or moderate in severity, and none were considered serious. Acne events mostly occurred in adults and those without a history of acne,

suggesting that this may not be classical acne. No patients discontinued ruxolitinib cream treatment due to acne, and only 1 patient interrupted treatment due to acne. Typical acne treatments were used for the treatment of these acne events.

#### Intralesional methotrexate in the treatment of localized vitiligo: A pilot study

Emad Elrewiny<sup>1</sup>, Ahmed Abolela<sup>1</sup>, Sameh Mohamed<sup>1</sup>, Amr Ammar<sup>1</sup>, Mofreh Mansour<sup>2</sup>, Mahmoud Rageh\*<sup>1</sup>

<sup>1</sup>Faculty of Medicine, Al-Azhar University, Department of Dermatology, Cairo, Egypt, <sup>2</sup>Faculty of Medicine, Al-Azhar University, Department of Dermatology, Assiut, Egypt

## Intralesional methotrexate in the treatment of localized vitiligo: A pilot study

## **Introduction & Objectives:**

Vitiligo is an immune-mediated skin disorder that targets epidermal melanocytes leading to the appearance of depigmented skin patches. Different treatment modalities have been reported with varied efficacy. We tried to evaluate the safety and efficacy of intralesional methotrexate in treating localized areas of vitiligo.

#### **Materials & Methods:**

Thirty participants with localized patches of vitiligo were recruited. They were treated with intralesional injections of methotrexate every 2 weeks for a maximum of six sessions. At the end of the study, the degree of repigmentation was categorized into: excellent improvement (>75% repigmentation), good improvement (50%-75% repigmentation), fair improvement (25%-50% repigmentation) and poor improvement (<25% repigmentation).

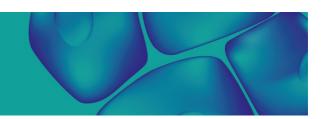
### **Results:**

We included 7 males (23.3%) and 23 females (76.7%). Their mean age was  $33.6 \pm 8.6$  years. The duration of the disease ranged from 1 to 22 years. Four patients had a family history of vitiligo. At the end of the study, there was a highly statistically significant improvement (p < 0.001) after treatment regarding repigmentation.

### **Conclusion:**

This study showed that intralesional methotrexate is a safe and effective treatment option for patients with localized vitiligo lesions. Further studies on a larger scale are needed to evaluate the long-term effects of treatment and detect the ideal dose to be injected.

PS: This study has been published at the Australasian Journal of Dermatologyhttps://doi.org/10.1111/ajd.14071



Clinicopathological Study of 307 Patients with Lichen Planus Actinicus and Pigmentosus Referred to Razi Skin Hospital From 2016 to 2021

Maryam Nasimi\*<sup>1</sup>, Kambiz Kamyab<sup>1</sup>, Zahra Gholi<sup>1</sup>, Maryam Ghiasi<sup>1</sup>, Marzieh Pirzadeh<sup>1</sup>

<sup>1</sup>Tehran university of medical sciences, Dermatology, Tehran, Iran

**Introduction & Objectives:** The two less-known subtypes of lichen planus (LP) are lichen planus actinicus (LPA) and lichen planus pigmentosus (LPP), with the highest prevalence in the Middle East. We aimed to evaluate the clinicopathological profile of these patients.

**Materials & Methods:** Three hundred and seven cases including 184 LPA and 123 LPP patients were recruited from the registered pathology reports of Razi Skin Hospital of Tehran from April 2016 to March 2021. The clinical features and pathological reports were extracted and analyzed.

**Results:** Among 307 patients, 117 (63.9%) in the LPA group and 88 (71.5%) in the LPP group were women. Duration of disease ranged from 1 month to 20 years and 1 month to 12 years in the LPA and LPP groups, respectively. Face (159 patients), limbs (68), and neck (23) were the most frequent sites of involvement in LPA patients, whereas face (60 patients), limbs (47), and trunk (42) were more commonly involved in the LPP patients. Pruritus and oral mucosal lesions were found with similar frequency in both groups. Pathological evaluation showed vacuolar degeneration of basal layer (100%), lymphocytes infiltration (97.3%), and melanin incontinence (58.2%) as the most frequent findings in LPA and vacuolar degeneration of basal layer (100%), lymphocytes infiltration (100%), and melanin incontinence (52/8%) as the most frequent findings in LPP cases.

**Conclusion:** LPA and LPP were both more prevalent among women. Face was the most common site of involvement in both LPA and LPP. Vacuolar degeneration, lymphocyte infiltration, melanin incontinence, and hyperkeratosis were more common histological findings in this study.

## Targeting hyperpigmentation on friction areas with an effective tyrosinase inhibitor and increased skin renewal

Katja Warnke<sup>1</sup>, Uta Meiring<sup>1</sup>, Angelina Waerncke<sup>1</sup>, Gesa-Meike Muhr<sup>1</sup>, Manuela Fürstenau<sup>1</sup>, Dylan Griffiths<sup>2</sup>

<sup>1</sup>Beiersdorf AG, Research and Development, Hamburg, Germany, <sup>2</sup>Beiersdorf AG, Medical Management, Hamburg, Germany

## **Introduction & Objectives:**

Hyperpigmentation incidence is 29 % on global average for body. Discolorations can occur on different body sites as pigment spots, imperfections, unevenness, and post-inflammatory hyperpigmentation (PIH). Especially on knees and elbows, skin is thickened and likely for PIH due to friction. A targeted special strategy is needed to target these areas.

We investigated the approach to combine exfoliating Lactic Acid, regenerating Dexpanthenol, moisturizing Hyaluronic Acid and the efficacious tyrosinase inhibitor Thiamidol (Isobutylamido Thiazolyl Resorcinol) to target hyperpigmented friction areas on knees and elbows. In a consumer survey, we assessed consumer perception.

#### **Materials & Methods:**

In a clinical study over 12 weeks, skin evenness and reduction of hyperpigmentation was assessed by clinical grading and self-grading after 2, 4, 8 and 12 weeks. Additionally, clinical photography was performed.

In a second study, corneocyte size was determined by image analysis of corneocytes, sampled with D-Squames, to evaluate **regenerative capacity** of the skin after 4 weeks of application twice daily.

**Skin moisture** was examined by means of Corneometer® CM 825 measurements at baseline, 24 hours after application and 2 weeks.

The test product's **tolerability** was determined by dermatological assessment in a study with 40 volunteers (50 % with sensitive skin and phototype II-VI) over 2 weeks applying the product twice daily.

A user survey was conducted with 124 volunteers over 4 weeks to assess**product performance** using a questionnaire.

#### **Results:**

After 12 weeks, over two thirds of volunteers showed improvement in clinical grading of skin tone evenness and overall skin tone. Discrete discoloration and discoloration size were significantly reduced in every second subject and 72.5 % showed an improved skin condition.

The results were further supported by self-grading of visibility and intensity of dark spots/discoloration, evenness, smoothness, overall skin condition and moisture. First significant results against baseline were visible after two weeks with further improvement until twelve weeks.

Image analysis of corneocytes showed significant reduction towards baseline and control site as a result of increased epidermal skin turnover due to improved skin renewal and regeneration. Skin moisture improved significantly after single and regular product application.

The dermatological assessment confirmed a very good skin tolerability on all skin types including sensitive skin and all phototypes.

In the survey with consumers with hyperpigmentation and discoloration especially on knees and elbows, after 4 weeks usage, 97 % confirmed that the product evens out the skin tone and smoothens skin longlasting, 98 % confirmed that skin feels immediately softer on elbows and knees. 92 % agreed that reduces thickened skin and 85 % that pigmentation is diminished.

#### **Conclusion:**

A new formula combining the skin the effective tyrosinase inhibitor Thiamidol (Isobutylamido Thiazolyl Resorcinol) with exfoliating Lactic Acid, regenerating Dexpanthenol and moisturizing Hyaluronic Acid significantly reduced hyperpigmentation and discoloration on friction areas on knees and elbows improving skin evenness and smoothness. The formula is very well tolerated, suitable for all skin and phototypes and offers a solution to target hyperpigmentation on thickened skin.

#### Platelet-rich plasma provides improvement of facial lichen planus pigmentosus: A pilot study

Chanisa Kiatsurayanonn<sup>1</sup>

<sup>1</sup>Institute of Dermatology, Bangkok, Thailand

#### **Introduction & Objectives:**

Lichen planus pigmentosus (LPP) is a rare variant of lichen planus most commonly affects middle-aged patients with skin of colour. Despite the multiple treatment modalities available for LPP, their efficacies are largely inconsistent and evidences are lacking, making management of LPP challenging and problematic. Recent studies have revealed versatile applications of platelet-rich plasma (PRP) in the treatment of various dermatologic indications. In this study, we investigated the use of PRP as a novel therapy in 5 LPP patients who demonstrated significant improvement of their facial lesions.

#### **Materials & Methods:**

Overall five patients (aged 35-56 years, four females and one male) received 3 sessions of intradermal PRP injection on both sides of facial LPP lesions at a 2-week interval (0th, 2nd and 4th week). The diagnosis of LPP was confirmed by clinical and histopathological findings. All patients were instructed to apply only provided moisturizer and sunscreen, and not to use any other topical preparations on their faces during the study period. PRP was prepared according to the manufacturer's instruction (e+ PRP kit®; MINOS, Neogenesis). Melanin index (MI) of the hyperpigmented lesion was objectively measured by narrow-band reflectance spectrophotometer (Mexameter® MX18; Courage + Khazaka electronic GmbH). Furthermore, two independent, blinded dermatologists were asked to grade clinical photographs taken by Canfield Visia-CR System® using a quartile grading scale (QGS), which 0= no improvement (less than 1%), 1= mild improvement (1–25%), 2= moderate improvement (26-50%), 3= good improvement (51–75%), 4= excellent improvement (>75%). Patient satisfaction scores were also recorded by visual analog scale from 0-10 where 0-1 = not satisfied, 2-4 = slightly satisfied, 5=neutral, 6-8= very satisfied, 9-10 = extremely satisfied.

#### **Results:**

Initial mean MI score of the subjects was 450.33±69.91 and declined to 392.60±73.88 at the end of the study (p<.05). All patients demonstrated significant reduction of MI score since the first PRP injection, with a trend towards a further decrease of MI score in their subsequent visits. Significant escalation of mean QGS was initially observed at 6th week. Interestingly, the mean MI score and QGS continued to improve substantially even after the last PRP treatment from 6th to 12th week. Finally, at 12th week 2 patients (40%) attained moderate improvement, 1 patient (20%) achieved good improvement and 2 patients (40%) accomplished excellent improvement. The mean patient self-assessment score at the end of the study was reported to be very satisfied. Finally, adverse effects were minimal including swelling at injection sites and bruising which spontaneously resolved in a few days without treatment. None of the patients developed infection nor worsening of hyperpigmentation.

#### **Conclusion:**

In conclusion, we report the first pilot study utilizing PRP in the treatment of LPP. We discovered that intradermal PRP injection successfully improved facial LPP lesions without causing significant side effects. We hereby propose PRP as a novel therapy for LPP which could be a promising alternative in treatment-resistant cases. Further well-designed studies with a larger sample size are necessary to confirm this preliminary observation.

# Prevalence of pigmentary disorders diagnosed by dermatologists and their impact: results of the first large international survey

Brigitte Dréno<sup>1</sup>, Suzana Puig<sup>2</sup>, Liu Wei<sup>3</sup>, Akimichi Morita<sup>4</sup>, Chee-Leok Goh<sup>5</sup>, Hee Young Kang<sup>6</sup>, Fatimata Ly<sup>7</sup>, Sérgio Schalka<sup>8</sup>, Jorge Ocampo-Candiani<sup>9</sup>, Anne-Laure Demessant-Flavigny<sup>10</sup>, Caroline Lefloch<sup>11</sup>, Delphine Kerob<sup>12</sup>, Andrew F. Alexis<sup>13</sup>, Jean Krutmann<sup>14</sup>, Henry W. Lim<sup>15</sup>, Thierry Passeron<sup>16</sup>

<sup>1</sup>Nantes Université, INSERM, CNRS, Immunology and New Concepts in ImmunoTherapy, INCIT, UMR 1302/EMR6001. F-44000 Nantes, France, <sup>2</sup>Melanoma Unit, Dermatology Department, Barcelona University Hospital Clinic, Barcelona, Spain, <sup>3</sup>Department of Dermatology, The General Hospital of Air Force PLA, Beijing, China, <sup>4</sup>Department of Geriatric and Environmental Dermatology, Nagoya City University Graduate School of Medical Sciences, Nagoya, Japan, <sup>5</sup>National Skin Centre, Singapore, Singapore, <sup>6</sup>Department of Dermatology, Ajou University School of Medicine, Suwon, South Korea, <sup>7</sup>Department of Dermatology, Cheikh Anta Diop Dakar University, EPS Institute of Social Hygiene, Dakar, Senegal, <sup>8</sup>Medcin Skin Research Center and Biochemistry Department, Chemistry Institute of Sao Paulo University, Sao Paulo, Brazil, <sup>9</sup>Department of Dermatology, Medical Faculty University Hospital of Nuevo Leon, Monterrey, Mexico, <sup>10</sup>Scientific Communication Director, La Roche-Posay International, <sup>11</sup>Head of Clinical Studies, La Roche-Posay International, <sup>12</sup>Scientific Director, La Roche-Posay International, <sup>13</sup>Department of Dermatology, Weill Cornell Medical College, New York, NY, USA, <sup>14</sup>IUF Leibniz Research Institute for Environmental Medicine, Dusseldorf, Germany Medical Faculty, Heinrich-Heine-University, Dusseldorf, Germany, <sup>15</sup>Department of Dermatology, Henry Ford Health, Detroit, MI, USA, <sup>16</sup>Department of Dermatology, Côte d'Azur University, Nice University Hospital Center, Nice, France INSERM U1065, C3M, Côte d'Azur University, Nice, France

## **Introduction & Objectives:**

Pigmentary disorders (PD) are frequent dermatological conditions, but little is known on their real-world prevalence and impact. This first worldwide survey evaluates the self-reported prevalence of PD such as Melasma, Post-inflammatory Hyperpigmentation (PIH), Solar Lentigo, Vitiligo, Peri-Orbital Hyperpigmentation (POH) and Axillary Hyperpigmentation (AH), their impact on quality of life (QOL) and stigmatization. We present here the results among people who had a diagnosis for their PD by a dermatologist (PDD) versus the ones who were diagnosed another way (self-diagnosed or by another HCP) (nPDD).

#### Materials and method:

Survey (N= 48,000) conducted in 34 countries from all continents (structured: North America (USA, Canada), Latin America (Brazil, Argentina, Mexico, Peru), Europe (France, Spain, Germany, UK, Italy, Greece, Sweden, Russia), SSA (South Africa, Ivory Coast, Nigeria, Kenya), North Asia (China, Japan, South Korea), SAP (Singapore, Malaysia, Thailand, Indonesia), MENA (Morocco, Egypt, Saudi Arabia, Qatar, United Arab Emirates, Kuwait, Oman), India and Australia) from December 2022-February 2023. An automated selection from the Ipsos Panel ensured representative samples (gender, age, employment status and country region) based on quota method.

The online auto-administered questionnaire covered demographics, phototype, self-reported pigmentation condition based on a descriptive text and image of each of the conditions; its impact on

QOL, stigmatization, and sun protection behavior.

#### **Results:**

50% of the population report having at least one PD such as solar lentigo 27%, AH 18%, PIH 15%, POH 15%, melasma 11% and vitiligo 8%, with an average age of 44yo and affecting more women (59%).

Among people who reported PD, 36% of them (n=8,482) had a diagnosis confirmed by a dermatologist (PDD): 49% for vitiligo, 41% for melasma, 38% for PIH, 34% for POH, 34% for AH and 33% for solar lentigo.

People diagnosed by a dermatologist (PDD) were more affected by their disorder than those whose PD have not been diagnosed by a dermatologist (nPDD): DLQI was >10/30 for 40% of them, vs 20% for nPDD. Social stigmatization was also more important among PDD: 54% have concealed the visible parts of their affected skin (vs 40% among nPDD), and 41% have avoided some people (vs 27% among nPDD). Impacts on stigmatization can be found in all aspects of people's lives and were more important among PDD: professional: 31% have felt discrimination at work (vs 15% among nPDD); familial: 27% have felt they brought shame to their family (vs 15% among nPDD); and affective: 28% have felt pushed away by their partner (vs 14% among nPDD).

Conclusion: This first large international survey shows the high prevalence of pigmentary disorders worldwide and the stronger impact on QOL and stigmatization of those with a diagnosis confirmed by a dermatologist (PDD).

# Prevalence of Vitiligo, impact on quality of life and social stigmatization: results of the first large international survey

Jean Krutmann<sup>1</sup>, Suzana Puig<sup>2</sup>, Brigitte Dréno<sup>3</sup>, Jorge Ocampo-Candiani<sup>4</sup>, Fatimata Ly<sup>5</sup>, Sérgio Schalka<sup>6</sup>, Liu Wei<sup>7</sup>, Akimichi Morita<sup>8</sup>, Chee-Leok Goh<sup>9</sup>, Hee Young Kang<sup>10</sup>, Anne-Laure Demessant-Flavigny<sup>11</sup>, Caroline Lefloch<sup>12</sup>, Delphine Kerob<sup>13</sup>, Henry W. Lim<sup>14</sup>, Andrew F. Alexis<sup>15</sup>, Thierry Passeron<sup>16</sup>

<sup>1</sup>IUF Leibniz Research Institute for Environmental Medicine, Dusseldorf, Germany Medical Faculty, Heinrich-Heine-University, Dusseldorf, Germany, <sup>2</sup>Melanoma Unit, Dermatology Department, Barcelona University Hospital Clinic, Barcelona, Spain, <sup>3</sup>Nantes Université, INSERM, CNRS, Immunology and New Concepts in ImmunoTherapy, INCIT, UMR 1302/EMR6001. F-44000 Nantes, France, <sup>4</sup>Department of Dermatology, Medical Faculty University Hospital of Nuevo Leon, Monterrey, Mexico, <sup>5</sup>Department of Dermatology, Cheikh Anta Diop Dakar University, EPS Institute of Social Hygiene, Dakar, Senegal, <sup>6</sup>Medcin Skin Research Center and Biochemistry Department, Chemistry Institute of Sao Paulo University, Sao Paulo, Brazil, <sup>7</sup>Department of Dermatology, The General Hospital of Air Force PLA, Beijing, China, <sup>8</sup>Department of Geriatric and Environmental Dermatology, Nagoya City University Graduate School of Medical Sciences, Nagoya, Japan, <sup>9</sup>National Skin Centre, Singapore, Singapore, <sup>10</sup>Department of Dermatology, Ajou University School of Medicine, Suwon, South Korea, <sup>11</sup>Scientific Communication Director, La Roche-Posay International, <sup>12</sup>Head of Clinical Studies, La Roche-Posay International, <sup>13</sup>Scientific Director, La Roche-Posay International, <sup>14</sup>Department of Dermatology, Henry Ford Health, Detroit, MI, USA, <sup>15</sup>Department of Dermatology, Weill Cornell Medical College, New York, NY, USA, <sup>16</sup>Department of Dermatology, Côte d'Azur University, Nice University, Hospital Center, Nice, France INSERM U1065, C3M, Côte d'Azur University, Nice, France

### **Introduction & Objectives:**

#### **Introduction and objectives:**

Pigmentary disorders (PD) are frequent even if little is known on their real-world prevalence and impact. This first worldwide survey evaluates the self-reported prevalence of PD such as Melasma, Post-inflammatory Hyperpigmentation (PIH), Solar Lentigo, Vitiligo, Peri-Orbital Hyperpigmentation (POH) and Axillary Hyperpigmentation (AH), their impact on quality of life (QOL) and stigmatization. We present here the results of Solar lentigo (SL).

#### Materials and method:

Survey (N= 48,000) conducted in 34 countries from all continents (structured: North America (USA, Canada), Latin America (Brazil, Argentina, Mexico, Peru), Europe (France, Spain, Germany, UK, Italy, Greece, Sweden, Russia), SSA (South Africa, Ivory Coast, Nigeria, Kenya), North Asia (China, Japan, South Korea), SAP (Singapore, Malaysia, Thailand, Indonesia), MENA (Morocco, Egypt, Saudi Arabia, Qatar, United Arab Emirates, Kuwait, Oman), India and Australia) from December 2022-February 2023. An automated selection from the Ipsos Panel ensured representative samples (gender, age, employment status and country region) based on quota method.

The online auto-administered questionnaire covered demographics, phototype, self-reported pigmentation condition based on a descriptive text and image of each of the conditions; its impact on QOL, stigmatization, and sun protection behavior.

#### **Results:**

27% of the population report suffering from SL (n= 13,192), mostly women (58%) with a mean age of 48.7 yo. Among people who reported SL, 81% declare they are phototype I, II or III, vs 75% worldwide.

SL seems a PD more frequent in Italy (41%), Spain (39%), Australia (37%), Mexico (35%), Peru (35%), Brazil (34%), Malaysia (32%), Indonesia (33%), and India (33%).

33% of them had a diagnosis confirmed by a dermatologist, while 23% made their diagnosis thanks to the questionnaire. In average, people were 41.3 yo when SL started. 67% present SL on their face, 30% on their hands and 27% on their arms.

Among all PD, solar lentigo is the one with the lowest impact on the quality of life and on stigmatization. Among people concerned by SL, 13% declares the PD bothered them significantly or a lot. A third of people (30%) have hidden the visible parts of their affected skin. Impacts on stigmatization are smaller in several aspects of people's lives: professional; familial; and affective.

It is recognized that solar lentigo worsens with sun exposure. People seem to be aware as 82% protect their skin from the sun. However, only 39% protect their skin all year-long and only 48% are aware that sun exposure is deleterious.

#### **Conclusion:**

This first large international survey shows the high prevalence of solar lentigo worldwide, but also demonstrated that among other PD, solar lentigo has the lower impact on QOL and stigmatization. This survey also highlights the need for photoprotection education.

## Treatment patterns, satisfaction, and disease progression in non-segmental vitiligo across Europe and the United States

David Rosmarin<sup>1</sup>, Ahmed M Soliman<sup>2</sup>, Simran Marwaha<sup>3</sup>, James Piercy<sup>3</sup>, Heidi Camp<sup>2</sup>, Peter Anderson<sup>3</sup>

<sup>1</sup>Indiana University School Of Medicine, Department of Dermatology, United States, <sup>2</sup>AbbVie Inc., United States, <sup>3</sup>Adelphi Real World, United Kingdom

## **Introduction & Objectives:**

Non-segmental vitiligo (NSV), an autoimmune disorder characterized by depigmented patches of skin, affects up to 2% of the worldwide population. We evaluated treatment patterns, satisfaction, disease progression and unmet need.

#### **Materials & Methods:**

Data were from the Adelphi Vitiligo Disease Specific Programme 2021, a survey of physicians and their adult and adolescent NSV patients in the US, France, Germany, Italy, Spain, and UK. Physicians classified patients by the extent of their NSV currently and at initiation of current treatment as: mild, moderate, or severe. They provided information on demographics, current/previously prescribed NSV therapies, satisfaction with treatment, reasons for dissatisfaction, and how noticeable NSV was compared with before current treatment. Patients provided information on treatment satisfaction, reasons for dissatisfaction and completed the Vitiligo Noticeability Scale (VNS). Patients were divided into 4 groups based on change in extent of vitiligo from current treatment initiation to the present: still mild, still moderate, improvers and treatment failures (condition worsened or remained severe). All analyses were descriptive.

#### **Results:**

This analysis included 1754 patients with NSV (n=1299 ≥18yrs, n=455 12-17yrs, 458 US, 1296 Europe). At treatment initiation, 715, 878 and 161 patients had mild, moderate, and severe NSV, respectively (Figure 1). At present, 96%, 62% and 57% of patients were still mild, still moderate and treatment failures, respectively; only 22% were improvers. Mean age was 31.2 years; 50% were female. Mean time from first symptoms of NSV, diagnosis of NSV, and on current treatment was 46, 37 and 11 months, respectively. Topical calcineurin inhibitors (TCI) or phototherapy were the most common treatments in improvers (38% or 39%), still moderate (41% or 39%) and treatment failures (30% or 42%). TCIs were used by 48% of still mild but phototherapy use was lower (22%). Lines of treatment analysis indicated patients repeatedly cycled through the same therapy classes - TCI, phototherapy, and topical corticosteroids. Using VNS, physicians reported that NSV was as or more noticeable than before treatment initiation in 46% of treatment failures vs 35%, 34% and 9% in still mild, still moderate and improvers, respectively; patient reported percentages were 60%, 25%, 32%, and 11%, respectively (Figure 2). For 78% of treatment failures, the physician was not satisfied with the current regimen vs 44% for still mild, 57% still moderate and 23% improvers; patient dissatisfaction was 74%, 40%, 49% and 26%, respectively (Figure 3). The main reason for physician dissatisfaction (73% of cases) was not inducing initial or sustaining repigmentation. Physician assessments of disease progression (improving, stable, deteriorating) were consistent with overall change in severity from treatment initiation to present (Figure 4). Disease control was considered not optimal in 58% of all patients, rising to 72% in treatment failures.

#### **Conclusion:**

While treatments may work for some patients with NSV, a considerable number fail on treatment or remain moderate. Patients appear to cycle through the same therapies as there are limited other options available. High levels of dissatisfaction were reported by physicians and patients, with physicians believing better control is achievable in most patients. This unmet need demonstrates a lack of effective therapies for NSV and a need for new treatment options.



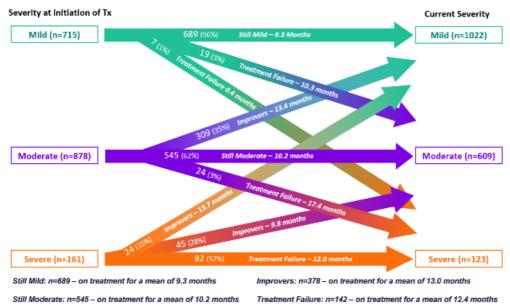


Figure 2. Physician- and patient-reported noticeability of vitiligo compared with before current treatment

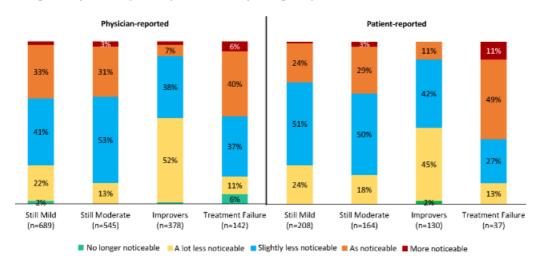


Figure 3. Physician- and patient-reported satisfaction with current treatment

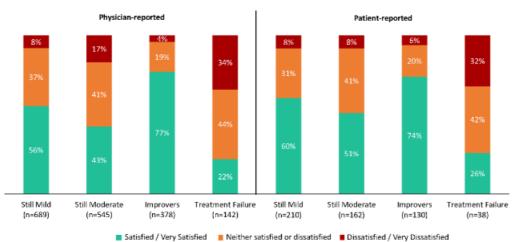
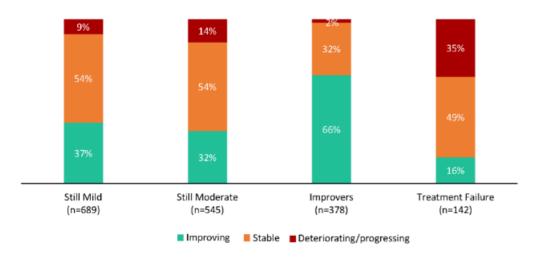


Figure 4. Physician-reported current disease progression



## Oral and Topical Retinoid Therapy for the Treatment of Lichen Planus Pigmentosus in a 21-year-old Filipino: A Case Report

MA Bernadette Beatrize Paredes<sup>1</sup>, Martha Joy Tapales<sup>1</sup>

<sup>1</sup>Rizal Medical Center, Dermatology, Pasig, Philippines

## **Introduction & Objectives:**

Lichen Planus Pigmentosus is a rare dyschromia that presents as acquired dark brown to gray macules and patches most commonly seen on sun-exposed areas of the face, neck, and flexures. Various treatment modalities have been reported to be beneficial in stabilizing the disease and improving pigmentation, however, an optimal treatment method is yet to be established.

#### **Materials & Methods:**

We report a case of a 21-year-old healthy Filipino female, who presented with a 1-year history of multiple grayish-brown macules and patches that were visible on the face, neck, trunk, limbs, and flexures. The patient was started on low-dose oral isotretinoin (20 mg/day) and nightly application of topical tretinoin 0.05% cream to the face and neck and was continued daily for 7 months. On the 8th month of treatment, oral isotretinoin was decreased to 10mg/day while nightly application of topical tretinoin 0.05% cream was continued.

#### **Results:**

Stabilization of disease was noted on the fourth month of treatment, as evidenced by the absence of any new lesions within three months from the start of treatment. On the seventh month of treatment, there was notable reduction in the severity of the hyperpigmentation compared to baseline.

### **Conclusion:**

The recalcitrant nature of Lichen Planus Pigmentosus makes therapy challenging, and there is still no definitive treatment for this condition. In our case, the combination of topical tretinoin 0.05% with low-dose oral isotretinoin has demonstrated good outcomes in both stabilizing the condition and reducing the severity of hyperpigmentation. Even yet, once the condition has stabilized, different treatment techniques for skin lightening may be required as retinoid therapy alone may not be sufficient to completely eliminate hyperpigmentation.

#### NAcM-OPT Protects Keratinocytes from H2O2-Induced Cell Damage via Promotion of Autophagy

Renxue Xiong<sup>1</sup>, Qingmei Shen<sup>2</sup>, Yan Zhao<sup>2</sup>, Xiuzu Song<sup>1</sup>, Cuiping Guan<sup>1</sup>

<sup>1</sup>Hangzhou Third People's Hospital, Department of Dermatology, <sup>2</sup>Zhejiang Chinese Medical University, School of Basic Medical Sciences

**Introduction & Objectives:** To investigate the protective effect of NAcM-OPT, a small molecule inhibitor of ubiquitine proteasome, on H2O2-induced oxidative damage in keratinocytes.

**Materials & Methods:** HaCaT cells were treated with NAcM-OPT under the stimulation of oxidative stress, and cell activity was detected by CCK-8 method; cell proliferation was detected by EdU method; the changes of autophagic flux were detected by mGFP-RFP-LC3 dual fluorescent autophagy indicator system; intracellular ROS were detected by DCF method; apoptosis was detected by DAPI staining; mitochondrial activity was detected by mitochondrial membrane potential. The expression of autophagy-related proteins Beclin1 and LC3 was detected by western blotting; mitochondrial morphology was observed by transmission electron microscopy; the expression of antioxidant genes was examined by qRT-PCR. Keratinocytes were supplemented with the autophagy activator rapamycin, melanocytes were added to the keratinocyte cell supernatant, and qRT-PCR was used to identify tyrosinase expression.

**Results:** In HaCaT cells, H2O2 stimulation led to an increase in intracellular ROS, a significant decrease in apoptosis, a slowdown in cell division, an impairment of mitochondrial activity, a decrease in the expression of the autophagy-related proteins Beclin1 and LC3, and a reduction in the antioxidant genes Nrf2, HO-1, NQO-1, and GCLM. The H2O2-induced increase in ROS and apoptosis in HaCaT cells could be attenuated by NAcM-OPT pretreatment, which also reduced cell proliferation and mitochondrial activity. In vivo experiments confirming that NAcM-OPT reduces the lack of melanin content in H2O2-stimulated mice and in vitro studies that NAcM-OPT enhances melanocyte tyrosinase expression by addiing the autophagy activator rapamycin.

**Conclusion:** NAcM-OPT was shown to increase cell viability and cell proliferation. Moreover, NAcM-OPT showed the ability to alleviate ROS accumulation and cell apoptosis in HaCaT cells under oxidative stress. Importantly, we found that autophagic flux was improved due to increased autophagy protein expression with NAcM-OPT treated under H2O2-induced oxidative stress, which reduced susceptibility to excessive ROS. Furthermore, Rap enhanced the mRNA levels of TYR in melanocytes. In addition, NAcM-OPT depicted the ability to alleviate mitochondrial damage and restore mitochondrial function and significantly upregulated the expression of Nrf2, HO-1, NQO-1, and GCLM. Most importantly, NAcM-OPT increased epidermal thickness, follicle length, and melanin synthesis under oxidative stress in vivo. Based on these findings, NAcM-OPT activated the expression of autophagy to alleviate mitochondrial damage in HaCaT cells and enhance TYR expression in melanocytes. Therefore, NAcM-OPT has clear potential as a promising small molecule antioxidant drug for the treatment of vitiligo.

#### The role of Polypodium leucotomos in vitiligo - what is the evidence?

Sue Liu\*1, Mason Crossman<sup>2</sup>, Samuel Morriss<sup>3</sup>, Yali Deng<sup>4</sup>, Lawrence Lin<sup>1</sup>, Zhao Feng Liu<sup>5</sup>, Chris Chew<sup>5</sup>

<sup>1</sup>Monash University Clayton Campus, Clayton, Australia, <sup>2</sup>Flinders University, Bedford Park, Australia, <sup>3</sup>The Royal Melbourne Hospital, Parkville, Australia, <sup>4</sup>University of Melbourne, Parkville, Australia, <sup>5</sup>The Alfred, Melbourne, Australia

## **Introduction & Objectives:**

Vitiligo is a common acquired pigmentary skin condition in which oxidative stress in melanocytes plays a key role in the development of autoimmunity and depigmentation. Current treatment to induce repigmentation includes phototherapy, topical and systemic agents, however results may be cosmetically unsatisfactory. Antioxidant treatments may play a role in the treatment of vitiligo, including *Polypodium leucotomos*, a tropical fern with demonstrated antioxidant, anti-inflammatory and immunomodulatory effects. We aimed to provide an overview of the current evidence evaluating the use of *Polypodium leucotomos* in vitiligo.

## Materials & Methods:

Human studies published until October 2022 on the use of *Polypodium Leucotomos* in vitiligo were searched in Embase, Ovid Medline and Cochrane Databases. Papers were screened for relevance and data extracted by three reviewers. The primary outcome of interest was the observed success rate and extent of repigmentation.

#### **Results:**

We identified four articles from our search. Three were randomised controlled trials of which two had been published in the past decade. Three of these studies used oral *Polypodium leucotomos* in adjuvant to narrowband UB phototherapy (NB-UVB) while one was in combination with photochemotherapy (PUVA). The largest study included a total of 57 patients. The addition of *Polypodoium leucotomos* to NB-UVB has been effective, improving the extent of repigmentation and response rate (47.8% vs. 22%). Efficacy may vary across sites, with greater efficacy observed in the head and neck compared to the trunk and extremities. It may also reduce NB-UVB-related adverse effect rates (52% vs. 86%) such as erythema, pruritis and dry skin. Higher repigmentation may be observed in lighter skin types. Across the existing studies of *Polypodium leucotomos*, there is large variation in duration, dosage and adjuvant treatment making it difficult to directly compare studies.

### **Conclusion:**

There have been limited studies analysing *Polypodium leucotomos* in vitiligo, however results appear promising, particularly in a disease where many therapies are unsuccessful and disease relapse is common. It has demonstrated efficacy in repigmentation rate as an adjuvant to phototherapy, however further studies are required to characterise its impacts on different types of vitiligo.

#### Knowledge and attitude study of vitiligo among final year medical students

Bharath Kumar J P\*1, Savitha Somaiah1, Chaitra Srinivas1

<sup>1</sup>Sapthagiri Institute of Medical Sciences and Research Centre, Bengaluru, India

**Introduction & Objectives:** Vitiligo is an acquired skin disorder caused due to destruction of melanocytes. It clinically presents with well-defined depigmented macules and patches with or without white hairs. About 1% of the world's population is estimated to be affected by vitiligo. This disease can occur at any age but usually has its onset at 10 to 30 years of age. The pathogenesis is usually multifactorial, autoimmunity, intrinsic defects of melanocytes, and oxidative stress are commonly implicated. Numerous studies have shown that patients with vitiligo experience low self-esteem, feel stigmatized, and suffer from psychosocial burden. Because of the lack of knowledge & attitude regarding this disease, a lot of taboos are present around the world. The present study is an attempt to document the prevalent knowledge and attitude among the medical students regarding this disease and to identify the determinants of good/poor knowledge and attitude.

**Materials & Methods:** A cross sectional study was conducted among college students studying in final year of MBBS. A total of 150 students were included in the study. A questionnaire containing 15 questions was given to students. Based on the questionnaire knowledge attitude of the students were assessed about Vitiligo.

**Results:** A total of 150 students from a tertiary care hospital were administered the questionnaire, 56 males and 93 females. Out of total 150 students, 149 completed the questionnaire giving 99% response rate.

Most of the people were aware about Vitiligo 145(97%). Majority of responders had knowledge that vitiligo is not communicable (94%) and not connected to Leprosy 112 (75%). 117(96%) thought it to be hereditary and 61(41%) associated vitiligo with dietary habits of certain food. Knowledge about flare up due to sun exposure 93(62%), and treatment 100(67%) was present in large number of students. 75(50%) had knowledge about surgical options, also majority of them knew that modern allopathic form were better than ayurvedic and homeopathic treatment. 74(49%) felt that if a single patch appears, it will always spread all over the body. 100% of the responders came with a positive attitude about empathizing with vitiligo patients, having a normal marital life, eating food prepared by these patients, and shaking hands with them.

**Conclusion:** There are a lot of misconceptions & myths regarding vitiligo observed in the studied population. The attitude scores were better than knowledge scores. This study gave us valuable information about the knowledge and awareness of final year MBBS medical students about vitiligo which will help us in overcoming the shortcomings and reduce stigma through the conduction of educational campaigns for the medical trainees. These campaigns will lead to a positive attitude and further decrease the discriminatory behavior towards vitiligo patients and their relatives. Consequently, an increased self-confidence, social integration, and psychological well-being of the patients will result in better treatment outcomes.

#### Treatment Patterns in Patients With Vitiligo: A Retrospective Real-World Data Analysis

Yuval Ramot\*<sup>1, 2</sup>, Vered Rosenberg<sup>3</sup>, Limei Zhou<sup>4</sup>, Stephanie Harbers<sup>5</sup>

<sup>1</sup>Hebrew University of Jerusalem, The Faculty of Medicine, Israel, <sup>2</sup>Hadassah Medical Center, Jerusalem, Israel, <sup>3</sup>Kahn-Sagol-Maccabi Research and Innovation Institute, Maccabi Healthcare Services, Tel Aviv, Israel, <sup>4</sup>AbbVie Inc., Toronto, Canada, <sup>5</sup>AbbVie Inc., Rungis, France

**Introduction & Objectives:** Current treatment for vitiligo relies largely on off-label interventions such as corticosteroids (CS), calcineurin inhibitors (CI), and phototherapy. However, limited data and clarity exist regarding treatment patterns and use in the real world. This study aims to describe treatment patterns for patients with vitiligo in Israel.

**Materials & Methods:** A cross-sectional analysis was conducted using the database of a large health services organization. Treatment patterns were assessed retrospectively for the 2021 prevalent population. Data are reported by the number and proportion of patients covered by treatment from the date of first vitiligo diagnosis until 31 December 2021. Treatment sequencing is presented as the proportions of patients treated with first-, second-, and third-line therapies. Disease severity was categorized by treatment received (mild received only topical treatments vs moderate-to-severe received systemic treatments, including phototherapy).

Results: Of\*\* 11,412 patients with vitiligo, 8,537 (74.8%) were found to have received any treatment ever. Median (interquartile range [IQR]) time from diagnosis to first treatment was 0 (0−14) months. Median (IQR) time for adults ≥18 years was 0 (0−17) months, adolescents 12−<18 years: 0 (0−7) months, and children <12 years: 0 (0−5) months (standardized mean difference [SMD]: 0.28; *P*<0.001). Median (IQR) time to first treatment was longer for those with moderate-to-severe disease (2 [0−22] months) versus mild disease (0 [0−8] months; [SMD: 0.30], *P*<0.001). Women were more likely than men to be treated (77.0% vs 72.5% [SMD: 0.1], *P*<0.001). Overall, 51.5% of patients received topical CS, 36.5% topical CI, 27.1% systemic CS, 1.7% systemic immunosuppressants, and 7.4% phototherapy ever. Adults were more likely to receive topical CS, systemic CS, and phototherapy (54.9%, 30.6%, and 8.1%) versus adolescents (42.0%, 12.6%, and 5.1%) or children (33.9%, 14.8%, and 3.6%, respectively; [SMD: 0.29, 0.30, and 0.13], *P*<0.001, for all). The most common first-line treatments were topical CS (42.4%) and CI (27.8%), whereas second-line and third-line treatments included systemic CS (36.9% and 32.0%), phototherapy (7.8% and 14.5%), and systemic immunosuppressants (1.2% and 12.2%). Only 16.3% of patients were receiving treatment at the end of the assessment year.

**Conclusion:** These findings demonstrate that the large majority (~75%) of patients receive one or more treatments for their vitiligo during the course of their disease. Topical CS and CI (particularly in children and adolescents) were the most commonly used therapies. The low number of patients actively receiving treatment at the end of the assessment year (16.3%) may be indicative of the discontinuity in treatment for many patients. Additionally, the longer time from diagnosis to first treatment in those with moderate-to-severe disease could suggest a role for early intervention in preventing longer-term disease progression.

Disease experience and perception of meaningful improvements among adults with non-segmental vitiligo: Evidence from qualitative embedded exit interviews of patients enrolled in the upadacitinib phase 2 clinical trial

Khaled Ezzedine<sup>1</sup>, Ahmed M Soliman<sup>2</sup>, Mary Kate Ladd<sup>3</sup>, Bethanee J Schlosser<sup>2</sup>, Heidi Camp<sup>2</sup>, Rohiniorro Sen<sup>2</sup>, Robin Pokrzywinski<sup>3</sup>

<sup>1</sup>Henri Mondor University Hospital, Department of Dermatology, Creteil, France, <sup>2</sup>AbbVie Inc., United States, <sup>3</sup>Evidera, Bethesda, United States

#### **Introduction & Objectives:**

Vitiligo is a chronic skin depigmentation disease which negatively impacts a patient's (pt's) health-related quality of life, resulting in social, emotional, and psychological issues. Through qualitative embedded phase 2 trial exit interviews, this study sought to obtain insight into the pt disease experience and meaningful treatment benefits for nonsegmental vitiligo (NSV).

#### **Materials & Methods:**

This cross-sectional, qualitative research study involved one-on-one interviews with pts with NSV participating in AbbVie's phase 2 upadacitinib clinical trial M19-051 (NCT04927975). Web-based telephone interviews occurred <4 weeks after the week 24 visit or early termination visit. Interviews queried vitiligo history, past treatment experience, other vitiligo symptoms, daily impacts of vitiligo, most bothersome aspect of vitiligo, vitiligo experience during the trial (expectations, results), meaningful change perceptions, and assessment of measures (Vitiligo Area Scoring Index [VASI], Vitiligo Noticeability Scale [VNS], Pt's Global Impression of Change-Vitiligo [PaGIC-V], Total-Pt Global Vitiligo Assessment [TPaGVA], and Face-PaGVA [F-PaGVA]).

#### **Results:**

Fourteen pts participated in the study. The body site where depigmentation was initially discovered varied greatly among pts. Almost all pts (n=13) indicated worsening of their vitiligo (i.e., spreading to new areas and losing more pigment in the same area) from their first symptoms until trial entry. The most common symptom experienced by pts, besides depigmentation, was sun sensitivity (n=10). Noted impacts that vitiligo had on pts' daily lives were the need to coverup the skin (n=10) and feeling self-conscious (n=4). A majority (n=13) experienced negative social impacts (e.g., social anxiety, feeling unattractive, and worrying about what to wear). Four pts reported an impact on their job, and three on their sexuality or intimacy. Six pts reported repigmentation over various body sites occurring during the trial, including two who described this as meaningful. Most pts (n=12) felt that 50% repigmentation or more would be meaningful to them, and seven indicated that at least 25% repigmentation would be a meaningful improvement in a clinical trial. For VNS, all pts believed "no longer noticeable" and "a lot less noticeable" represented a meaningful improvement, while >70% felt "slightly less noticeable" was meaningful. For the PaGIC-V, 100% of pts believed "much better" represented a meaningful improvement, while 86% considered "a little better" a meaningful improvement. For T-PaGVA and F-PaGVA, most pts indicated that moving down from any level to the next (e.g., very extensive to extensive; moderate to limited) would be viewed as a meaningful change. However, some pts (six for T-PaGVA and four for F-PaGVA) felt that going from "very extensive depigmentation" to "extensive depigmentation" at the end of the clinical trial would not be a meaningful change.

## **Conclusion:**

The findings from this study provide insight into pts' perspectives on meaningful treatment targets, which can aid in the choice of relevant outcomes and clinically meaningful response definitions for clinical trials for NSV.

#### Comorbidities Associated With Vitiligo: A Retrospective Real-World Data Analysis

Yuval Ramot\*<sup>1, 2</sup>, Vered Rosenberg<sup>3</sup>, Limei Zhou<sup>4</sup>, Stephanie Harbers<sup>5</sup>

<sup>1</sup>Hebrew University of Jerusalem, The Faculty of Medicine, Jerusalem, Israel, <sup>2</sup>Hadassah Medical Center, Department of Dermatology, Jerusalem, Israel, <sup>3</sup>Kahn-Sagol-Maccabi Research and Innovation Institute, Maccabi Healthcare Services, Tel Aviv, Israel, <sup>4</sup>AbbVie Inc., Toronto, Canada, <sup>5</sup>AbbVie Inc., Rungis, France

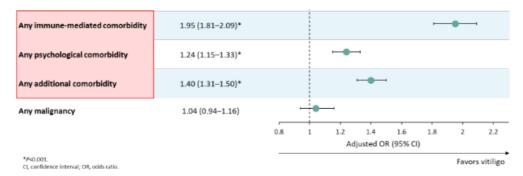
**Introduction & Objectives:** Current understanding of the holistic burden of vitiligo remains limited. It is frequently seen as a cosmetic condition, with underappreciation of the comorbid and psychosocial impact of the disease for patients. The objective of this analysis was to describe real-world comorbidities in patients with vitiligo in Israel.

**Materials & Methods:** A cross-sectional retrospective cohort analysis was conducted using the database of a large health services organization. Patients diagnosed with vitiligo (based on International Classification of Diseases, Ninth Revision, Clinical Modification [ICD-9] codes) and non-vitiligo controls from the general population were matched for age group, sex, and socioeconomic status in a 1:1 ratio. Disease severity was categorized by treatment received (mild received only topical treatment vs moderate-to-severe received systemic treatments, including phototherapy). Data are reported as the proportion of patients and standardized mean difference (SMD) and *P*-value; *P*<0.05 was considered statistically significant, and an SMD >0.1 was defined as a notable difference. Odds ratios were derived from logistic regression with adjustment of age, sex, socioeconomic status, birth country, sector, smoking status, and body mass index.

Results: A total of 11,412 patients with vitiligo were matched with 11,412 non-vitiligo controls. The mean (SD) age was 42 (21) years, with 51.1% of patients being female. Patients with vitiligo were significantly more likely to have any immune-mediated disease vs the general population (29.7% vs 18.4% [SMD: 0.27]; P<0.001), with the most common being atopic dermatitis (12.5%), psoriasis (5.8%), Hashimoto thyroiditis (2.9%), alopecia areata (2.2%), and prurigo nodularis (2.2%). Immune-mediated comorbidities were more common in females (33.7% vs 25.6% [P<0.001; SMD: 0.18]), younger age groups (<12 years, 34.2% and 12-<18 years, 36.9% vs ≥18 years, 28.1% [P<0.001; SMD: 0.13]), and in those with moderate-to-severe disease (37.0% vs mild, 29.7% [P<0.001; SMD: 0.26]). A higher proportion of patients with vitiligo also had any psychological comorbidity compared with the general population (18.7% vs 15.9% [P<0.001; SMD: 0.07]), most commonly depression (10.8%), sleep disorder/insomnia (5.9%), and anxiety (3.7%). Psychological comorbidities were more common in females (19.7% vs 17.5% [P=0.003; SMD: 0.06]), adults (≥18 years, 21.8% vs 12-<18 years, 7.7% and <12 years, 4.6% [P<0.001; SMD: 0.35]), and in those with moderate-to-severe disease (24.8% vs mild, 15.9% [P<0.001; SMD: 0.17]). Sexual dysfunction was more common in males (0.6% vs 0.0% [P<0.001; SMD: 0.11]). Among additional comorbidities, anemia (22.5% vs 17.5% [P<0.001; SMD: 0.14]) was more common in patients with vitiligo. In adult patients with vitiligo, the odds of immune-mediated, psychological, and additional comorbidities were higher vs the general population, but the odds of malignancy were not higher (Figure 1).

**Conclusion:** These findings demonstrate that patients with vitiligo were more likely to suffer from a variety of immune-mediated as well as psychological comorbidities compared with the general population, providing insight into the significant patient burden of this disease.

Figure 1. Comorbidities Among Adult Vitiligo Population and General Population



## MitoQ alleviates H2O2-induced mitochondrial dysfunction in keratinocytes through the NRF2/PINK1 pathway

Cuiping Guan<sup>1</sup>, Yan Zhao<sup>2</sup>, Renxue Xiong<sup>1</sup>, Qingmei Shen<sup>2</sup>, Xiuzu Song<sup>1</sup>

<sup>1</sup>Hangzhou Third People's Hospital, Department of Dermatology, <sup>2</sup>Zhejiang Chinese Medical University, School of Basic Medical Sciences

**Introduction & Objectives:** Oxidative stress is involved in the development of vitiligo, and mitochondria are the major source of reactive oxygen species. Mitochondrial abnormalities in keratinocytes of vitiligo patients in the lesional area suggest mitochondrial dysfunction, but the mechanism of its occurrence is unclear. Here, we investigate the regulatory role of the central antioxidant regulator molecule NRF2 on PINK1/Parkin and the intervention role of MitoQ in this process to provide new clues for mitochondrial abnormalities in vitiligo and new antioxidant therapeutic agents for vitiligo treatment.

Materials & Methods: Skin samples from vitiligo patients and healthy controls were collected from the Dermatology Outpatient Clinic of Hangzhou Third People's Hospital for detection of NRF2, PINK1, Parkin and LC3 levels by immunofluorescence. HaCaT cells were treated with H2O2 or MitoQ/H2O2, and the following assays were performed, including DCFH-DA fluorescent ROS probe to detect reactive oxygen species levels, Western blotting to detect cellular antioxidant factors and mitochondrial autophagy-related protein expression, DAPI staining and caspase3 activity assay to evaluate apoptosis, and mitochondrial membrane potential and apoptosis assay kit to detect mitochondrial activity; Transmission electron microscopy to observe mitochondrial morphology.

**Results:** Reduced or absent expression of NRF2, PINK1, Parkin, and LC3 was found in skin tissue from vitiligo lesions compared to skin tissue from healthy controls. MitoQ was shown to reduce the accumulation of intracellular reactive oxygen species. MitoQ inhibited H2O2-induced apoptosis in keratinocytes and preserved mitochondrial function in keratinocytes under oxidative stress. Furthermore, MitoQ induced the activation of the nuclear factor E2-related factor 2 (NRF2) pathway, whereas the knockdown of the Nrf2 gene reduced the protective effect of MitoQ. In addition, the mitophagy-related protein PINK1/Parkin was positively regulated by MitoQ, and PINK1/Parkin was involved in the MitoQ-induced activation of NRF2. This suggests that MitoQ can activate the NRF2-mediated PINK1 /Parkin pathway and reduce mitochondrial dysfunction caused by oxidative stress damage.

**Conclusion:** MitoQ was effective in preventing H2O2-stimulated keratinocyte apoptosis. The underlying process was found to be strongly associated with restoration of mitochondrial homeostasis and oxidative stability via restoration of mitochondrial functional balance and activation of NRF2/PINK1 signaling, all of which promoted keratinocyte survival. Taken together, these findings indicate that restoring mitochondrial function and eliminating oxidative insults are effective therapeutic methods for the treatment of vitiligo, suggesting that MitoQ is a promising therapeutic agent for the treatment of vitiligo.

Hypopigmented interface T-cell dyscrasia evolving to mycosis fungoides: A case report with 6 years follow-up and literature review

Panpan Wang<sup>1</sup>, Ping Wang<sup>1</sup>

<sup>1</sup>Hangzhou Third People's Hospital, Department of Dermatology, Hangzhou

**Introduction & Objectives:** Hypopigmented interface T-cell dyscrasia (HITCD) presents clinically as hypopigmented skin, is pathologically characterized by abnormal T-lymphocyte proliferation and is often accompanied by vacuolar degeneration of the basal layer. Although the clinical presentation is similar to the of hypopigmented mycosis fungoides (HMF), the pathology does not meet the diagnostic criteria for mycosis fungoides (MF), is considered a separate entity from MF and rarely progresses to MF. We report a case involving diagnosis of hypopigmented patches with pathology of HITCD untreated; after 6 years, the lesions developed multiple infiltrative erythematous patches with pathology consistent with MF.

Materials & Methods: We report a case of a patient with both HITCD and MF features.

Results: The patient was largely cured after 5 months of NB-UVB treatment.

**Conclusion:** HITCD has often been considered in previous studies as a disease independent of MF and rarely progresses to MF. The presence of HITCD in this patient suggests that HITCD may be a premalignant lesion of MF and that HITCD should be considered a lymphoproliferative disorder with the potential to progress to MF. Our report suggests a new view that HITCD requires early intervention and treatment.

## The effect of topical tranexamic acid with micro-needling and micro-needling alone in treatment of macular amyloidosis

Mehdi Gheisari<sup>1</sup>, Shima Moslemi Haghighi<sup>1</sup>, Sahar Dadkhahfar<sup>1</sup>, Shirin Zaresharifi<sup>1</sup>, Fariba Ghalamkarpour<sup>1</sup>

<sup>1</sup>skin research center, Shahid Beheshti University of Medical Sciences, dermatology

## **Introduction & Objectives:**

Macular amyloidosis is a form of primary localized cutaneous amyloidosis presented by pruritic pigmented macules in rippled or reticulate pattern. The aim of this study was to assess the efficacy of using topical tranexamic acid with micro-needling comparing to micro-needling alone in patients with macular amyloidosis.

#### **Materials & Methods:**

\*\* Patients with bilaterally located macular amyloidosis on trunk or upper extremities were recruited in this trial. The skin lesions in all patients were divided into two parts which were randomly assigned to the group of treatment with micro-needling plus tranexamic acid and the group of micro-needling alone. There were four sessions of treatment with two weeks interval. The percentage of improvement in pigmentation (based on photographs and dermoscopy) and rippling of each group was determined by three blinded dermatologists. The level of patient satisfaction and reduction of pruritus was measured by a questionnaire and defined as a percentage.

#### Results:

Twenty females were enrolled in this study. The mean (SD) patients' age was  $39.7(\pm 10.13)$  years. Both groups showed improvement in pigmentation based on images, dermoscopy, and rippling pattern. Patients' satisfaction was 46.5% in tranexamic acid group and 47.5% in micro-needling alone. Nevertheless, there was no significant difference between both groups (p value>0.05). Interestingly, the pruritus improved 61.66% after four sessions of treatment in both groups.

## **Conclusion:**

Micro-needling is a suitable modality for decreasing pruritus and pigmentation in macular amyloidosis. However, topical application of tranexamic acid does not lead to additional improvement.

# Discovery of 2-mercaptonicotinoyl glycine, a new potent skin lightening agent with a proven clinical efficacy

Peggy Sextius<sup>1</sup>, Romain De Dormael<sup>1</sup>, Guillaume Lereaux<sup>1</sup>, Delphine Kerob\*<sup>2</sup>, Emilie Warrick<sup>1</sup>, Stephane Diridollou<sup>1</sup>

<sup>1</sup>L'Oréal Research and Innovation, Aulnay sous Bois, France, <sup>2</sup>La Roche-Posay Laboratoire Dermatologique, Levallois-Perret, France

## **Introduction & Objectives:**

The majority of melanin production inhibitors currently marketed inhibit tyrosinase. Only few have demonstrated clinical efficacy while their compounds present safety issues. Moreover, environmental respect is barely taken into consideration. Research on skin lightening agents considering efficacy, safety but also environmental respect is of great importance to significantly improve marketed actives, to avoid side effects and to have a low environmental impact.

#### **Materials & Methods:**

A high-throughput screening test evaluating melanin production on a large chemical diversity and *in silico* predictive methodology were used to eco-design original and performant chemical structures. Efficacy was assessed via topical application on 3D organotypic skin models. Performance and mechanism studies were conducted *in tubo, in vitro* on melanocyte, as well as *in vivo* following UV-daylight exposures on volunteers with phototype III/IV/V originating from Southeast Asia. 4-*n*-butylresorcinol, a tyrosinase inhibitor, was chosen as a marketed reference product.

#### **Results:**

In vitro screening combined with in silico methodologies gave access to 2-mercaptonicotinoyl glycine, an innovative technology for the management of cutaneous hyperpigmentation. It is highly efficient, with a good melanocyte safety and has a low environmental impact. Its efficacy was confirmed via topical application on pigmented reconstructed epidermis and ex vivo human skin explants with an efficacy superior to 4-n-butylresorcinol. Moreover, 2-mercaptonicotinoyl glycine has a unique mode of action consisting in conjugating with melanin precursors, avoiding their integration into growing eumelanin and pheomelanin.

An *in vivo* dose effect at 0.5 and 1% has been shown versus the vehicle allowing to prevent immediate pigmentation, or to reduce neo-melanin production. 2-mercaptonicotinoyl glycine was safe.

## **Conclusion:**

The presented new technology significantly improves the overall performance of skin lightening agents on the market.

Evaluation of the anti-pigmenting efficacy of the association of vitamin B3, vitamin C and AHA in a topical serum, compared to the reference ingredient in the management of melasma

Juliane Rocio<sup>1</sup>, Mukta Sachdev<sup>2</sup>, Claire Deloche<sup>3</sup>, Stéphanie Lerclerc-Mercier<sup>3</sup>, Camila Valpaços<sup>4</sup>, Alessandro Nascimento<sup>4</sup>, Priscila Correia<sup>5</sup>, Beatriz Santanna<sup>3</sup>, Thierry Passeron<sup>6</sup>

<sup>1</sup>Institute of Dermatology and Aesthetics, Brazil, <sup>2</sup>MS Skin Centre and MSCR , India, <sup>3</sup>L'Oréal France, France, <sup>4</sup>CIDP Brasil, Brazil, <sup>5</sup>L'Oréal Brasil, Brazil, <sup>6</sup>University Hospital Centre Nice, France

## **Introduction & Objectives:**

The management of melasma remains challenging. Despite therapeutic options that act at different stages of melanogenesis, results are sometimes disappointing, and relapses are common. For hydroquinone, the ingredient showing the most effective results, there is a concern regarding its tolerability and the possibility of prolonged use. The study aimed at evaluating the anti-pigmenting efficacy of a topical serum (B3) containing an association of 5% vitamin B3, vitamin C and 8% AHA in the treatment of melasma for 5 months and its comparison with hydroquinone 4% (HQ4).

#### **Materials & Methods:**

The study consisted of a prospective monocentric, double-blind randomized trial, including 65 women between 20 and 50 years old, of multiple ethnicities, phototypes II to VI and presenting melasma for more than 1 year. In the first 2 weeks of the study, subjects used face moisturizer and SPF 50+ sunscreen daily. From the third week onwards, subjects were randomized into 2 groups. One group applied the B3 serum daily in the morning and at night for 5 months. The other group applied HQ4 at night for 3 months. At the end of the 3 months, this group interrupted the treatment with HQ4 and started the treatment with the B3 serum twice a day for 2 additional months. Both groups applied SPF 50+ sunscreen daily throughout the study. At initial visit and during the 5 months, subjects were monitored monthly by a dermatologist. Melasma was evaluated by MASI scale, which quantifies the affected area, pigmentation darkness and skin homogeneity. mMASI, disregarding the homogeneity parameter, was also measured. Erythema was assessed using IGA scale and clinical tolerability, by a skin reaction scale. To illustrate the efficacy of the treatment, standardized photographs were taken. In addition, reflectance confocal microscopy was performed.

## **Results:**

Reduction in MASI score was observed after 3 months for both treatments (3.47 for the B3 serum and 3.71 for HQ4). Reduction of the mMASI score was also similar for both groups (1.97 for the B3 serum and 2.05 for HQ4). After replacing HQ4 in the third month, the efficacy was maintained and improved with the daily application of the B3 serum at the end of the 5 months (5.68 for MASI and 3.31 for mMASI [full treatment with the B3 serum] and 5.38 for MASI and 2.81 for mMASI [HQ4 3 months and B3 serum 2 months]). This corresponds to more than 40% decrease in the MASI score in the 2 groups after 5 months of treatment compared to baseline. No statistical significance was found in treatment comparison. Regarding the erythema, more promising results (statistical difference, p value=0.05) were observed with the B3 serum, especially in 1 month of treatment. Skin tolerance was better in B3 serum group compared to the HQ4 group (85% improvement versus 59%) during the first 3 months of treatment. Reflectance confocal microscopy showed decrease in keratinocyte pigmentation from beginning to the end of the treatment for both products in more than 90% of subjects.

#### **Conclusion:**

The serum containing combination of 5% vitamin B3, vitamin C and 8% AHA demonstrated superior results in tolerance and erythema assessment after 1 month when compared to Hydroquinone 4%, suggesting a better compliance to the treatment. Both treatments showed, after 3 months, a parity in melasma improvement based on MASI assessment and confocal microscopy methodology, with no statistical difference, ie, the B3 serum is a safe and efficacious alternative for melasma management in monotherapy and/or as an adjuvant.

Real-Word Evidence: Efficacy of a dermocosmetic regimen containing tyrosinase inhibitor Thiamidol to reduce hyperpigmentation.

Dylan Griffiths<sup>1</sup>, Katja Warnke<sup>1</sup>, Sandra Radenkovic<sup>1</sup>, Barbara Schuster<sup>1</sup>

<sup>1</sup>Beiersdorf, Hamburg, Germany

## **Introduction & Objectives:**

Hyperpigmentation is characterized by irregular brown macules occurring on sun-exposed areas of the body, particularly on the face. It affects mainly women and darker skin types (Fitzpatrick skin photo types III-IV). This acquired hypermelanosis of the skin impacts patients' quality of life resulting in a need for dermatological skin care. In this study, we investigated the efficacy and tolerability of a skin care regimen with the tyrosinase inhibitor Thiamidol (Isobutylamido Thiozolyl Resorcinol) in patients with facial hyperpigmentation.

#### **Materials & Methods:**

In the presented real-world-evidence European study, 629 subjects (mean age 47 y, 98% women, 2% men) from 11 countries (Belgium, Bulgaria, Croatia, Czech Republic, Hungary, Lithuania, Russia, Slovakia, Slovania, United Kingdom, Ukraine) suffering from hyperpigmentation applied a dermocosmetic regimen consisting of a twice daily serum formulation (with Thiamidol, Licochalcone A, and Hyaluronic Acid), day care SPF30 formulation (with Thiamidol, and Licochalcone A) and a night care formulation (Thiamidol, and Licochalcone A).

The regimen was used over 12 weeks. The evaluated parameters were patient's self-assessment and expert assessment.

#### **Results:**

Self-assessment demonstrated a hyperpigmentation improvement in 92% of subjects after 12 weeks, with 98% of subjects confirming the products were suitable for their skin. Expert assessment demonstrated an evenness improvement in 91% of subjects after 12 weeks with 98% of experts rating the tolerability as very good or good.

Significant and continuous improvement was seen in a modified MASI score, with a median MASI score improvement of 74% after 12 weeks. An improvement in MASI was seen in 97% of subjects.

99% of experts would recommend the products to their patients following the study.

## **Conclusion:**

The skin care regimen with Thiamidol was well tolerated and offers an effective daily skin care solution to significantly reduced mild-to-moderate facial hyperpigmentation.

### Core outcome set for congenital melanocytic naevi

Anne Fledderus<sup>1, 2</sup>, Suzanne Pasmans<sup>1</sup>, Claire Van Eijsden<sup>1</sup>, Phyllis Spuls<sup>2</sup>, Albert Wolkerstorfer<sup>2</sup>, Chantal Van der Horst<sup>2</sup>, Oren Lapid<sup>2</sup>, Marjolein Van Kesse<sup>3</sup>, Heather Etchevers<sup>4</sup>

<sup>1</sup>Erasmus MC Sophia Kinderziekenhuis, Rotterdam, Netherlands, <sup>2</sup>Amsterdam UMC, locatie AMC, Amsterdam, Netherlands, <sup>3</sup>Neavus Global, <sup>4</sup>Marseille Medical Genetics, Marseille, France

## **Introduction & Objectives:**

The Outcomes in Congenital Melanocytic Naevi (OCOMEN) project aims to reach uniformity in care and research of medium-to-giant congenital melanocytic naevi (CMN). CMN can impose a psychosocial burden on patients and their families and are associated with risk of developing melanoma or neurological complications. Comparison of treatment efficacy is currently hindered by the lack of standard and uniform outcome reporting; this impedes guidance on optimal management policy. To address this, the OCOMEN project aims to develop a Core Outcome Set (COS) for CMN care and research. A COS is a minimum set of outcomes to measure and report in all clinical practice and clinical trials of a specific health condition. This project focused on the 'what' to measure, i.e. the domains and the specific outcomes describing the domains and the first step of 'how' the measure i.e. the measurement instruments.

#### Materials & Methods:

This study was performed according to the guidelines of the Core Outcome Measures in Effectiveness Trials initiative and received methodological support from the CHORD COUSIN Collaboration. This project entailed the following: (1) A systematic review to identify outcomes reported in previous performed studies. 2) Seven focus groups to identify outcomes important for patients. (3) The classification of all these outcomes into domains. (4) Through e-Delphi surveys, 144 relevant stakeholders (patients, parents, dermatologists, surgeon, neurologist, pathologist, and researchers) from 27 countries iteratively rated the importance of domains and outcomes. (5) A consensus meeting with relevant stakeholders to reach consensus on the core domains. (6) A second consensus procedure with relevant stakeholders to reach consensus on the core outcomes that describe the core domains. (7) A systematic review to find and assess measurement instruments measuring the core outcomes.

#### **Results:**

We reached consensus on the following domains and outcomes for both care and research: anatomy of skin: size, colour, texture of the CMN and satellite naevi number, quality of life: emotional distress, neoplasms: presence of melanoma, nervous system: neurological symptoms and signs, adverse events: wound problems of the CMN, skar problems. The domain and outcome pathology: molecular characteristics, was specified for the COS of research. A list of measurement instruments assessing the core outcomes was identified through a systematic review.

#### **Conclusion:**

We reached consensus on the domains and outcomes for the COS of medium-to-giant CMN (figure 1). The next step will be to reach consensus on what instruments should be used to measure these domains and outcomes. Uniformity and standardization of outcomes is of utmost important to compare management strategies. The application of the COS for CMN will harmonize care and research and facilitate treatment comparisons.

|                 | RESEARCH   | CARE  |
|-----------------|--|---|
| Skin appearance | Size of CMN Colour of CMN Texture of CMN Satellite nevi number | Size of CMN<br>Colour of CMN<br>Texture of CMN<br>Satellite nevi number |
| Quality of life | Emotional distress   | Emotional distress  |
| Neoplasm        | Presence of melanoma   | Presence of melanoma  |
| Neurology       | Neurological symptoms and signs                                | Neurological symptoms and signs   |
| Adverse events  | Wound problems of the CMN<br>Scar problems                     | Wound problems of the CMN<br>Scar problems                              |
| Pathology       | Molecular characteristics                                      |   |



### Upregulation of granulysin expression in halo nevus lesions

Nika Hlaca<sup>1</sup>, Katarina Skender<sup>2</sup>, Marijana Vicic<sup>3</sup>, Marija Kastelan<sup>1</sup>, Andrea Dekanic<sup>4</sup>, Larisa Prpic-Massari<sup>1</sup>

<sup>1</sup>Clinical Hospital Centre Rijeka, Faculty Of Medicine University Of Rijeka, Dermatovenerology, Rijeka, Croatia,

<sup>2</sup>Clinical Hospital Centre Rijeka, <sup>3</sup>Clinical Hospital Centre Rijeka, Faculty Of Medicine University Of Rijeka,

<sup>4</sup>Department of Pathology Medical University of Rijeka

## **Introduction & Objectives:**

Halo nevus is a melanocytic nevus surrounded by a white halo. The current findings emphasize the role of cytotoxic T-cells in the destruction of melanocytes. Granulysin is a cytotoxic mediator found in cytotoxic T-cells and natural killer cells. The data regarding the role of granulysin-mediated cytotoxicity in halo nevus are lacking. The aim is to analyse the expression and distribution of granulysin, T cells and natural killer cells subsets in the epidermis and dermis of lesional and perilesional skin of patients with halo nevus.

## **Materials & Methods:**

Skin biopsy specimens from lesional and perilesional skin of five patients with halo nevus and five healthy controls were analysed by immunohistochemistry.

#### **Results:**

Dense infiltrates of T cells, particularly of CD4+ and CD8+ subsets, were found in halo nevus lesions. Granulysin positive cells were mainly accumulated in the upper dermis of halo nevus lesions. Granulysin expression was significantly upregulated in the lesions of halo nevus in comparison to perilesional and healthy skin. CD8+granulysin+ T lymphocytes, and CD56+granulysin+ NK cells were found with higher frequency in the dermal infiltrate of lesional skin compared to perilesional and healthy skin.

### **Conclusion:**

In conclusion, accumulation of granulysin-positive cells in the halo nevus lesions suggests a potential role of granulysin in the destruction of lesional melanocytes, a typical feature of halo nevus.

Impact of empathic and competent management of pediatric vitiligo on disease evolution and parental and juvenile disease-related quality of life. A follow-up study on 47 children.

Harpain Lucie\*1, Sonja Radakovic1, Marculescu Rodrig2, Adrian Tanew3

<sup>1</sup>Medical University of Vienna, Dept. of Dermatology, Vienna, Austria, <sup>2</sup>Medical University of Vienna, Dept. of Laboratory Medicine, Vienna, Austria, <sup>3</sup>Private Practice, Vienna, Austria

Key words: Vitiligo, children, counselling, treatment, health-related quality of life

**Introduction & Objectives:** Vitiligo is an autoimmune disease characterized by immune-mediated loss of melanocytes resulting in depigmentation of affected skin areas. It is a common pigmentary disorder with an estimated prevalence in Europe of 1.6%. Although in general not associated with symptoms such as pruritus of pain vitiligo due to its cosmetic stigmatization may have a huge impact on patients' quality of life. There is still a lack of general awareness of the influence of vitiligo on patients' well-being and guidance and treatment of affected patients is often unsatisfactory. In the present study we assessed disease evolution and parental and juvenile disease-related quality of life after empathic and competent management of children with vitiligo.

Materials & Methods: Children with vitiligo accompanied by at least one parent were examined and counselled in a tertiary care centre specialised on vitiligo. Treatment was initiated and a follow-up performed after a time interval of ≥6 months. Besides baseline demographic and clinical data the following parameters were assessed at both the baseline and follow-up visit: vitiligo disease activity (VIDA), vitiligo area scoring index (VASI), family dermatology life quality index (FDLQI) and the vitiligo specific quality of life index (VitiQoL).

**Results:** 47 children (male 23, female 24) were included in the study. Their mean age was 10.6 years (range, 3-17 years) and the mean disease duration 15.1 months (range, 0-98 months). The mean time period between baseline and follow-up visit was 27.1 months (range, 6-114 months). 39 children had non-segmental vitiligo (NSV) and 8 segmental vitiligo (SV). During the study period the baseline VIDA deceased significantly from  $2.8 \pm 1.5$  to  $0.8 \pm 1.8$  (p<0.001) whereas no significant change was found for the VASI which was  $5.0 \pm 12.7$  at baseline and  $5.3 \pm 15.2$  at the follow-up visit (p=0.664). Both the FDLQI and VitiQoL decreased significantly over the observation period from  $8.1 \pm 5.3$  to  $4.6 \pm 4.7$  (p<0.001) and  $16.3 \pm 16.2$  to  $11.5 \pm 13.4$  (p=0.004), respectively.

**Conclusion:** Our findings indicate that empathic and competent counselling and treatment of children with vitiligo can result in disease arrest and empower both children and their parents to better cope with the substantial disease-related impairment of quality of life. However, a guarded interpretation of our findings is required since for ethical reasons our study did not include an untreated control group.

### Raccoon eyes under the dermoscope: think of localized lichen planus

Kenza Tahri Joutei Hassani<sup>1</sup>, Zakia Douhi<sup>1</sup>, Khalil Bouayad<sup>1</sup>, Hanane Bay Bay<sup>1</sup>, Sara Elloudi<sup>1</sup>, Meryem Soughi<sup>1</sup>, Fatima Zahra Mernissi<sup>1</sup>

<sup>1</sup>Hassan II university hospital center

## **Introduction & Objectives:**

Lichen planus (LP) is a well-known inflammatory condition that affects both the skin and mucous membranes . LP typically presents as shiny, violaceous, flat-topped, pruritic polygonal papules or plaques with fine white lines forming a superficial network known as Wickham striae . While LP can occur anywhere on the body, it rarely affects the eyelids. Isolated lesions of eyelid LP can pose a challenge for clinical diagnosis. We present a unique case of LP affecting both upper and lower eyelids bilaterally presenting as "raccoon eyes."

#### **Materials & Methods:**

An otherwise healthy 40-year-old woman presented with a 4-month history of pruritic lesions on her bilateral eyelids. The patient had not applied any medication or any cosmetic product to the site prior to the onset of the lesions. On examination, she had a violaceous slightly pigmented plaque over the upper and lower eyelids. Examination of the entire body did not reveal any similar lesion. Dermoscopy of the lesions revealed grey-brown dots and globules, a granular annular pattern with an erythematous background. A skin biopsy of the upper eyelid showed acanthosis, hypergranulosis, overlying hyperkeratosis, a dense lichenoid inflammatory infiltrate with mild to moderate vacuolar interface dermatitis, and prominent melanophagocytosis in the superficial dermis, confirming the diagnosis of LP. She was prescribed a topical desonide 0,1% for three months with good improvement.

#### Results:

Eyelid dermatosis involve various conditions including contact dermatitis, seborrheic dermatitis, and atopic dermatitis, among others. Lichen planus of the eyelid is rare, with only a few reported cases prior to 1995. Typically, lichen planus lesions on the eyelids are part of generalized lesions seen elsewhere on the body. However, our case is unique as the eyelid were the only affected area. The lesions of lichen planus on the eyelids can be categorized into three types: (1) classic lilac-colored papules with slight indentations and filigree scaling, usually accompanied by similar lesions elsewhere on the body, (2) annular papules or small medallion plaques often seen in conjunction with lesions on other body parts, and (3) lesions occurring exclusively on the eyelids.

The characteristic dermoscopic features suggestive of lichen planus are Wickham's striae (WS) that corresponds histologically to the focal thickening of the granular layer. We didn't find any WS in our case but we found greybrown dots and globules with a granular annular pattern.

There are various other manifestations of ocular lichen planus, such as cicatrizing conjunctivitis, blepharitis, keratitis, and symblepharon, which can potentially result in corneal ulceration or long-term visual impairment. Therefore, it is crucial for both dermatologists and ophthalmologists to be vigilant and knowledgeable about this diagnosis to ensure timely and appropriate management.

#### **Conclusion:**

Lichen planus of the eyelid is a condition that is often overlooked and should be considered in the list of possible

diagnoses for eyelid dermatosis. Although topical steroids have shown efficacy in treating eyelid LP, further research is needed to determine the most optimal therapeutic approach for this condition.

# rare association of Laugier Hunziker syndrome and rheumatoid arthritis :a case report and review of the literature

Oumaima Lafdali<sup>1</sup>, Oumayma Handi<sup>1</sup>, Maryem Aboudourib<sup>1</sup>, Ouafae Hocar<sup>1</sup>, Said Amal<sup>1</sup>

<sup>1</sup>CHU MOHAMMED VI, Dermatology and venereology, marrakech, Morocco

## **Introduction & Objectives:**

Laugier-Hunziker syndrome (LHS) is a rare acquired disorder characterized by diffuse macular hyperpigmentation of the oral mucosa and less frequently a longitudinal melanonychia. Although LHS is considered as a benign disease with no systemic manifestations or malignant potential. The ethiopathogenesis remains unknown . We report a case of a 64 years old woman with Laugier-Hunziker syndrome associated to rheumatoid arthritis

#### **Materials & Methods:**

A 64 years old non smoking woman, presented with diagnosis of rheumatoid arthritis established 3 years ago. The patient was well managed with corticosteroids. She had no history of chronic drug use nor had familial history of pigmentary disorders and digestive polyposis or tumors. The patient presented with diffuse nail melanonychia developed over the 10 last years. She also complained of asymptomatic hyper pigmentation on the lower lip and the buccal mucosa. Those skin and nails changes appeared almost 7 years before the start of corticosteroids.

The physical examination revealed multiple longitudinal and heterogeneous pigmented bands affecting all the finger nails. Toenails were spared. The pseudo Hutchinson sign was positif. Irregular brown homogeneous macules were present on the lips and one single macule was in the buccal mucosa.

in the laboratory examinations, the peripheral blood cell count and biochemical parameters were all within normal limits. Rheumatoid factor, anti-CCP and antinuclear antibody profiles were negative. Plasma cortisol levels, adrenocorticotropic hormone (ACTH) values and thyroid function tests (TSH) were within normal limits. No pathological findings were determined in the abdominal ultrasonography, upper gastrointestinal track endoscopy, colonoscopy and mammography. Therefore, most systemic disorders were ruled out and the diagnosis of LHS was made.

#### **Results:**

Laugier-Hunziker syndrome is a diagnosis of exclusion. If a patient has focal pigmentation, a biopsy should be done to exclude melanoma. Addison disease should be excluded by biological tests. The apparition of the melanonychia at an adult age excluded other differential diagnosis like Petz Jegher syndrome, Bandler syndrome and idiopathic melanonychia. Many external conditions like drugs, cigarette and systemic exposure to heavy metals may be responsible of mucocutaneous discoloration.

Although there are approximately 200 cases of LHS in the literature, there are only one familial case, one case of LHS associated with rheumatoid arthritis by a Turkish team and two patients with LHS associated with Sjogren syndrome.

The most common sites for the lesions are the lips and the oral cavity, particularly the buccal mucosa. In literature, not all the cases reported both oral and nail involvement, and the incidence of a pigmented nail band is 44%–60%. Racial factors are highly suggested. Longitudinal melanonychia, has been reported to occur in 77%–96% of blacks and 11% of Asians. Also the irregular or stippled pigmentation in our case seems to be a new feature of nail

pigmentation associated with LHS.

# **Conclusion:**

The association of LHS with rheumatoid arthritis and Sjögren syndrome should throw new light on the possible role of autoimmunity in the ethiopathogenesis of this rare disease .

## Glutathione between Myth and Reality

Amera Bayumi<sup>1</sup>

العيادات الأمريكية التخصصية العذيبة $^{
m 1}$ , Dermatology, Muscat, Oman

#### 1-GLUTATHIONE BETWEEN MYTHS AND REALITY.

## **Introduction & Objectives:**

Glutathione is well known as the master of antioxidant but there is a myth nowadays about it that it is the magic stick of skin whitening. A lot of people do not know that it can be simply supplied in food. In most dermatology clinics used as whitening mesotherapy materials and considered major component in most brands in few clinics it is supplied to the patients in parenteral form which in the last few years denied by so many international organizations and professors as it causes major harm to the body

#### **Materials & Methods:**

In this lecture we will spotlight on the truth behind glutathione whitening effect is it really effective? Is it harmful? What is the best way of administration? What is the mechanism of action of whitening effect of glutathione?.....

#### **Results:**

## **Conclusion:**

Glutathione is well known as the master of antioxidant but there is a myth nowadays about it that it is the magic stick of skin whitening. A lot of people do not know that it can be simply supplied in food. In most dermatology clinics used as whitening mesotherapy materials and considered major component in most brands in few clinics it is supplied to the patients in parenteral form which in the last few years denied by so many international organizations and professors as it causes major harm to the body. In this lecture we will spotlight on the truth behind glutathione whitening effect is it really effective? Is it harmful? What is the best way of administration? What is the mechanism of action of whitening effect of glutathione?.....

# Association Between Treatment Patterns and Comorbidities in Patients With Vitiligo: A Retrospective Real-World Data Analysis

Yuval Ramot\*<sup>1, 2</sup>, Vered Rosenberg<sup>3</sup>, Limei Zhou<sup>4</sup>, Stephanie Harbers<sup>5</sup>

<sup>1</sup>Hebrew University of Jerusalem, The Faculty of Medicine, Jerusalem, Israel, <sup>2</sup>Hadassah Medical Center, Department of Dermatology, Jerusalem, Israel, <sup>3</sup>Kahn-Sagol-Maccabi Research and Innovation Institute, Maccabi Healthcare Services, Tel Aviv, Israel, <sup>4</sup>AbbVie Inc., Toronto, Canada, <sup>5</sup>AbbVie Inc., Rungis, France

**Introduction & Objectives:** Standard of care treatment for vitiligo relies largely on off-label interventions such as corticosteroids (CS), calcineurin inhibitors (CI), and phototherapy. The impact of comorbidities, including psychological comorbidities, on treatment choice is currently unknown. This analysis describes real-world treatment patterns by comorbidities for patients with vitiligo in Israel.

**Materials & Methods:** A cross-sectional cohort analysis was conducted using the database of a large health service organization. Treatment patterns were assessed retrospectively for the 2021 prevalent population. Data were reported on the number and proportion of patients covered by treatment from the date of first vitiligo diagnosis until 31 December 2021. Treatment sequencing is presented as the proportion of patients treated with first-, second-, and third-line therapies, overall and by presence of comorbidities.

Results: Among the 2021 prevalent vitiligo population (N=11,412), immune-mediated comorbidities were present in 3389 (29.7%) patients and psychological comorbidities in 2129 (18.7%). Atopic dermatitis (12.5%), psoriasis (5.8%), Hashimoto's thyroiditis (2.9%), alopecia areata (2.2%) and prurigo nodularis (2.2%) were the most common immune-mediated comorbidities. Depression (10.8%; among adults: 1218/9082 [13.4%]), sleep disturbance/insomnia (5.9%), and anxiety (3.7%) were the most common psychological comorbidities.\*\* Patients with ≥1 immune-mediated comorbidity were significantly more likely to receive any treatment (83.0% vs 71.3% [P<0.001; standard mean difference (SMD): 0.28]), including topical CS (62.6% vs 46.9% P<0.001; SMD: 0.32]), topical CI (40.4% vs 34.8% [P<0.001; SMD: 0.12]), systemic CS (33.7% vs 24.3% [P<0.001; SMD: 0.21]), systemic immunosuppressants (4.8% vs 0.4% [P<0.001; SMD: 0.28]), and phototherapy (9.5% vs 6.5% [P<0.001; SMD: 0.11]) than those without an immune-mediated comorbidity. Likewise, adult patients with depression were significantly more likely to receive any treatment (81.2% vs 76.3% [P<0.001; SMD 0.12]), including topical CS (60.2% vs 54.0% [P<0.001; SMD: 0.12]) and systemic CS (44.5% vs 28.4% [P<0.001; SMD: 0.34]) compared with patients without depression.\*\* Significant differences in first- and second-line therapy overall by presence of ≥1 immune-mediated comorbidity (vs none) or depression (vs no depression [adult patients]) were observed (P<0.05; SMD >0.1). For first-and second-line therapy, differences in topical and systemic therapy patterns were minor; for third-line therapy, patients with ≥1 immune-mediated comorbidity (vs none) and adult patients with depression (vs no depression) were more commonly prescribed systemic immunosuppressants (19.0% vs 2.8% and 17.9% vs 11.7%) and less commonly prescribed phototherapy (9.0% vs 22.2% and 7.1% vs 16.1%).

**Conclusion:** These data show that patients with vitiligo and immune-mediated comorbidities or depression are more likely to receive treatment than patients without these comorbidities. Patients with these comorbidities may also progress more rapidly to systemic therapy as evidenced by greater use of systemic interventions at third line. These findings suggest that the increased impact of additional physical or psychosocial burden may potentially drive treatment decision making.

### Vitiligo and its comorbidities: an Italian tertiary centre experience

Maria Efenesia Baffa\*<sup>1</sup>, Stefano Senatore<sup>1</sup>, Carlo Pipitò<sup>1</sup>, Roberto Maglie<sup>1</sup>, Silvia Moretti<sup>1</sup>, Emiliano Antiga<sup>1</sup>

<sup>1</sup>University of Florence, Department of Health Sciences, Section of Dermatology, Firenze, Italy

#### **Introduction & Objectives:**

Vitiligo is the most common depigmenting disorder, affecting the 0.5-2% of the population. It is characterized by the selective loss of melanocytes which results in the typical non scaly, irregular, totally achromic (chalk-white) lesions. It has been often associated with other immune-mediated diseases. Here we report the data of our tertiary centre regarding the most common immune-mediated comorbidities associated with vitiligo. Our aim is to identify and describe the immune-mediated comorbidities associated with vitiligo in a cohort of 987 patients.

## Materials & Methods:

All medical records of vitiligo patients, dating from January 1, 1999 to December, 2020 were evaluated retrospectively. The following items were investigated: personal history of 1) autoimmune thyroiditis, 2) psoriasis, 3) alopecia areata, 4) atopic dermatitis, 5) lichen sclerosus, 6) atrophic gastritis. Anti-nuclear anti-bodies (ANA) and anti-thyroid autoantibodies were evaluated as well.

#### **Results:**

Our population consisted in 987 patients,582 females (59%) and 405 males (41%). Two-hundred and thirty-four (24%) patients had one of the following comorbidities: 207 thyroid-related (21%), 47 psoriasis (4.8%), 35 atopic dermatitis (3.5%), 15 alopecia areata (1.5%), 7 lichen sclerosus (0.7%), 14 atrophic gastritis (1.4%), 9 type I diabetes mellitus (0.9%). ANA titers were elevated in 214 (42%) patients out of the 510 in which the value was tested. Of interest is that only one patient in our dataset had a history of systemic and/or cutaneous lupus erythematosus. The 60% of patients had positive anti-thyroid peroxidase auto-antibodies (148 out of the 248 that were tested). Only 5 patients out of the 9 who were positive for anti-TSH receptor auto-antibodies had a diagnosis of Basedow disease.

#### **Conclusion:**

We found a high prevalence of comorbidities among individuals with vitiligo presenting to our centre. Comorbid autoimmune conditions were seen in 24% of vitiligo patients. Our data overlap those from the international literature, confirming the higher risk of immune-mediated disorders in vitiligo population. On the other hand, the prevalence of lupus erythematosus was close to zero, suggesting the possibility to interpret the ANA positivity as a non-specific indicator of autoimmune diathesis rather than a value to be further investigated in the absence of clinical signs and/or symptoms of lupus erythematosus.

# Immune Checkpoint Proteins in Vitiligo: Potential Biomarkers for Disease Activity and Novel Therapeutic Targets

Arno Belpaire<sup>1, 2</sup>, Reinhart Speeckaert<sup>1, 2</sup>, Nanja Van Geel<sup>1, 2</sup>

<sup>1</sup>Ghent University Hospital, Head and Skin, Gent, Belgium, <sup>2</sup>Ghent University, Head and Skin, Gent, Belgium

# Immune Checkpoint Proteins in Vitiligo: Potential Biomarkers for Disease Activity and Novel Therapeutic Targets

#### **Introduction & Objectives:**

Despite substantial advancements in understanding the pathogenesis of vitiligo, effective targeted therapies are limited. Clinical assessment of disease activity is currently based on subjective expert interpretation, underscoring the need for reliable biomarkers. This study explores immune checkpoint biomarkers involved in the regulation of (auto-)immune responses, driving advancements in disease monitoring and treatment of vitiligo.

#### **Materials & Methods:**

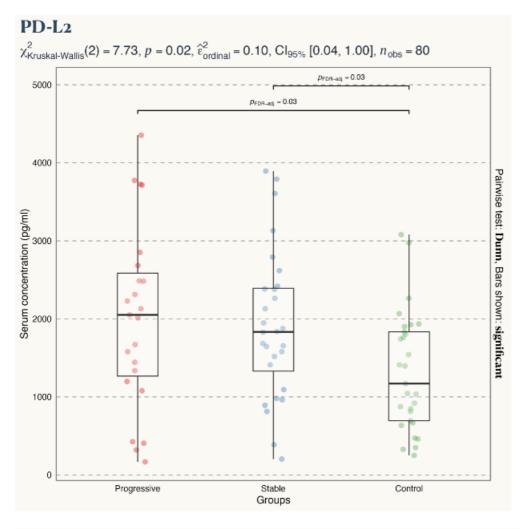
A prospective study was conducted at the Dermatology Department of Ghent University Hospital between October 2021 and March 2023, enrolling 51 patients with nonsegmental vitiligo and 29 healthy controls. Patients were classified into progressive (n=23) and stable (n=28) vitiligo groups based on clinical evaluations using the Vitiligo Disease Activity Score (VDAS) and Vitiligo Disease Extent Score (VDIS). Immune checkpoint proteins in the serum samples were analyzed using a commercial multiplex immunoassay kit, with results read and data acquired using a multiplexing-capable analyzer and a standard analytical software tool. Statistical analyses were performed using Rstudio (Version 2023.03.1+446). Comparisons across the groups were performed using a nonparametric Kruskal-Wallis test with a post-hoc Dunn test.

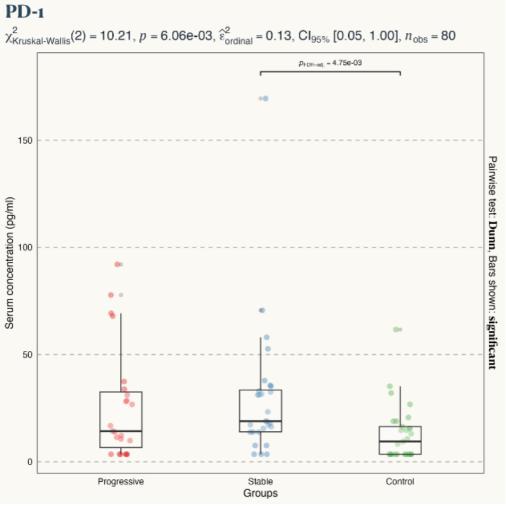
#### **Results:**

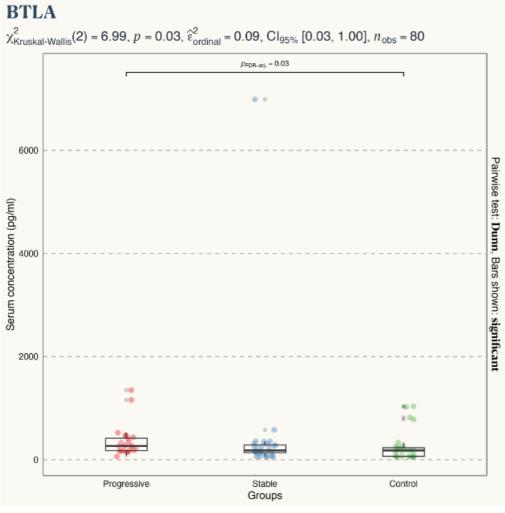
The serum concentration levels of PD-1, PD-L2, BTLA, and LAG-3 significantly differed between vitiligo patients and controls. Specifically, PD-L2 levels were higher in both progressive (median=2052.0 pg/mL, IQR: 1267.5-2586.4 pg/mL, P = .002) and stable (median=1833.5 pg/mL, IQR: 694.6-1833.5 pg/mL, P = .002) vitiligo patients compared to controls. The progressive group exhibited elevated levels of LAG-3 (median=20.3 pg/mL, IQR: 16.7-26.6 pg/mL, P = .009) and BTLA (median=260.0 pg/mL, IQR: 177.3-416.6 pg/mL, P = .003). In contrast, the stable group showed higher PD-1 levels (median=18.9 pg/mL, IQR: 13.9-33.5 pg/mL, P = 0.006).

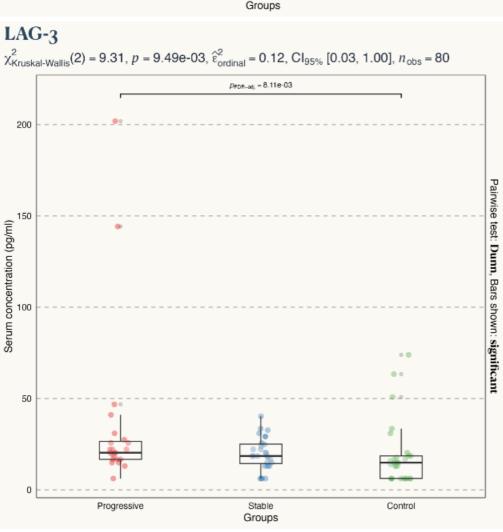
## **Conclusion:**

Differential expression of immune checkpoint proteins in vitiligo patients may serve as potential biomarkers for disease activity, providing a non-invasive approach to disease monitoring. Immune checkpoint inhibition is known for its efficacy in melanoma therapy, yet might reversely represent a promising therapeutic strategy for vitiligo. Additional research is needed to validate these potential biomarkers and to further investigate the therapeutic implications of immune checkpoint modulation in vitiligo treatment.









#### Modulation of melanogenesis in vitiligo

Małgorzata Grochocka<sup>1</sup>, Tadeusz Tadrowski<sup>1</sup>, Jakub Kuta<sup>1</sup>, Rafał Czajkowski<sup>1</sup>

<sup>1</sup>Nicolaus Copernicus University in Torun, Poland, Department of Dermatology and Venerology , Bydgoszcz, Poland

### Introduction & Objectives:

Vitiligo is a pigmentary disorder that leads to selective loss of melanocytes, resulting in discoloration of the skin, its appendages, and mucous membranes. Patients with vitiligo have melanocytes that exhibit an increased cellular response to stress. These cells are targeted and destroyed by the immune system (CD8+ cytotoxic T lymphocytes), leading to the formation of depigmented patches. Development of disease is influenced by oxidative stress, which can directly disrupt melanin metabolism and impair melanocyte survival through excessive accumulation of cytotoxic hydrogen peroxide. Antioxidants such as polyphenols and ginkgolides have the ability to modulate the expression levels of various genes involved in cell cycle regulation, apoptosis, and DNA repair. Providing antioxidants may help restore the impaired intracellular balance between oxidants and antioxidants observed in vitiligo patients.

### Materials & Methods:

The project was based on hTERT- Dermal Melanocyte cell line. The main aim was to determine the effects and dosage of natural compounds (ginkgolides) in mono-doses and combinations of two compounds (IC50 values determination). Additionally, the study investigated the combined effect of UVB radiation and natural compounds (ginkgolides). The effects of analyzed compounds and UVB radiation on changes in melanin synthesis levels were examined for doses ≤ IC50. In the conducted experiment, the effect of selected compounds on melanocyte survival was examined using the MTT assay. Measurements were taken after 24 and 48 hours of exposure to various compounds, including ginkgolides (A, K, J, B, and C), kaempferol, bilobalide, ginkgolic acid, and isoginketin. The compounds were used at concentrations ranging from 15,625 nM to 500 nM. Statistical analysis of the results was performed using either one-way ANOVA or the Kruskal-Wallis test.

### Results:

Among the tested compounds, ginkgolides A, B, and C showed promising results as they did not adversely affect cell survival under most tested conditions. Furthermore, ginkgolide C exhibited an increase in cell numbers compared to controls when used at a concentration of 500 nM and 24 hours of exposure. Other compounds that could be further explored under appropriate conditions are kaempferol, ginkgolide J, bilobalide, and ginkgolic acid. However, ginkgolide K and isoginketin showed significant negative effects on cell survival, suggesting that they may not be suitable for further testing.

#### Conclusion:

The search for melanogenesis modulators serves as a significant starting point for the creation of an innovative therapy with long-lasting clinical effects. Under appropriate in vitro culture conditions, utilizing the correct combination and doses of the aforementioned compounds, this method would achieve constitutive melanin expression. The study's results could contribute to enhancing the treatment approach by incorporating selected compounds.

### cyclophosphamide-induced skin hyperpigmentation: a rare presentation

Syrine Nahali<sup>1</sup>, Mariem Tabka<sup>1</sup>, Ismahene Souissi<sup>1</sup>, Alaoui Fatima<sup>1</sup>, Mourad Mokni<sup>1</sup>

<sup>1</sup>la rabta, dermatology and venereology, ariana

## **Introduction & Objectives:**

Cyclophosphamide is a chemotherapeutic agent used in treatment of neoplasms and severe manifestations of auto-immune diseases.

Pigmentary changes present one of its rare side effects.

#### **Materials & Methods:**

We describe a patient with chronic kidney disease in whom a rare presentation of skin hyperpigmentation occurred.

#### **Results:**

A 56-year-old man with a history of extra-membranous glomerulonephritis was offered a trial of treatment with cyclophosphamide and prednisone.

Two weeks later, he developed a pruritic hyperpigmented eruption on the popliteal, axillary and interfessional folds, the trunk and the arms. No associated pigmentary changes on the nails and mucosae were identified.

A biopsy specimen revealed a subtle presence of pigment incontinence within the superficial dermis. There was no other triggering factor (medication or pathology) identified.

A wide range of chemotherapeutic agents has been associated with pigmentary disorders, with cyclophosphamide being one of the most frequently involved.

In fact, Cyclophosphamide is known to induce hyperpigmentation that can affect skin, nails, or mucous membranes. However, isolated skin pigmentation is an infrequent side effect and almost exclusively limited to the palms and soles. In our observation, neither the nails nor the palms and soles were affected. The pigmented lesions were predominant in the areas of friction. The tendency for cyclophosphamide-induced hyperpigmentation to develop at areas of skin prone to friction or trauma has previously been noted. Local proliferation of melanocytes may have happened in response to local pressure.

The pathogenesis of hyperpigmentation due to cyclophosphamide remain unclear. The drug may cause a direct toxic effect on melanocytes inducing an increased epidermal melanin production.

Most published reports showed no direct linear relationship with either the treatment dosage or duration. Pigmentary disorders occur after a variable period and may vary from seven days to many months following the start of treatment. The pigmentary changes usually tend to fade gradually, without specific intervention after interrupting the causative drug.

## **Conclusion:**

Isolated cyclophosphamide-related skin hyperpigmentation and its particular localisation on folds and areas of

friction has not been published before.

We are reporting this complication to increase awareness about this uncommon side effect of a very common chemotherapeutic agent, to avoid unnecessary biopsies and for reassurance to patients.

# Efficacy of topical gabapentin in women with primary macular amyloidosis: A side-by-side triple-blinded randomized clinical trial

Bahareh Abtahi\*<sup>1, 2</sup>, Elahe Hemati<sup>3</sup>, Gita Faghihi<sup>4</sup>, Zabihollah Shahmoradi<sup>4</sup>, Fatemeh Paknazar<sup>5</sup>, Fereshte Rastegarnasab<sup>6</sup>, Jaleh Varshosaz<sup>7</sup>, Mahdi Hadian<sup>4</sup>, Mojtaba Akbari<sup>8</sup>, Ali Mohammad Sabzghabaee<sup>9</sup>

<sup>1</sup>Pediatric Dermatology Division of Department of Pediatrics, Imam Hossein Children's Hospital, Isfahan University of Medical Sciences, Isfahan Iran, <sup>2</sup>Skin Diseases and Leishmaniasis Research Center, Isfahan University of Medical Sciences, Isfahan Iran, <sup>3</sup>Pediatric Dermatology Division of Department of Pediatrics, Imam Hossein Children's Hospital, Isfahan University of Medical Sciences, Isfahan, Iran, <sup>4</sup>Skin Diseases and Leishmaniasis Research Center, Isfahan University of Medical Sciences, Isfahan, Iran, <sup>5</sup>Social Determinants of Health Research Center, Semnan University of Medical Sciences, Semnan, Iran, <sup>6</sup>Student Research Committee, Isfahan University of Medical Sciences, Isfahan Iran, <sup>7</sup>Department of Pharmaceutics, Faculty of Pharmacy and Novel Drug Delivery Systems Research Center, Isfahan University of Medical Sciences, Isfahan, Iran, <sup>8</sup>Department of Epidemiology, School of Health, Isfahan University of Medical Sciences, Iran, <sup>9</sup>Isfahan Clinical Toxicology Research Center, Isfahan University of Medical Sciences, Isfahan, Iran

#### **Introduction & Objectives:**

This study aimed to evaluate the efficacy of topical 6% gabapentin cream for the treatment of patients with primary cutaneous macular amyloidosis (PCMA).

### **Materials & Methods:**

In this triple-blind clinical trial, a total of 34 patients, who were diagnosed with PCMA, were treated with two different methods of topical gabapentin as the active group and vehicle cream as the control group.

**Trial registration:** The trial was registered in the Iranian registry of clinical trials (http://www.irct.ir; registration No.: IRCT20131119015455N4).

## Results:

Pruritus score reduction in both groups was statistically significant compared with the baseline value (P: <0.001). There was a significant pigmentation score reduction in intervention group compared with control group after one month of the study (P: <0.001). The differences of pigmentation score changes between the groups were not significant at month 2 (P = 0.52), and month 3 (P = 0.22).

#### **Conclusion:**

The results of this study suggest that topical gabapentin cream may be effective as a topical agent in the treatment of pruritus associated with PCMA without any significant adverse effects. It is recommended to perform similar studies with a larger sample size and longer duration in both sexes.

Successful treatment of recalcitrant non-segmental vitiligo of the dorsum of the hands with a topical formulation containing MIA-inhibiting peptides in combination with sun exposure

Sergi Hernández Navarro<sup>1</sup>, Marta Bajona Roig<sup>1</sup>, Jordi Segura Tejedor<sup>1</sup>, Mauro Alaibac<sup>2</sup>, Matteo Bordignon\*<sup>2</sup>

<sup>1</sup>Bella Aurora Labs, R&D Department, Santa Coloma de Cervelló, Spain, <sup>2</sup>University of Padua, Dermatology, Padua, Italy

## **Introduction & Objectives:**

Vitiligo is an acquired chronic pigmentation disorder of the skin that affects 0.5–2% of the population worldwide. The exact pathogenesis of the dermatosis is still to be fully clarified.

It has been recently suggested that the final step of the formation of the achromic patches could be mediated by the action of a protein called Melanoma Inhibitory Activity (MIA). MIA is a small protein firstly described as secreted from malignant melanoma cells, which is able to interact with a particular group of adhesion molecules called alpha5beta1 integrins (a5b1ints). The binding of MIA to these proteins at the cell surface is responsible for the detachment of melanocytes from extracellular matrix proteins, creating the depigmented macules through melanocytorrhagy, as also demonstrated in an animal model.

Recently, it has been shown that a topical preparation containing MIA-inhibiting peptides is useful for the treatment of non-segmental vitiligo of face and trunk in combination with UV lamps.

#### **Materials & Methods:**

A 45-years-old female patient, affected by non-segmental vitiligo on the hands for 3 years, came to our observation. The patient was already treated with various therapies including oral and topical steroids, topical immunomodulators, kelline, UVB lamps, without any benefit and with progressive enlargement of the spots reaching almost the 90% of depigmentation in that area.

The MIA-inhibitors topical treatment was applied twice a day for 6 months on the affected skin together with sun exposure (suggested to do on a daily basis, at least 30 minutes).

### **Results:**

After 6 months, the patient achieved a significative repigmentation of the affected areas reaching about 90% of the basal situation of the dorsum of left hand and about 80% of the basal situation of the dorsum of right hand. During the treatment, no side effects locally or systemically of any type were observed.

#### **Conclusion:**

The treatment of vitiligo in hands is challenging for every dermatologist, due to the particularly refractivity of this anatomic site to any so far used therapy. At the same time, due to the high visibility of this site, the demanding for cure of the patients is at a very high level and new therapeutic options are surely required. The possibility to have a new topical treatment characterized by the use of custom-design peptides with no pharmacological action and with an elevated safety profile could surely represent a very interesting approach for treating this hypopigmentary disorder in this difficult-to-treat site.

A treatment based on the MIA-inhibitor technology (an oligopeptide specifically designed to block the activity of

the protein) has been recently introduced on the market for the treatment of vitiligo, with already proven efficacy on adults in common disease site such as face and trunk (5).

In this study we present a clinical case of successful treatment in a very difficult-to-treat anatomic site such as the dorsum of hands. Moreover, differently to the previous case report, the repigmentation was achieved without any UV lamps but only with direct sunlight exposure, confirming the independent role of the MIA-inhibiting peptides technology for the treatment of non-segmental vitiligo.

Considering the very good achieved results without any side effects, this treatment could be considered a possible therapeutic option of non-segmental vitiligo of this anatomic site. Other studies are mandatory to establish the efficacy of this treatment in more wide range of patients.

# Efficacy of Prolonged Ruxolitinib Cream Treatment for Vitiligo Among Patients With Limited or No Initial Response at 6 Months

Albert Wolkerstorfer\*<sup>1</sup>, Melinda J. Gooderham<sup>2</sup>, Michael Sebastian<sup>3</sup>, David Rosmarin<sup>4</sup>, Andrew Blauvelt<sup>5</sup>, Maryam Shayesteh Alam<sup>6</sup>, Jacek Zdybski<sup>7</sup>, Shaoceng Wei<sup>8</sup>, Deanna Kornacki<sup>8</sup>, Thierry Passeron<sup>9, 10</sup>, John E. Harris<sup>11</sup>

<sup>1</sup>Amsterdam University Medical Center, Amsterdam, Netherlands, <sup>2</sup>SKiN Centre for Dermatology, Peterborough, ON, Canada, <sup>3</sup>Hautarztpraxis Mahlow, Blankenfelde-Mahlow, Germany, <sup>4</sup>Indiana University School of Medicine, Indianapolis, IN, United States, <sup>5</sup>Oregon Medical Research Center, Portland, OR, United States, <sup>6</sup>SimcoDerm Medical and Surgical Dermatology Centre, Barrie, ON, Canada, <sup>7</sup>Klinika Zdybski – Dermedic, Ostrowiec Swietokrzyski, Poland, <sup>8</sup>Incyte Corporation, Wilmington, DE, United States, <sup>9</sup>Centre Hospitalier Universitaire de Nice, Université Côte d'Azur, Nice, France, <sup>10</sup>INSERM U1065, C3M, Université Côte d'Azur, Nice, France, <sup>11</sup>University of Massachusetts Chan Medical School, Worcester, MA, United States

## **Introduction & Objectives:**

Vitiligo is a chronic autoimmune disease characterized by melanocyte destruction, leading to skin depigmentation. Limited data are available regarding the efficacy of long-term topical vitiligo treatment. In 2 randomized, double-blinded, vehicle-controlled phase 3 studies in adults and adolescents (aged ≥12 y) with nonsegmental vitiligo (TRuE-V1 [NCT04052425]; TRuE-V2 [NCT04057573]), ruxolitinib cream application resulted in statistically superior improvements in repigmentation vs. vehicle in the primary and all key secondary endpoints at Week 24 and was well tolerated. In the open-label period of TRuE-V1/TRuE-V2 (Weeks 24–52) and the TRuE-V long-term extension (LTE; Weeks 52–104) study (NCT04530344), further improvements in facial and body repigmentation (as assessed by Vitiligo Area Scoring Index [VASI] responses) were observed through Week 104 among patients who continued to apply ruxolitinib cream. In this pooled analysis, we evaluated shifts in facial and total body VASI (F-VASI/T-VASI) responses among patients with vitiligo who had limited or no repigmentation at Week 24 and who continued to apply ruxolitinib cream for an additional 80 weeks.

#### **Materials & Methods:**

In TRuE-V1/TRuE-V2, patients were randomized 2:1 to apply twice-daily 1.5% ruxolitinib cream or vehicle for 24 weeks, after which all patients could apply 1.5% ruxolitinib cream through Week 52. Patients who completed TRuE-V1/TRuE-V2 were eligible to enroll in the TRuE-V LTE. Patients who did not achieve ≥90% improvement in F-VASI at Week 52 continued to apply open-label 1.5% ruxolitinib cream until Week 104. Patients initially randomized to apply ruxolitinib cream who had <25% improvement from baseline in F-VASI or T-VASI at Week 24 and had non-missing VASI assessments at the evaluated time points were included in this analysis. Shifts in F-VASI and T-VASI were assessed among patients with no facial/body repigmentation or worsening depigmentation (≤0% improvement in F-VASI/T-VASI) and patients with limited facial/body repigmentation (>0%-<25% improvement in F-VASI/T-VASI) at Week 24.

### **Results:**

Among patients with no facial repigmentation at Week 24, improvements in F-VASI at Weeks 52 and 104 were observed in 77.8% (49/63) and 97.1% (34/35) of patients, respectively. Among patients with limited facial repigmentation at Week 24, F-VASI improvements at Weeks 52 and 104 were observed in 64.0% (32/50) and 83.3% (30/36) of patients, respectively. Across both groups, 54.9% (39/71) of patients achieved ≥75%

improvement from baseline in F-VASI (F-VASI75) at Week 104.

Among those with no body repigmentation at Week 24, T-VASI improvements at Weeks 52 and 104 were observed in 79.6% (39/49) and 93.3% (28/30) of patients, respectively. For those with limited body repigmentation at Week 24, T-VASI improvements at Weeks 52 and 104 were observed in 64.5% (80/124) and 81.6% (62/76) of patients, respectively. Across both groups who had <25% improvement in total body repigmentation at Week 24, 50.0% (53/106) of patients achieved ≥50% improvement in T-VASI (T-VASI50) at Week 104.

#### **Conclusion:**

In the TRuE-V studies, ruxolitinib cream application for an additional 80 weeks resulted in improved repigmentation among patients with nonsegmental vitiligo who had limited or no repigmentation at Week 24. These 2-year TRuE-V results highlight the importance of prolonged treatment in patients with vitiligo, even when minimal or no repigmentation is achieved after 6 months of treatment.

# Efficacy and Safety of the combination of oral Baricitinib and NB-UVB for the Treatment of Active Vitiligo: Results from a Randomized, Double-Blind, Phase 2 Proof Of Concept Study

Julien Seneschal\*<sup>1</sup>, Guyon Mathilde<sup>1</sup>, Ribal Merhi<sup>1</sup>, Nicolas Andreu<sup>1</sup>, Sarah Cazenave<sup>1</sup>, Khaled Ezzedine<sup>2</sup>, Juliette Mazereeuw-Hautier<sup>3</sup>, Thierry Passeron<sup>4</sup>

<sup>1</sup>University of Bordeaux, Dermatology, Bordeaux, France, <sup>2</sup>University of Creteil, dermatology, Paris, France, <sup>3</sup>University of Toulouse, Dermatology, Toulouse, <sup>4</sup>University of Nice, Dermatology, Nice, France

## **Introduction & Objectives:**

Vitiligo is a chronic autoimmune disease associated with skin depigmentation. Disease activity is largely regulated by interferon-γ-induced activation of the Janus kinase (JAK) signaling pathway. The JAK1/JAK2 inhibitor oral baricitinib (BARI) could be an option to dampen skin inflammation and halt the spreading of the disease. NB-UVB is the standard treatment in vitiligo to promote repigmentation. The objective of this trial was to evaluate the efficacy and safety of oral BARI in adult patients with active vitiligo in combination with NB-UVB during a 36-wk randomized, double-blind, multicenter phase 2 study (NCT04822584).

#### **Materials & Methods:**

Patients (Pts) with active disease were randomized (3/1) to daily BARI or PLA for 36 weeks. Patients received BARI (4mg once a day) or placebo (PLA) alone for the first 12 weeks and then all patients received NB-UVB (twice a week) in combination with BARI or PLA for additional 24 weeks. Adult Patients diagnosed with active non-segmental vitiligo with depigmentation covering ≥5% total body surface area (BSA) were eligible for enrolment. The primary endpoint was the mean percent change from baseline (%CFB) of the Total-VASI (T-VASI) score at week 36. Key secondary endpoints at Week 36 included T-VASI50, T-VASI75, T-VASI90, F-VASI75, F-VASI90, the mean percent change from baseline of the F-VASI, DLQI, the SkinDex29 scores and the Vitiligo Impact Patient Scale (VIPs). Safety and tolerability were also assessed.

#### **Results:**

Forty nine pts were randomized (BARI, n=37; PLA, n=12); 7 pts (14.28%) discontinued treatment. Mean (SD) age was 49.2 (13.8) y, 71.4% were female, and 87.7% had skin phototypes II-III. Baseline mean (SD) T-VASI and F-VASI values were respectively 17.7 (10.6) and 0.7 (0.7), in the BARI group and 27.0 (25.7) and 0.7 (0.9), respectively in the PLA group. Efficacy of oral BARI in combination with NB-UVB was superior to PLA combined with NB-UVB, with statistically significant differences for the primary endpoint at wk 36 (Table1). The %CFB of the T-VASI and F-VASI scores at week 36 was -44.8% (p=0.0223) and -65.2% (p=0.0011) in the BARI group, respectively and -9.2% and +4.2% in the PLA group, respectively. Response rate differences versus (vs) PLA were 52.9% vs 9.1% for T-VASI50, 26.5% vs 0% for T-VASI75, 6.1% vs 0% for T-VASI90, 55.9% vs 9.1% for F-VASI75, 50% vs 9.1% for F-VASI90. The %CFB in the BARI group vs PLA, at week 36 for the DLQI score was -29.8% vs +25.4%, for the SkinDex29 was -14% vs +0.6%, and for VIPs was -27.4 vs -16.9%. Treatment-emergent adverse events (TEAEs) occurred in 64.9%/58.3% in the BARI and PLA groups, respectively, most were mild or moderate; 3.2% vs 7.1% in the BARI and PLA groups, respectively, had a serious AE, one patient in the BARI group developed pulmonary embolism leading to the discontinuation of the study.

#### **Conclusion:**

BARI in combination with NB-UVB demonstrated rapid and clinically meaningful superiority to PLA combined with

Table1. Efficacy Results at Week 36 (Intent-to-Treat Population)

|   | BARVIT                     |
|---|----------------------------|
|   | BARICITINIB +NB-UVB (n=37) |
| Primary endpoint                                  |                            |
| Percentage Change From Baseline (%CFB) T-VASI(SD) | -44.8*(38.8)               |
| Key secondary endpoints                           |                            |
| %CFB F-VASI(SD)                                   | -65.2**(49.3)              |
| T-VASI50, %                                       | 52.9                       |
| T-VASI75, %                                       | 26.5                       |
| T-VASI90, %                                       | 6.1                        |
| F-VASI75  | 55.9                       |
| F-VASI90  | 50                         |
| %CFB DLQI(SD)                                     | -29.8(61.3)                |
| %CFB Skindex29(SD)                                | -14(23.5)                  |
| %CFB VIPs (SD)                                    | -27.4(47.9)                |

<sup>\*</sup> *P*<0.05, \*\*P<0.01

# Efficacy and Safety of Povorcitinib for Extensive Vitiligo: 52-Week Results From a Double-Blinded, Placebo-Controlled, Dose-Ranging Phase 2b Study

Amit Pandya\*<sup>1</sup>, Khaled Ezzedine<sup>2</sup>, Thierry Passeron<sup>3</sup>, Nanja Van Geel<sup>4</sup>, Kurt Brown<sup>5</sup>, Leandro L. Santos<sup>5</sup>, Lois Erskine<sup>5</sup>, Kofi Wagya<sup>5</sup>, Andrew Blauvelt<sup>6</sup>

<sup>1</sup>UT Southwestern Medical Center: Dermatology, Dermatology, Dallas, United States, <sup>2</sup>Paris 12 Val de Marne University, Créteil, France, <sup>3</sup>Hospital Center Universitaire De Nice, Dermatology, Nice, France, <sup>4</sup>Ghent University Hospital, Gent, Belgium, <sup>5</sup>Incyte- Wilmington, DE, Wilmington, United States, <sup>6</sup>Oregon Medical Research Center, Portland, United States

## **Introduction & Objectives:**

Vitiligo is an autoimmune disease characterized by depigmentation of skin due to the progressive loss of melanocytes. The often highly visible and chronic nature of vitiligo as well as its unpredictable disease course have negative psychosocial impacts on most patients (pts), affecting quality of life. Disease pathogenesis is largely regulated by interferon- $\gamma$  activation of the Janus kinase (JAK) signaling pathway. Povorcitinib is an oral, small-molecule, selective JAK1 inhibitor with potential activity in the treatment of nonsegmental vitiligo (NSV). This phase 2b study (NCT04818346) evaluated the efficacy and safety of povorcitinib in pts with extensive NSV.

#### **Materials & Methods:**

Adults with NSV affecting  $\geq$ 0.5% facial and  $\geq$ 8% total body surface areas were eligible. Pts were randomized 1:1:1:1 to once daily povorcitinib 15/45/75 mg or placebo for 24 wks; subsequently, pts received povorcitinib 45 or 75 mg for an additional 28 wks, with a 24-wk off-treatment follow-up period. The primary endpoint was the percentage change from baseline in total Vitiligo Area Scoring Index (T-VASI) at Wk 24. Other endpoints included percentage of pts achieving  $\geq$ 50% reduction from baseline in T-VASI (T-VASI50),  $\geq$ 50%/ $\geq$ 75% reduction in facial VASI (F-VASI50/75), and safety.

### **Results:**

Of 171 randomized pts, 54.4% were female and 66.7% had Fitzpatrick skin types I-III. Median (range) age was 50 (23-74) y and disease duration was 16.4 (0.8-58.9) y. At Wk 24, the primary efficacy endpoint, T-VASI percent change from baseline with povorcitinib (15 mg, -19.1%; 45 mg, -17.8%; 75 mg, -15.7%; least square means povorcitinib vs placebo, P<0.01) was statistically superior to placebo (+2.3%). Percentages of pts with F-VASI50 at Wk 24 were higher for povorcitinib (16.3%, 34.9%, and 23.8% for 15, 45, and 75 mg, respectively) than placebo (7.0%). Improved repigmentation was seen across treatment groups at Wk 52; mean percentage changes from baseline in T-VASI for povorcitinib 15-to-75-mg, 45-mg, 75-mg, and placebo-to-75-mg subgroups were -40.7%, -42.7%, -41.3%, and -18.1%, respectively; F-VASI mean percentage changes from baseline were -63.6%, -63.8%, -64.4%, and -54.8%, respectively. T-VASI50 was achieved by 45.2%, 37.0%, 37.9%, and 15.2%; F-VASI50 by 71.0%, 77.8%, 69.0%, and 63.6%; and F-VASI75 by 48.4%, 55.6%, 58.6%, and 45.5% of pts, respectively. A total of 34 pts entered the follow-up period, with 32 completing Wk 76. T-VASI median (range) percentage changes from Wk 52 to Wk 76 were 2.1% (-61.2%, 33.9%), 4.9% (-25.4%, 33.8%), 21.0% (3.8%, 295.1%), and -0.4% (-17.9%, 24.3%), respectively; F-VASI median (range) changes were 0% (-80.0%, 33.3%), 0% (-100.0%, 200.0%), 55.6% (-86.6%, 2900.0%), and 66.7% (-20.0%, 400.0%), suggesting durability of response after discontinuation of povorcitinib. Treatment-emergent/serious adverse events (TEAEs/SAEs) were 89.2%/2.4% among pts who received povorcitinib 45 or 75 mg through 52 wks. The most common TEAEs were COVID-19 (36.1%), blood creatine phosphokinase

increased (13.3%), acne (12.0%), fatigue (10.8%), and headache (9.6%).

# **Conclusion:**

Oral povorcitinib was associated with substantial facial and total body repigmentation in pts with extensive NSV through 52 wks of treatment in this phase 2b study. Pts who were off treatment for 24 wks demonstrated durable response, maintaining their level of response achieved at Wk 52. All doses of povorcitinib were generally well tolerated.