Assessment of VITISKIN® tolerance effect againts a neutral gel combined with or without UVB TL01 treatment on subjects suffering from vitiligo

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Vitiligo is an acquired skin disease that affects between 0.5 and 2% of the population throughout the world. It is characterised by the appearance of white patches and depigmentation that spread and increase in number over time. Despite recent progress, the mechanisms of this disease have not yet been fully understood. Several hypotheses have been retained: vitiligo may be due to a specific melanocyte deficit [Nordling and Ortonne (1), Ortonne and Bose (2), Lepoole (3)], to immune system mechanisms involved in the development of depigmentation (cytotoxic T lymphocytes may be responsible for the destruction of melanocytes [Naeyaert et al. (4), Norris et al. (5)] or the disease may even be due to stress caused by oxidation of the entire epidermis and melanocytes [Schallreuter et al. (6)].

Isispharma Laboratories have developed a hydrogel called VITISKIN® that contains an SOD complex (superoxide dismutase, reductase catalase) from the Saccharomyces cerevisiae yeast – Dismutin BT. This complex has a detoxifying action with anti-radical properties (7) that can stimulate the general metabolism of the cells [Chambon et al. (8)]. This formula has been enriched with vitamin B12, with calcium pantothenate (precursor of melanin) and zinc and copper acetate.

Several trials have demonstrated the efficacy of the SOD complex:
- an in vitro trial (8) showed that the product stimulates the metabolism of fibroblasts and has anti-radical properties, neutralising superoxide ions;
- another study showed that the same SOD in concentrated form can help keratocytes in patients with Xeroderma Pigmentosum to recover a normal appearance.

Aim of the trial
The aim of the trial is to study the efficacy (compared with a neutral gel) and the tolerance of VITISKIN® gel as a complementary care treatment for vitiligo patches in subjects who are undergoing or not UVB TL01 treatment in three therapeutic strategies. This trial has received the approval of the C.C.P.P.R.B. (Consultative Committee for the Protection of Persons in Biomedical Research) and was carried out in Professor Humbert’s dermatology department at the university hospital of Besançon, France.

Inclusion criteria
Twenty-four individuals were included in 3 groups of 8. The volunteers were over 18 years of age and presented vitiligo on their body with 2 symmetrical patches (not including the face), and were considered healthy following a clinical examination; they accepted the possibility (2 chances in 3) of being treated with selective phototherapy using UVB TL01, and gave their informed consent. They are not in an exclusion period (pregnancy or breast feeding for female subjects), are not suffering from dermatitis, or a serious acute or chronic illness that might interfere with the trial; they have no history of known allergies to the products being studied or to one of the related components; they have not undergone systemic or topical treatment for vitiligo in the 4 weeks prior to the start of the trial (UV, topical immunoregulator: tacrolimus and pimecrolimus, topical corticosteroids, calcipotriol).

Assessment methods and criteria monitored
The subjects applied the product, VITISKIN®, topically on one side (twice a day on the patch and surrounding area) and applied a neutral product on the other side for 10 or 14 weeks depending on which group they were in.
Group 1 was pre-treated for 4 weeks then treated for 10 weeks in combination with UVB TL01 treatment (3 sessions a week), at an initial dose of 0.07 d/cm² increased by 0.01 d/cm² per session until they obtained a pinkish erythema and finally reaching a plateau.
Group 2 was treated for 10 weeks in combination with UVB TL01 treatment (same irradiation conditions as Group 1).
Group 3 was treated for 14 weeks without UVB TL01 irradiation (Tab. 1).
The following criteria were appraised.

**Overall efficacy**

Overall efficacy was assessed (except for D0) against a 6-point scale (worsened; unchanged; slight improvement; moderate improvement; significant improvement; disappearance of the patches).

**Progression of the vitiligo patches**

The progression of the vitiligo patches was assessed (except for D0) on a 7-point graded scale (unchanged; slight repigmentation but diffuse; slight repigmentation evenly distributed; moderate repigmentation but diffuse; moderate repigmentation but evenly distributed; almost total repigmentation but not covering entirely the affected area; total repigmentation).

**Tolerance**

Tolerance was graded on a 0 to 4 scale (0: no secondary effects; 1: slight effect; 2: moderate; 3: moderately severe; 4: severe) for the erythema, drying, flakiness, itching, burning and tingling sensations.

**Photography**

The aim of the standardised macrophotographic system is to ensure that the camera is in the same position, that the same light is produced, and that the same distance from the skin is achieved for each shot for a given area of skin. It is therefore possible to assess the condition of the skin at different points in time in the same conditions.

**Self-assessment of the cosmetic qualities**

During the last session, volunteers assess the texture, the application, the penetration time and the fragrance.

**Results**

**Overall efficacy**

An improvement in the patches was observed for group 1 at V2 and for group 2 at V3 (significant trend).

Group 2 is the only group that shows an important improvement for all subjects on the active side (at V3), **83% of whom showed moderate improvement and 17% of whom showed important improvement** (Fig. 1a, b).
Progression of the vitiligo patches

In group 1, the appearance of moderate, but uniform repigmentation was observed at visit V3 (13% of subjects) on the active substance side only (non-significant difference) and at visit V4 (13% of subjects) on the active substance and excipient side.

In group 2, a significant difference was observed at V2 (p = 0.017) between the active substance and the excipient. In addition, we would like to stress that at visit V3, 100% of the subjects had a repigmentation on the active substance side, of which 50% had homogeneous and moderate repigmentation (significant difference). The level (important but diffuse) of repigmentation is only present on the active substance side.

In group 3, no important difference was shown (V2, V3, V4 p > 0.05) (Fig. 2).

Tolerance

- Erythema (assessed at visit V4):
  - Group 1: 5 subjects had an erythema on both sides.
  - Group 2: no subject had an erythema.
  - Group 3: 3 subjects had an erythema on both sides.

- Dryness: 1 subject at V1, improvement between V2 and V3. No dryness at V4.
- Tingling: 1 subject in group 1 (slight) at V2.
- Flakiness: slight flaking for 2 subjects.

Self-assessment of the cosmetic qualities

VITISKIN® was appreciated on the whole. 86% liked the texture; the application was considered easy for 100% of the subjects and the fragrance was pleasant for 91% of the subjects. The penetration time appeared fast for 86% of subjects. The efficacy was deemed good by 32% of the subjects for the active substance.

Conclusion

VITISKIN® as a skin care treatment associated to UVB treatment improves significantly vitiligo patches in particular for therapeutic treatment where the application is combined with UVB treatment for 10 weeks.

VITISKIN® can therefore be recommended for topical application

In combination with UVB therapy during treatment of patches of vitiligo vulgaris.

BIBLIOGRAPHY