Clinical in-use study under dermatological control of a newly developed medical device: Remescar Stretch Marks

ABSTRACT

AIM: The aim of this clinical in-use study is to determine whether a newly developed product treating stretch marks (commercialized under the brand name *Remescar Stretch Marks*) provided efficacy and appropriate patient usability. This will be objectively assessed by a dermatologist based on a clinical scoring (visual and tactile) using a specific 4-point ordinal scale on the area(s) concerned with stretched marks (stomach / hips / legs), over a skin surface of about 100 cm² on D1T0, before any product application then on D29, after 28 consecutive days of use at home.

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RESULT: The clinical in-use study yielded significant decrease in the average scores of stretch marks on the experimental areas (stomach / hips / legs), after 28 consecutive days of product use.

CONCLUSION: The test product (*Remescar Stretch Marks*) induces a statistically significant decrease in the scores of stretch marks on stomach/hips/legs, has good skin acceptability and scores very high on patient usability.

Introduction

Stretch marks or striae are a form of scarring on the skin. Stretch marks are irregular areas of skin that look like bands, stripes, or lines.

Stretch marks first appear as reddish or purple lines, but tend to gradually fade to a lighter range. The affected areas appear empty and are soft to the touch. Stretch marks occur in the dermis. No stretch marks will form as long as there is support within the dermis.

Medical terminology for these kinds of markings includes striae atrophicae, vergetures, stria distensae, striae cutis distensae, striae gravidarum (in cases where it is caused by pregnancy), lineae atrophicae, linea albicante, or simply striae.

The general prevalence of stretch marks is high, up to 80% in most populations[2]. It is estimated that up to 90% of pregnant women develop stretch marks[3]. Many women experience stretch marks during their first pregnancy. Often, the lesions appear earlier than expected with one study demonstrating 43% of the women enrolled developing striae before 24 weeks of pregnancy[4]. We see a high incidence in women but also men. In addition to this, obesity is the number one health threat and leads to striae.

Pathogenesis

The cause of stretch marks remains unknown but clearly relates to changes in the structures that provide the skin with its tensile strength and elasticity. Mechanical stretching of the skin in association with hormonal factors has been implicated in the pathogenesis. It has been postulated that some hormones, like estrogen, decrease the adhesiveness between collagen fibers and increase ground substance, which results in the formation of stretch marks in areas of stretching[1].
Stretch marks are often associated with weight gain (e.g. pregnancy, obesity), rapid growth (e.g. puberty) or sickness (e.g. Cushing's disease).
The most common sites to be affected by stretch marks include the abdomen, breasts, thighs, or buttocks.
Clinical complications of those skin tears can cause itching, inflammation and/or pain. Scratching can cause the marks to break open and increase pain.

Test product

The test product is an OTC device, developed by the company Sylphar and classified as a class IIa medical device. The product is commercially available under the brand name *Remescar Stretch Marks*. Remescar Stretch Marks is a device which will treat scarred skin and therefore it falls under the umbrella brand Remescar. Remescar Stretch Marks is a cream designed for the prevention, management and treatment of stretch marks. The product will protect the skin and moderate inflammation. It will lead to an excellent integration of the cream into the skin lipid barrier, thanks to the phospholipid-induced spherical film. The formula number of the product which has been used for this study is 2827 B1.

Methods

Aim

This study intended to confirm, in a panel of healthy human subjects, the skin acceptability and the effect on the stretch marks of the investigational product and to appreciate its cosmetic qualities and efficacy, after application under the normal conditions of use.

The primary objective of the study is to investigate the effect of *Remescar Stretch Marks* on stretch marks after 28 days.
Secondary objective is the skin acceptability of the product.
The final objective is the assessment of the treatment in regards to the patient usability and product characteristics.

Study specifications

Ethics

The study was performed in the spirit of:

- the general principles of medical ethics in clinical research coming from the Declaration of Helsinki (June 1964) and its successive amendments,
- the international recommendations relating to Good Clinical Practices for conducting clinical trials for drugs ICH E6(R1) of 10/06/1996 (CPMP/ICH/135/95),
- the Directive of the European Parliament and Council 2001/20/EC concerning the harmonization of legislative, statutory and administrative provisions of the member States relating to the application of good clinical practices when conducting clinical trials for drugs for human use – OJ/EC of 01/05/2001,
- the French Code of Public Health (last edition),
- the recommendations of Colipa - August 1997: "guidelines for the assessment of human skin compatibility",

and was in accordance with the European Directive 95/46/EC on the protection of individuals with regard to the processing of personal data and on the free movement of such data and law n° 78/17 of 06/01/1978 related to data processing, files and liberty, and its successive amendments ("Commission Nationale de l'Informatique et des Libertés" - CNIL).

The main aim of the study being a better knowledge of the skin safety and efficacy of the investigational product and this product being used under normal conditions, the foreseeable risk incurred by the test subjects was minor. So, there was suitability between the aim of the study and its eventual risks and the foreseeable troubles related to the experimental conditions of the protocol. The experimental conditions adopted (application area, quantity of investigational product applied, and frequency of the applications…) reproduced the normal conditions of use advocated and the test performed on a "small scale" reflected the use by the future consumers. The observance of the experimental conditions by the test subjects was assessed by a questionnaire at the end of the study.
The test subject's opinion was taken into account since it could reflect that of the potential consumers. The skin examination and clinical scoring (stretch marks) was performed by the investigator, having the appropriate experience.

The study had to be devoid of any foreseeable serious risk for the safety of the test subjects. So, the protocol and the preclinical information concerning the investigational product (particularly referring to its safety) were submitted to the opinion of the internal committee of the investigating center. The committee got sure that the project met the conditions of optimal scientific rigor, assessed its general relevance, the suitability between the aim followed and the means implemented and gave an opinion on the protection of the test subjects.
The internal committee of the investigating center gave a previous agreement.

The information about the study was given to each test subject before the start of the study. This information was accessible, understandable and suitable for each test subject. It was orally given and then in a written specific document. This information was completed. At the beginning of the study, 2 copies of this document were dated and signed by the test subject and by the investigator or the competent person designated. One copy was given to the test subject; the other one was kept at the investigating center.

Location and date

The study was performed at the Institute of Dermo-Cosmetic (Idec), department of Evic France, located in rue Ulysse Gayon 57 33000 BORDEAUX, certified ISO 9001 equipped with material and technical means suitable for non-invasive clinical researches, compatible with the safety requirements for human subjects.

The initiation date of study performance was the 20th of March 2012 and the completion date was the 20th of April 2012.

Methodological approach

This monocentric clinical study was performed in a panel of healthy human subjects. This study was defined as a non-interventional clinical research, according to the French law 2004-806 of 09/08/2004 relating to the policy of public health. The test subject was used as own control.

The potential effect of the product on stretch marks was assessed by clinical scoring on the concerned area(s) and on the basis of the statistical analysis of the data.
The study was performed on the basis of the protocol, reference 12-0313/0, version 1 of 19.03.12. The investigational product had to be applied, under the normal conditions of use, by the test subjects at home.
The checking of the skin acceptability (local tolerance) was based on:

- a clinical examination of the skin, on the experimental area(s), performed by the same investigator, at the investigating center on:
    - D1, before the first application
    - D29.
- the analysis of the sensations of discomfort reported directly by the test subjects to the investigator during the study or in the daily log.

The qualities and efficacy were appreciated after analysis of a questionnaire adapted to the investigational product, elaborated with the study monitor and completed by each test subject, after 28 consecutive days of use of the investigational product.
The results concerning the skin acceptability were descriptively expressed.
The investigating center has at its disposal a general panel of subjects coming from all social categories. For the study, the test subjects were selected on the basis of inclusion criteria and non-inclusion criteria specific to the study and on their ability to respect the constraints required by the protocol.

The number of test subjects with exploitable data at the end of the study was 20. This empirically defined number was sufficient to achieve the study objectives.
The inclusion criteria were the following:

- suitable to participate in the study (after the clinical examination and questioning) and corresponding to the quality of "healthy subject" as defined in the corresponding procedure of the investigating center,
- declaring to have a health coverage, signing an "informed consent form" for this study,
- certifying not to take part in another clinical study,
- certifying the truth of the personal information declared to the investigator,
- capable of following directions and reliable to respect the constraints of the protocol (living not too far from the investigating center, no linguistic and intellectual barrier),
- free to ensure the visits to the investigating center, aged from 18 to 40,
- female,
- 100% of the panel having all type of skin on body,
- exhibiting recent, setting up, immature stretch marks on body, on at least one of the areas (stomach, hips, legs) with recent meaning stretch marks which have a rose, pale or purplish red lilac color by score,
- with a photo type (Fitzpatrick): I to V, users of cosmetic products similar to the investigational product,
- declaring not to have exposed themselves to a risk of pregnancy for at least 3 months before the beginning of the study and committing themselves to use effective contraceptive method throughout the study (for the women of childbearing potential).

PRIMARY OBJECTIVE

The primary objective of the study is the effect of Remescar Stretch Marks on stretch marks after 28 days assessed by an investigator:

- on the defined area(s) exhibiting stretch marks (stomach / hips / legs), over a skin surface of about 100 cm²,
- on D1T0, before any product application then on D29, after 28 consecutive days of use at home.

An assessment was done by clinical scoring using a specific 4-point ordinal scale, this is a score based on a visual and tactile appreciation of the importance of stretch marks (immature, recent progression):

- Score 0: no stretch marks
- Score 1: presence of stretch marks of slight importance:
    - few stretch marks
    - and / or thin (≤ 1 mm)
    - very pale pink
- Score 2: presence stretch marks of moderate importance:
    - numerous stretch marks
    - and / or of moderate wideness (> 1 mm and ≤ 2 mm)
    - frank pink
- Score 3: presence stretch marks of severe importance:
    - very numerous stretch marks
    - and / or of important wideness (> 2 mm)
    - red / purple / lilac

SECONDARY OBJECTIVE

The test subjects were requested to note every day any reaction observed and sensation of discomfort felt on the daily log they were given at the beginning of the study.
A skin examination was performed:

- visually, under standard "daylight" source, by the same investigator, at the investigating center,
- at the following experimental times:
    - D1
    - D29
- on: body, on the application area(s) exhibiting stretched marks (stomach / hips / legs)

Concurrently with the clinical examinations performed after use of the investigational product, the test subjects were questioned about the possible sensations of discomfort they felt.

The test subjects had to note any reaction or sensation of discomfort on the daily log, using their own words to express what they felt.
In case of reactivity, the investigator had to note:

- the visible clinical signs: Erythema, Edema, Dryness/Desquamation...
- the sensations of discomfort declared by the test subjects: Heating, Burning, Stinging, Itching, Pulling, Redness, Watering or Foreign body sensation (in case of accidental contact with the eye mucous membrane)…

The investigator had to specify for the clinical signs and the sensations of discomfort, the location, duration, period of occurrence after application of the investigational product, frequency, intensity, evolution and medical

treatment possibly undertaken then had to calculate the percentage of reactive test subjects.

The intensity of the main visible clinical signs and the sensations of discomfort had to be assessed according to ordinal scales (as defined in the procedures of the investigating center).

The test subjects had to be questioned about the effects observed when using similar products and the clinical signs observed or sensations of discomfort described after use of the investigational product had to be defined as usual or not.

The information, gathered during the questioning, was compared to that noted every day by the test subjects on their daily logs. The interpretation was performed by the investigator who took into account the possible visible reactions of irritation (clinical signs) as well as the possible sensations of discomfort described by the test subjects and will be based on his expertise and categorized as very good, good, medium or poor skin acceptability.

TERTIARY OBJECTIVE

The final objective is the patient usability and appreciation. These are assessed through a qualitative scoring system.

The test subjects had to answer a questionnaire, orally asked by the technician, at the end of the study which gathered the items concerning the cosmetic qualities and efficacy of the investigational product, defined with the study monitor.

According to the items, the test subjects, if they had an opinion, had to answer by "yes" or "no" and an ordinal scale (4 scores): 3 = agree, 2 = slightly agree, 1 = slightly disagree, 0 = disagree.

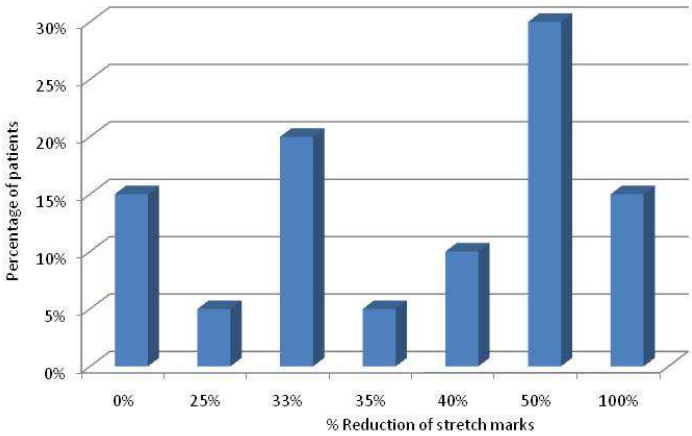
If they had no opinion, or if they were not concerned by the question, the technician had to note it in the case report form.

Results

The comparison of the scores of D29 with those of D1T0 showed a significant decrease in the average scores of stretch marks on the experimental areas (stomach/hips/legs), after 28 consecutive days of product use.

The mean score of the percentage decrease of the stretch mark is 44% based on the decrease between D1 and D29 of every subject.

The overall distribution of the percentages reduction in stretch marks in correlation with the amount of patients is given in graph 1.

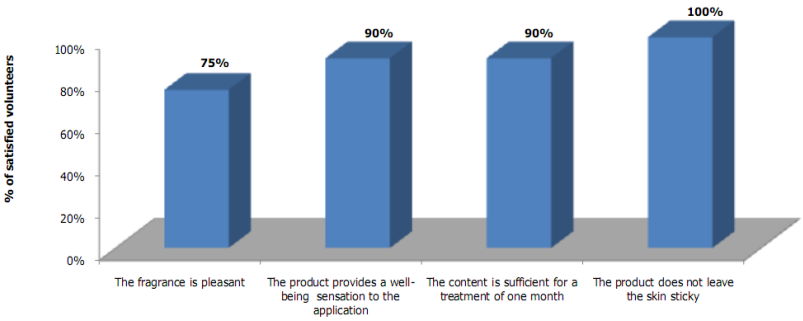


Graph1: Distribution of the percentages reduction of stretch marks

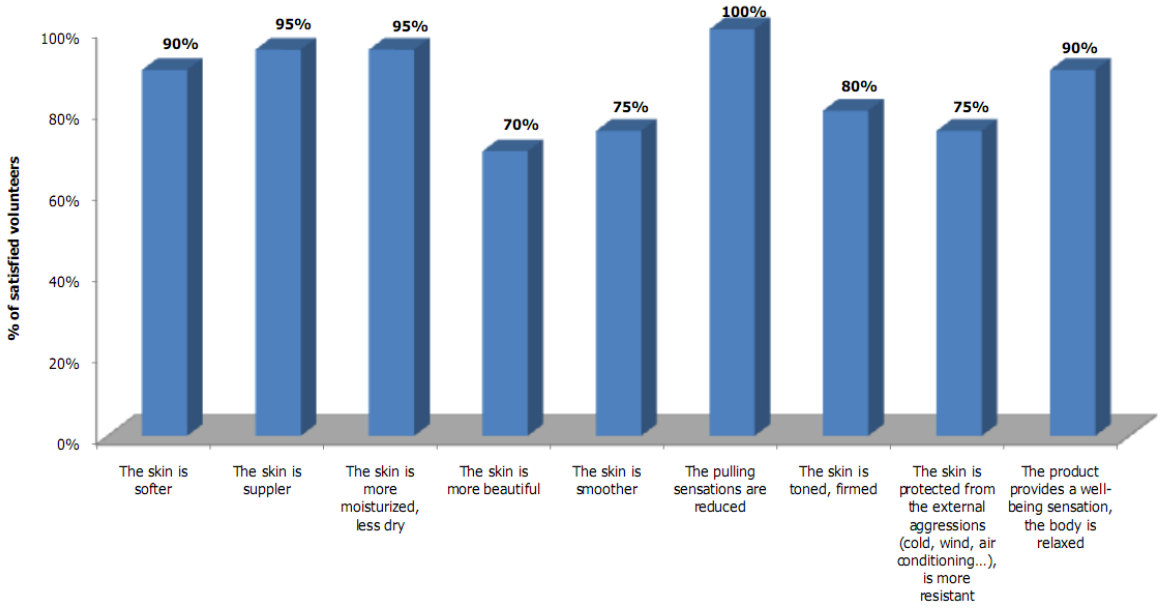
During the study the investigator detected that the mode of the study population had 50% decrease of the stretch marks. Besides that it was also observed that several patients had a decrease of 100% based on the 4-point ordinal scale.

The results on the acceptability of the product towards the skin were good. No clinical sign which could be imputable to the investigational product was observed by the investigator during the study.

Finally the acceptability and usability of the product was scored by the volunteers. 100% of the patients assessed that the product was pleasant and gave it an overall average rating of 87% on the different elements relevant to stretch marks. Graph 2 and 3 give an overview of the results on patient usability.



Graph2: Distribution of patient-usability scores



Graph3: Distribution of patient-usability scores

Conclusion

According to the experimental conditions adopted (repeated application under normal conditions of use, for 28 consecutive days, by a panel of 20 test subjects) and taking into account the grading scale established by the investigator; the test product Remescar Stretch Marks, induces a statistically significant decrease in the scores of stretch marks on stomach/hips/legs, has a good skin acceptability and scores very high on patient usability.

References

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