The use of reflectance confocal microscopy for the monitoring of Demodex density and degree of inflammation in rosacea patients using topical Ivermectin 1% (Soolantra)

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Primary Objective: To determine the monitoring and quantificational use of RCM in patients with rosacea using topical Ivermectin.Secondary Objective(s): 1. To correlate the in vivo skin changes, identified by RCM, to the clinical assessment.2. To...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Skin and subcutaneous tissue disorders NEC
Study type	Observational non invasive

Summary

ID

NL-OMON45450

Source
ToetsingOnline

Brief title
RCM in rosacea patients using Soolantra.

Condition

- Skin and subcutaneous tissue disorders NEC

Synonym
rosacea

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W,Galderma,Galderma S.A.

Intervention

Keyword: Ivermectine 1% cream (Soolantra), Reflectance confocal microscopy, Rosacea

Outcome measures

Primary outcome

1. Difference between the Demodex density before (t=0 weeks) and after (t=16

weeks) treatment.

Secondary outcome

1. Difference among the Demodex density before (t=0 weeks), during (t= 6, 12

weeks) treatment and after follow up (t=28 weeks).

2. Difference in the degree of inflammation before and after treatment.

3. The difference in vascular diameter before and after treatment.

4. The presence of parakeratosis, acanthosis and hyperkeratosis before and

after treatment.

Study description

Background summary

Rosacea is a common inflammatory skin disease with a wide spectrum of clinical features including erythema, teleangiectasia, edema, papules and pustules, hypertrophy, and/ or ocular features. Common triggers for rosacea are e.g. sun exposure, spicy food and alcohol consumption. The pathogenesis of rosacea is unknown, although it is generally considered to be related to factors such as abnormality in innate immunity, inflammatory reactions to cutaneous micro-organisms (e.g. Demodex mites), ultraviolet damage, and vascular dysfunction. Demodex folliculorum and Demodex brevis mites reside in sebaceous

follicles. Since their discovery, the pathogenicity of these mites have been under debate. Steadily increasing with age, there is up to a 100% colonization rate of Demodex mites in adults. High densities of demodex mites have been found in rosacea-affected skin, which is correlated with a generalized increase in inflammation markers. In a meta-analysis of case control studies a statistically significant association between Demodex infestation and rosacea was found.
In a multicenter, prospective study assessing the relationship between Demodex load, rosacea, and skin innate immune markers, a 6-fold increase in Demodex density in rosacea versus age-matched controls was demonstrated. Demodex mites can be found during histopathological examination of tissues from a punch biopsy from patients with rosacea. Other histopathological features of rosacea include, parakeratosis, acanthosis, hyperkeratosis, perivascular and perifollicular infiltrations, follicular spongiosis, exocytosis of inflammatory cells into the hairfollicles, vascular dilatation and solar elastosis.

Reflectance confocale microscopy (RCM) is a non-invasive technique for in vivo imaging of the skin that uses a near-infrared laser beam of 830nm. This technique produces horizontal (en face) images of the skin up to approximately 200-250 micrometers in depth with a resolution comparable to conventional histology. Currently, it is used for diagnosing melanoma skin cancer, nonmelanoma skin cancer, inflammatory skin diseases and the detection of infestation with fungi or parasites (e.g. scabies, Demodex mites). With the RCM, Demodex mites are visualized as roundish or cone-shaped structures with a bright contour, which are easily recognizable. Non-experienced RCM users can therefore easily learn how to detect Demodex mites. Other established diagnostic tests for the detection and quantification of Demodex mites include standardized superficial skin biopsy, skin scraping, direct microscopic evaluation of fresh secretions from sebaceous glands, and histopathological evaluation of tissue from a punch biopsy. All these methods lead to alteration of examined skin and can cause possible skin irritation, inflammation and bleeding. RCM, on the other hand, allows non-invasive, in vivo visualization of the upper layers of the skin at almost histological resolution without alterations of the examined site. RCM also has the advantage, over the punch biopsy, that it can monitor the same location over time. Furthermore, Erdermir et al. concluded that RCM was superior to a standardized surface skin biopsy for Demodex mite detection and quantification. In the study of Sattler et al., Harmelin et al., and Erdemir et al. the value of RCM for the detection and quantification of Demodex folliculorum in patients with rosacea was shown. Patients with rosacea had significantly higher numbers of mites in the skin compared to healthy controls.

Just recently, topical Ivermectine (Soolantra®) has been introduced in the treatment of rosacea. This cream has anti-parasitic and anti-inflammatory properties resulting in the reduction of rosacea manifestations. Van Zuuren, et al. showed in their Cochrane systematic review that topical Ivermectin was more effective than placebo and Metronidazole cream in the treatment of rosacea. The

exact mechanism of action of topical Ivermectine is unknown, but it is hypothesized that its anti-parasitic activity might play a role in the reduction of Demodex population, contributing in positive treatment effects. Because the amount of Demodex mites and some features of inflammation are not visible to the naked eye, this study aims to monitor the in vivo changes in the skin of rosacea patients using Ivermectin 1% (Soolantra®) cream with the RCM during a treatment period of 16 weeks, with a follow up of 12 weeks after ending the treatment.

Study objective

Primary Objective:
To determine the monitoring and quantificational use of RCM in patients with rosacea using topical Ivermectin.

Secondary Objective(s):
1. To correlate the in vivo skin changes, identified by RCM, to the clinical assessment.
2. To determine prognostic RCM features that correlate to a successful clinical response to topical Ivermectin in patients with rosacea.

Study design

Design: Prospective, observational, investigator-initiated, post marketing study.

Study burden and risks

Patients are able to chose which rosacea treatment they prefer and in case they chose for topical Ivermectin, they will be asked to participate in this study. If necessary, a washout-period of topical and systemic rosacea treatments will take place (in order to evaluate the treatment effect of topical Ivermectine more accurately). They will be monitored using RCM-imaging, which is non-invasive, safe and painless. More information on the pathogenesis of rosacea and the mechanism of action of topical Ivermectin can be gained in this way. The RCM-imaging and skin assessment (all non-invasive) may ask some time.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

- Healthy, male and non-pregnant female subjects, 16 years of age or older
- Clinical diagnosis of papulopustular (PPR) or erythematoteleangiectatic (ETR) rosacea
- Preference for treatment with topical Ivermectin 1% cream (within the standard care) above other rosacea treatments
- Washout period of topical and systemic treatment for rosacea
- In case of PPR subjects should have more than 15 papules or pustules and an Investigators Global Assessment (IGA) scale of > 3 (moderate)
- In case of ETR subjects should have an erythema scale of > 3 (moderate) and teleangiectasia scale of >2 (moderate)

Exclusion criteria

- Subjects with other facial dermatological condition or underlying disease, which requires the use of interfering topical or systemic therapy or may interfere with the rosacea diagnosis or its assessment
- Preference of the patient to receive another rosacea treatment.

Study design

Design

Study type: Observational non invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	19-02-2018
Enrollment:	20
Type:	Actual

Ethics review

Approved WMO

Date:	06-07-2017
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

Approved WMO

Date:	04-01-2018
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

Approved WMO

Date:	16-04-2018
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL60799.091.17