A randomized, double-blind, placebo controlled, single center study to assess the efficacy and pharmacodynamics of Gladskin eczema cream BID in patients with mild to moderate atopic dermatitis.

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Primary ObjectiveTo assess the efficacy of Gladskin Eczema Cream BID in patients with mild to moderate AD as assessed by EASI ScoreSecondary Objectives* To assess the pharmacodynamic effects of Gladskin Eczema Cream on the skin-microbiome, with...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Epidermal and dermal conditions
Study type	Interventional

Summary

ID

NL-OMON49563

Source
ToetsingOnline

Brief title
Gladskin BID in patients with mild to moderate atopic dermatitis

Condition

- Epidermal and dermal conditions

Synonym
Atopic Dermatitis / Eczema

Research involving
Human

Sponsors and support

Primary sponsor: Micreos Human Health
Source(s) of monetary or material Support: Micreos Human Health

Intervention

Keyword: Atopic dermatitis, Eczema, Gladskin

Outcome measures

Primary outcome

Tolerability / safety endpoints

Adverse events (AE) will be collected throughout the study, at every study visit.

Pharmacodynamic endpoints

Pharmacodynamic effects of Gladskin will be assessed at the time points indicated in the Visit and Assessment Schedule (Table 1) by:

- Multispectral imaging (erythema and roughness of target lesion)

- Laser speckle contrast imaging (LSCI, blood flow of target lesion)

- Microbiome of skin lesions (of target lesion and non-lesional skin)

- Bacterial colonization of skin lesions (S. aureus cultures of target lesion and non-lesional skin)

- Local (biopsy) biomarkers may comprise, but are not limited to: IL-13, IL-4, IL-5, IL-33, TSLP, IL-31, IL-22, eotaxin

- Transepidermal water loss of lesional and non-lesional skin

Efficacy endpoints

Efficacy will be assessed at the time points indicated in the Visit and

Assessment Schedule (Table 1):

- Clinical assessment using oSCORAD; EASI, IGA

- Target lesion oSCORAD and Total Signs and Symptoms (TSS)

- Patient-reported itch (daily NRS by ediary(app) and POEM)

- Dermatology Life Quality Index (DLQI)

- Standardized total body clinical photography

- Electronic diary for medical device compliance and use of escape medication

Secondary outcome

N.A.

Study description

Background summary

The pathophysiology of AD is complex and still not completely understood. Genetic susceptibility, environmental factors, epidermal barrier abnormalities, immunological disturbances and dysbiosis of the skin microbiota all play a role in the disease and the variability of these mechanisms may explain the heterogeneous character of AD. It remains hard to discern which of these mechanisms are primary events (causing AD), secondary events (resulting from AD), or both (Weidinger et al., 2018).

Staphylococcus aureus is an important player regarding dysbiosis in AD. Colonization with this pathogen and a lower general microbial diversity is apparent in approximately 70-90% of the AD patients (Totte et al., 2016). Several factors contribute to enhanced S. aureus adhesion to AD skin. After adhesion S. aureus may cause or exacerbate inflammation by binding of its superantigens (SAgs) to MHCII molecules which induces an excessive production of T cell cytokines (Spaulding et al., 2013). In addition, SAgs are also allergens and generate an IgE response (Geoghegan et al., 2018).

Based on the hypothesis that dysbiosis plays an important role in the pathogenesis of AD the microbiome and especially S. aureus might be a target for novel therapies (Geoghegan et al., 2018, Nakatsuji et al., 2017). A topical

treatment targeting the perturbed microbiome is Gladskin Eczema Cream. Gladskin is a topical cream registered as medical device class I, with Staphefekt SA.100, a recombinant chimeric endolysin, as active ingredient. Endolysins are bacteria-killing enzymes that originate from bacteriophages. Gladskin specifically targets Staphylococcus aureus, leaving the other bacteria unharmed. It is currently on the market as medical device for skin conditions with an infectious component, e.g. acne vulgaris, rosacea and atopic dermatitis. Questionnaire studies, both prospective and retrospective, indicate the potential for using Gladskin in patients with eczema. However, no randomized controlled clinical study has been performed to explore the potential of Gladskin as monotherapy in patients with mild to moderate atopic dermatitis.
The objective of this study is to assess the efficacy and pharmacodynamic effects of Gladskin after twice daily application in patients with mild to moderate atopic dermatitis.

Study objective

Primary Objective
To assess the efficacy of Gladskin Eczema Cream BID in patients with mild to moderate AD as assessed by EASI Score

Secondary Objectives
* To assess the pharmacodynamic effects of Gladskin Eczema Cream on the skin-microbiome, with emphasis on Staphylococcus aureus
* To assess the clinical and pharmacodynamic effects of Gladskin Eczema Cream as assessed by (oSCORAD, IGA, target lesion oSCORAD, TSS, 3D imaging, laser speckle contrast imaging, TEWL, itch and biopsy biomarkers)
* To assess the safety and tolerability of Gladskin Eczema Cream

Study design

A randomized, double-blind, placebo controlled, single center study.

Intervention

Gladskin eczema cream

Study burden and risks

Gladskin eczema cream is registered as medical device class I with CE marking, and over the counter available.
In vitro skin sensitisation and irritation tests showed that Gladskin eczema cream is not considered to be irritant. No prediction could be made in respect of its potential to cause eye irritation, therefore general instructions in this study will include a warning to avoid spill of cream in the eyes, when

applied to the face.

In addition to the in vitro work, the medical device currently has 5 years of marketing experience. Very few adverse events are reported by customers. The most frequently reported adverse events are redness, worsening of disease, burning sensation, itching, and swelling. During the application in clinical trial for a period of 12 weeks no substantial safety issues were reported (De Wit J. et al.). In general it can be concluded that Gladskin eczema cream is well tolerated without substantial risks for the trial subject. The short treatment period of 14 days and the visit schedule will enable to monitor closely potential adverse events.

The invasive measurements in this study consist of small, 3mm, skin punch biopsies. These will be limited to 3 skin biopsies in total.

In conclusion, we assess the risks associated with the medical device and methods as low and acceptable for the patients to participate in the study.

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

For enrollment of subjects the following criteria must be met:
1. Male and female subjects with mild to moderate AD (IGA 2 or 3) 18 to 55 years of age, inclusive. The health status is verified by absence of evidence of any clinically significant active or uncontrolled chronic disease other than AD following a detailed medical history and a complete physical examination
2. Diagnosed with AD according to the Hanifin criteria
3. EASI *4
4. Suitable target lesion defined as an eczema lesion of at least 1% BSA (preferably the antecubital fossa) with at least mild erythema and mild induration
5. *5% body surface area (BSA) affected at screening and baseline
6. Willing to not wash the target lesion 12 hours before every study visit
7. Willing to use microbiome friendly wash solution and refrain from other products for washing from screening until end-of-study
8. Able to participate and willing to give written informed consent and to comply with the study restrictions
9. Has sufficient Dutch language skills to be able to communicate well with the Investigator, understand the informed consent and complete questionnaires and e-diary.

Exclusion criteria

1. Any current and / or recurrent clinically significant skin condition other than AD
2. Ongoing use of prohibited atopic dermatitis treatments. Washout periods prior to baseline (first dose of the study medical device) are as follows:
a. Any topical medication (prescription or over-the-counter [OTC]): 14 days. Continued use of emollients during wash-out is allowed.
b. Cyclosporine/oral steroids/azathioprine/mycophenolate mofetil/other systemic AD treatments: 4 weeks
c. Phototherapy: 3 weeks
d. Biologics: 5 half-lives of the drug
e. Systemic antibiotics: 14 days
3. Tanning due to sunbathing, excessive sun exposure or a tanning booth within 3 weeks of enrolment
4. Known hypersensitivity to the compound or excipients of the compound

5. Pregnant, a positive pregnancy test, intending to become pregnant, or breastfeeding;
6. Participation in an investigational drug or device study within 3 months prior to screening or more than 4 times a year
7. Any (medical) condition that would, in the opinion of the investigator, potentially compromise the safety or compliance of the patient or may preclude the patient*s successful completion of the clinical trial.
8. Subject has a body temperature of >38°C at any visit;.

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	30-12-2019
Enrollment:	50
Type:	Actual

Medical products/devices used

Generic name:	Gladskin eczema cream
Registration:	Yes - CE intended use

Ethics review

Approved WMO

Date:	11-12-2019

Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	12-06-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

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

ID: 24034
Source: Nationaal Trial Register
Title:

In other registers

Register	ID
CCMO	NL71660.056.19
OMON	NL-OMON24034