A randomized, double-blind, placebo controlled study to assess the pharmacodynamics, safety/tolerability and efficacy of omiganan in patients with mild to moderate atopic dermatitis

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Primary objective• To explore the pharmacodynamic effects on a target lesion of topically applied omiganan in AD patientsSecondary Objectives• To assess safety and tolerability in AD patients• To evaluate the efficacy of omiganan compared to placebo...

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

Summary

ID

NL-OMON42598

Source
ToetsingOnline

Brief title
Omiganan in atopic dermatitis

Condition

- Epidermal and dermal conditions

Synonym
atopic dermatitis, eczema

Research involving
Human

Sponsors and support

Primary sponsor: Cutanea Life Sciences
Source(s) of monetary or material Support: Cutanea Life Sciences

Intervention

Keyword: antimicrobial peptide, pharmacodynamics, topical gel

Outcome measures

Primary outcome

Pharmacodynamic endpoints

Pharmacodynamic effects of CLS001 on the target lesion will be assessed at the time points indicated in the Visit and Assessment Schedule (Table 1).

- Local (biopsy) biomarkers (IgE, IFN- γ IL-1b, IL4, IL-6, IL-8, IL-9, IL-10, IL-13, IL-18, IL-31, TARC, eotaxin, oncostatin, TLR-2, TSLP, fillagrin)
- Microbiome of skin lesion
- Bacterial colonization of skin lesions (S. aureus) including biomarkers (enterotoxins)
- Transepidermal water loss of lesional and non-lesional skin

Secondary outcome

Safety and tolerability in AD patients

Adverse events (AE) will be collected throughout the study, at every study visit. Laboratory safety testing, 12-Lead ECGs and vital signs will be performed and measured multiple times during the course the study according to the Visit and Assessment Schedule. Skin tolerance and cosmetic scores by

patients will be collected on day 28.

Efficacy endpoints

Change from baseline to each time point of measurement during each treatment period for the following assessments:

• Clinical assessment of lesion on-site with local objective SCORAD and pruritus VAS

• Lesion size and morphology assessment by standardized clinical photography and 3D photography

Study description

Background summary

Atopic dermatitis (AD) is a chronic, pruritic, in*ammatory skin disease that occurs frequently in children, but also affects many adults. Clinical features of AD include skin dryness, erythema, oozing, crusting and lichenification. Pruritus is a major criterion for the diagnosis of AD and is the main driver of the high disease burden for patients and their families.
Two major models currently exist to explain the pathogenesis of AD. The predominant model describes AD as a result of impaired epidermal barrier function due to intrinsic structural and functional abnormalities in the skin. In this model, the disease evolves from the outside in, with an abnormal epidermal barrier as the primary defect. The second and more traditional model views AD primarily as an immune function disorder in which Langerhans cells, T-cells, and immune effector cells modulate an inflammatory response to environmental factors.
Colonization of S. aureus is found in 90% of chronic AD patients versus 5% in healthy individuals. Biofilm formation by AD-associated staphylococci almost certainly plays a major role in the occlusion of sweat ducts. This leads to inflammation and pruritus and may therefore play a role in exacerbation.
Endogenous antimicrobial peptides are critical elements of the skin*s innate immunity. In healthy skin, these peptides such as cathelicidins are induced upon colonization with certain bacteria or other external stimuli. However, in

atopic skin the upregulation of cathelicidins is abrogated by the presence of Th2 cytokines. This results in lower levels of antimicrobial peptides, which could be a possible mechanism for staphylococcal colonization and superinfection.

LL-37 and indolicidin are antimicrobial peptides that are members of the cathelicidin family. Omiganan is a synthetic indolicidin analogue with antimicrobial and immunomodulatory activity. Recently it has been demonstrated that enhanced LL-37 expression improves barrier function in the skin. It disrupts the cytoplasmic wall of microorganisms, resulting in depolarization and cell death. Omiganan has shown to be effective against a wide variety of bacteria and fungi, including S. aureus. Immunomodulatory effects of omiganan were observed in a mouse model with TPA-induced ear edema. To date, omiganan was assessed in various clinical studies including patients with acne or rosacea where anti-inflammatory activity of this compound was demonstrated. Due to its antimicrobial properties, the skin barrier enhancing properties of LL-37 and the immunomodulatory activity, we hypothesize that omiganan is a potential new treatment for AD.
This study is intended to investigate the pharmacodynamics of omiganan as a potential treatment for AD. Furthermore, exploratory efficacy by means of clinical outcomes (i.e. improvement in itch VAS and clearance of the lesion) and biomarkers will be assessed.

Study objective

Primary objective
• To explore the pharmacodynamic effects on a target lesion of topically applied omiganan in AD patients

Secondary Objectives
• To assess safety and tolerability in AD patients
• To evaluate the efficacy of omiganan compared to placebo in AD patients

Study design

A randomized, double-blind, vehicle controlled study to assess the pharmacodynamics, safety/tolerability, and efficacy of omiganan in patients with mild to moderate AD.

Intervention

The study will consist of one treatment arm with 2.5% omiganan*5HCL gel, one treatment arm with 1% omiganan*5HCL gel and one treatment arm with the vehicle gel.

Subjects will administer a gel for four (4) weeks once daily on one antecubital

fossa ((the target lesion and treatment period). During treatment period and two weeks prior to first administration of the gel (run-in period), subjects administer emollients BID on the remaining affected skin and if necessary triamcinolone (TCA) topical 0.1% QD. During the run-in period the target lesion will be left untreated.

Study burden and risks

The risks associated with the topical administration of CLS001 to humans has been identified in over 2500 subjects in total in fourteen clinical trials completed with topical applications of omiganan in formulations ranging from 0.5% to 3% in an aqueous gel and from 1% to 5% in an alcoholic solution for the indications of various indications including treatment of the inflammatory lesions of rosacea, treatment of acne and treatment of S. aureus in the nasal carriage. Omiganan when applied topically to intact or abraded skin, intranasally or at peripheral and central venous catheter sites appears to be safe and well tolerated. In addition, omiganan was not detected in the plasma of subjects after topical application to intact or abraded skin, to the nasal mucosa or at peripheral catheter sites. The risk of topical application to a very restricted lesional area can be considered minimal. Potential beneficial effects on atopic dermatitis lesions are to be explored in this study.

Therefore, providing the protocol is adhered to, careful observation and medical management will minimize any associated risk in this 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

1. Male and female subjects with mild to moderate AD 18 to 65 years of age, inclusive. The health status is verified by absence of evidence of any clinical significant active or uncontrolled chronic disease other than AD following a detailed medical history, a complete physical examination including vital signs, 12-lead ECG, haematology, blood chemistry, and urinalysis.
2. AD diagnosed by the physician / medical specialist and that has been present for at least 1 year.
3. At least one of the antecubital fossae must have an affected body surface area (BSA) of 0.5% with active dermatitis characterized by erythema and squamae at screening and end of the run-in period
4. Pruritus VAS score of target lesion of >=30 at screening and end of the run-in period
5. oSCORAD-score of total body <= 40.
6. 2-15% body surface area (BSA) involved with AD lesions at screening.
7. Able to participate and willing to give written informed consent and to comply with the study restrictions.

Exclusion criteria

1. Have any current and / or recurrent clinically significant skin condition in the treatment area other than AD.;2. Use of topical medication (prescription or over-the-counter [OTC]) within 14 days of study drug administration, or less than 5 half-lives (whichever is longer) in local treatment area.;3. Tanning due to sunbathing, excessive sun exposure, or a tanning booth within 3 weeks of enrollment.;4. Any confirmed, active significant allergic reactions (urticaria or anaphylaxis) including allergic reactions against any drug, multiple drug allergies or (ingredients of) emollients.;5. Participation in an investigational drug or device study within 3 months prior to screening or more than 4 times a year.;6. Loss or donation of blood over 500 mL within three months (males) or four months (females) prior to screening.;7. Unwillingness or inability to comply with the study protocol for any other reason.;Other qualifying criteria:
1. Subjects and their partners of childbearing potential must use two methods of contraception, one of which must be a barrier method for the duration of the study and for 3

months after the last dose (section 4.4.1).
2. Subjects must not have received treatments for AD within the intervals for the following medications:
a. Cyclosporine/oral steroids/azathioprine/mycophenolate mofetil/other systemic immunosuppressants: 4 weeks
b. Phototherapy: 3 weeks
c. Topical calcineurin-inhibitors: 10 days

Study design

Design

Study phase:	2
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):	19-05-2015
Enrollment:	36
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Omiganan Topical Gel
Generic name:	omiganan

Ethics review

Approved WMO

Date:	02-04-2015
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	16-04-2015
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	30-06-2015
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

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2014-003689-26-NL
CCMO	NL52919.056.15