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

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Primary Objective- To assess efficacy and pharmacodynamic effects of topical omiganan BID
Secondary Objectives- To assess safety and tolerability of topical omiganan BID

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

Summary

ID

NL-OMON42963

Source
ToetsingOnline

Brief title
Pharmacodynamics of omiganan BID in patients with atopic dermatitis

Condition

- Skin and subcutaneous tissue disorders NEC

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, eczema, pharmacodynamics, topical gel

Outcome measures

Primary outcome

Pharmacodynamic endpoints

Pharmacodynamic effects of Omiganan will be assessed at the time points

indicated in the Visit and Assessment Schedule (Table 1) by:

- Local (biopsy) biomarkers (IFN-alpha, IFN-gamma, IL 6, IL13, IL31, eotaxin3)

- Microbiome of skin lesions (in comparison to non-lesional skin)

- Bacterial colonization of skin lesions (S. aureus)

- Transepidermal water loss of lesional and non-lesional skin

- Transdermal analysis patch (TAP) biomarkers: IFN-gamma, IL-6, IL-10, IL-13,

IL-31, eotaxin3.

- Circulating cytokines (TARC, IFN-alpha, IFN-gamma, IL 6, IL13, IL31, eotaxin3)

- Thermography

Efficacy endpoints

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

Assessment Schedule (Table 1) by:

- Clinical assessment using SCORAD; EASI and IGA

- Patient-reported itch (daily NRS and weekly POEM)

- General clinical assessment

- Standardized total body clinical photography

- Diary for drug compliance and use of escape medication

- Partial / complete clearance of AD lesions

Secondary outcome

Tolerability / safety endpoints

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.

Pharmacokinetic endpoints

Following PK samples will be analyzed:

- Day 28; Pre-dose, 10, 20, 30, 60, 120 and 180 minutes

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 and crusting, and lichenification. Pruritus is a hallmark of the condition 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 traditional model views AD as primarily 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 and leads to inflammation, pruritus and may therefor 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 or other external stimuli. However, in atopic skin cathelicidins upregulation is abrogated by the presence of Th2 cytokines. This results in lower levels of antimicrobial peptides, which could be a possible mechanism of staphylococcal superinfection.

LL-37 and indolicidin are antimicrobial peptides that are members of the cathelicidin family. Omiganan is a synthetic indolicidin analogue with antimicrobial and immuno-modulatory activity. Recently it has been demonstrated that enhanced LL-37 expression improves barrier function of the skin. Regarding the mechanism of action, omiganan disrupts the cytoplasmic wall of microorganisms, resulting in depolarization and cell death. Omiganan was 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 varying anti-inflammatory activity of this compound could be demonstrated.

A previous study investigated the administration of 2.5% omiganan QD in patients with mild to moderate atopic dermatitis on one target lesion. The results of this trial showed statistical significant improvement of patient reported morning itch and the local objective SCORAD compared to placebo. Since the outcomes suggest dose dependency to a certain degree, we hypothesize that administration of omiganan twice daily will lead to a more effective treatment of mild to moderate AD.

This study is intended to assess the clinical efficacy and pharmacodynamics of omiganan as a potential treatment for AD. Clinical efficacy by means of clinical outcomes (i.e. clearance of the lesions, oSCORAD, EASI) and sub-clinical parameters / biomarkers on the skin and systemic ones will be assessed.

Study objective

Primary Objective
- To assess efficacy and pharmacodynamic effects of topical omiganan BID
Secondary Objectives
- To assess safety and tolerability of topical omiganan BID

Study design

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

Intervention

Volunteers with AD will apply gel on all AD lesions bidaily for a period of 4 weeks. Based on randomization this gel is placebo (only vehicle), contains 1%, 1.75% or 2.5% Omiganan*5HCL.

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, hematology, blood chemistry, virology and urinalysis;
2. AD diagnosis confirmed;
3. Symptoms present for at least 1 year;
4. EASI between 7.1 - 50.0, inclusive at screening;
5. 2-20% body surface area (BSA) affected at screening;
6. Body mass index (BMI) between 18 and 35 kg/m2, inclusive, and with a minimum weight of 50 kg;
7. Able to participate and willing to give written informed consent and to comply with the study restrictions;
8. Subjects and their partners of childbearing potential must use effective contraception, for the duration of the study and for 3 months after the last dose.

Exclusion criteria

1. Any current and / or recurrent clinical significant skin condition other than AD;
2. Pregnant, a positive pregnancy test, intending to become pregnant, or breastfeeding;
3. Ongoing use of prohibited atopic dermatitis treatments. Washout periods prior to baseline (first dose of the study drug) are as follows:
a. Cyclosporine/oral steroids/azathioprine/mycophenolate mofetil/other systemic immunosuppressants: 4 weeks
b. Phototherapy: 3 weeks
c. Biologics: 5 half-lives of the drug
d. Topical calcineurin-inhibitors: 10 days;

4. 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;
5. Tanning due to sunbathing, excessive sun exposure or a tanning booth within 3 weeks of enrollment;
6. Known hypersensitivity to the compound or excipients of the compound or known hypersensitivity to one or more different emollients;
7. Participation in an investigational drug or device study within 3 months prior to screening or more than 4 times a year;
8. Loss or donation of blood over 500 mL within three months (males) or four months (females) prior to screening;

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):	02-02-2017
Enrollment:	80
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Omiganan topical gel
Generic name:	Omiganan

Ethics review

Approved WMO Date:	01-12-2016
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	15-12-2016
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	19-09-2017
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	EUCTR2016-003849-28-NL
CCMO	NL59314.056.16