XZ.700 in patients with mild to moderate atopic dermatitis

No registrations found.

Ethical review	Positive opinion
Status	Pending
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON21515

Source
NTR

Brief title
CHDR1942

Health condition

Atopic Dermatitis / Eczema

Sponsors and support

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

Intervention

Outcome measures

Primary outcome

Tolerability / safety endpoints
• Adverse events (AE)
• Laboratory safety testing (blood and urine)
• 12-Lead ECGs
• Vital signs

• Physical examination
• Skin irritation by local irritation grading scale (Part A only)

Adherence
• Electronic diary with photo capture function to monitor treatment compliance

Secondary outcome

Pharmacodynamic endpoints
Pharmacodynamic effects of XZ.700 will be assessed at the time points indicated in the Visit and Assessment Schedule (Table 1 & 2) by:
• Multispectral imaging (erythema and roughness of target lesion)
• Laser speckle contrast imaging (LSCI, blood flow of target lesion)
• 2D photo documentation of the 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
• Blood-based biomarkers

Efficacy endpoints
Efficacy of XZ.700 will be assessed at the time points indicated in the Visit and Assessment Schedule (Table 1 & 2):
• SCORAD; EASI, IGA, lesion count, lesion clearance
• Target lesion oSCORAD, TSS and surface area (BSA in cm2)
• Patient-reported itch (twice daily NRS by e-diary / mobile app and POEM)
• DLQI

Study description

Background summary

The pathophysiology of atopic dermatitis (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 (S. aureus) is an important player regarding dysbiosis in AD. Colonization with this pathogen combined with 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), next to being conventional allergens that can generate an IgE response. In addition, S. aureus produces alpha toxin, which causes lysis of keratinocytes and aureolysin which inactivates antimicrobial peptides (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 novel topical treatment targeting the perturbed microbiome is XZ.700. XZ.700 is a recombinant chimeric endolysin that specifically targets S. aureus. Endolysins are phage derived enzymes that are produced at the end of the reproduction cycle of bacteriophages in the bacteria to lyse the
peptidoglycan cell wall and to allow the newly assembled phages to leave the host-cell. XZ.700 is produced via recombinant technology. It is highly specific against the S. aureus species (both MSSA and MRSA) and unlikely to induce bacterial resistance, allowing it to be used for the long-term treatment of chronic skin diseases such as AD.
This first-in-human study is intended to evaluate the safety and tolerability of XZ.700 as well as exploring the pharmacodynamics effects in patients with mild to moderate AD. Clinical efficacy will be investigated by means of clinical outcomes (i.e. clearance of the target lesion, target lesion oSCORAD, target lesion TSS) and local biomarkers will be assessed.

Study objective

Primary Objective
To evaluate the safety and tolerability of topical XZ.700 in patients with mild to moderate atopic dermatitis

Secondary Objectives
To investigate the PD effects of XZ.700 in patients with mild to moderate atopic dermatitis
To evaluate the efficacy of three dose levels of topical XZ.700 in patients with mild to moderate atopic dermatitis

Study design

Day -28 till EOS

Intervention

XZ.700 or placebo

Contacts

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Eligibility criteria

Inclusion criteria

1. Male and female subjects with mild to moderate AD (IGA 2 or 3) 18 to 65 years (during covid-19 restriction period subjects will be included from 18 to 54 years of age inclusive) of age, inclusive. The health status is verified by absence of evidence of any clinically significant active or uncontrolled chronic disease other than AD that potentially may influence the adherence to the study and/or assessments in the study, following a detailed medical history and a complete physical examination including vital signs, 12-lead ECG, hematology, blood chemistry, virology and urinalysis;
2. Diagnosed with AD according to the Hanifin criteria (Hanifin 1980);
3. Suitable target lesion (preferably the antecubital fossa) defined as an eczema lesion of 1%≤BSA≤5% (excluding the face and hands) with at least mild erythema and mild induration at screening and baseline day 1;
4. Target lesion is cultured positive for S. aureus on two consecutive occasions during the screening period;
5. Extent of lesional, atopic dermatits affected skin for Part A: 1%≤ BSA≤5%; for Part B: 1%≤BSA≤10%; at screening and baseline (day 1);
6. Willing to refrain from washing the target lesion 12 hours before every study visit that includes microbiology samples;
7. Willing to use microbiome friendly wash solution as provided by sponsor and refrain from other products for washing from screening until end-of-study;
8. Willing to refrain from all topical products for lesional skin during the treatment period;
9. 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;
10. Able to Participate and willing to give written informed consent and to comply with the study restrictions;
11. Has the ability to communicate well with the Investigator in the Dutch language.

Exclusion criteria

1. Any current and / or recurrent clinically significant skin condition which will interfere with

the clinical findings of the study as assessed by the investigator;
2. Ongoing use of prohibited atopic dermatitis treatments. Washout periods prior to baseline (first dose of the study drug) are as follows:
- All atopic dermatitis lesions: any topical medication (prescription or over-the-counter [OTC]): 14 days. For emollients target lesion only: 7 days. On other atopic dermatitis lesions use of emollients is allowed, however must
be discontinued prior to Day 1.
- Cyclosporine/oral steroids/azathioprine/mycophenolate mofetil/other systemic AD drugs: 4 weeks
- Phototherapy: 3 weeks
- Biologics: 5 half-lives of the drug
- Systemic antibiotics: 14 days
3. Tanning due to sunbathing, excessive sun exposure or a tanning booth within 3 weeks of enrolment and/or not willing to refrain from these during the study;
4. Known hypersensitivity to the investigational compound or its excipients;
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. Loss or donation of blood over 500 mL within three months (males) or four months (females) prior to screening;
8. A positive drug and/or alcohol test at screening (rescreening is allowed).
9. Subject has a body temperature of >38.0 °C at any visit, only during SARS-CoV-2 measures;
10. Only during SARS-CoV-2 measures: Subject has a BMI of >30 kg/m2

Study design

Design

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

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-09-2020
Enrollment:	48

Type: Anticipated

IPD sharing statement

Plan to share IPD: No

Plan description
N.A.

Ethics review

Positive opinion
Date: 03-09-2020

Application type: First submission

Study registrations

Followed up by the following (possibly more current) registration

ID: 54877
Bron: ToetsingOnline
Titel:

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

No registrations found.

In other registers

Register	ID
NTR-new	NL8876
CCMO	NL74232.056.20
OMON	NL-OMON54877

Study results

Summary results
N.A.