

XZ.700 in patients with mild to moderate atopic dermatitis

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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...

Ethische beoordeling	Positief advies
Status	Werving nog niet gestart
Type aandoening	-
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON21515

Bron

NTR

Verkorte titel

CHDR1942

Aandoening

Atopic Dermatitis / Eczema

Ondersteuning

Primaire sponsor: Microcos Human Health

Overige ondersteuning: Sponsor

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

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

Toelichting onderzoek

Achtergrond van het onderzoek

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.

Doel van het onderzoek

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

Onderzoeksopzet

Day -28 till EOS

Onderzoeksproduct en/of interventie

XZ.700 or placebo

Contactpersonen

Publiek

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

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 $1\% \leq \text{BSA} \leq 5\%$ (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 dermatitis affected skin for Part A: $1\% \leq \text{BSA} \leq 5\%$; for Part B: $1\% \leq \text{BSA} \leq 10\%$; 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.

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

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 $>38.0^{\circ}\text{C}$ at any visit, only during SARS-CoV-2 measures;
10. Only during SARS-CoV-2 measures: Subject has a BMI of $>30\text{ kg/m}^2$

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Parallel
Toewijzing:	Gerandomiseerd
Blinding:	Dubbelblind
Controle:	Placebo

Deelname

Nederland	
Status:	Werving nog niet gestart
(Verwachte) startdatum:	01-09-2020
Aantal proefpersonen:	48
Type:	Verwachte startdatum

Voornemen beschikbaar stellen Individuele Patiënten Data (IPD)

Wordt de data na het onderzoek gedeeld: Nee

Toelichting

N.A.

Ethische beoordeling

Positief advies

Datum: 03-09-2020

Soort:

Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

ID: 54877

Bron: ToetsingOnline

Titel:

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

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

Resultaten

Samenvatting resultaten

N.A.