A randomized, evaluator-blinded, vehicle-controlled study to explore the pharmacodynamic effects of omiganan and omiganan in combination with imiquimod in healthy volunteers.

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Primary ObjectiveTo explore the pharmacodynamics effects of topically applied OMN ono Tape-stripped skin of healthy volunteerso Tape-stripped and IMQ-primed skin of healthy volunteerso Tape-stripped skin prior to IMQ applicationSecondary Objectives...

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

Summary

ID

NL-OMON45716

Source
ToetsingOnline

Brief title
Topical challenge with omiganan and imiquimod in healthy volunteers

Condition

- Skin and subcutaneous tissue disorders NEC

Synonym
dermatological challenge model, skin inflammation model

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Imiquimod, Omiganan, Pharmacodynamics, Topical challenge

Outcome measures

Primary outcome

Pharmacodynamic effects of this study will be assessed at the time points

indicated in the Visit and Assessment Schedule (Table 3) by:

- Local (biopsy) biomarkers ((including but not limited to IL-8, IFN-*, IFN-*,

IFN-*, MXA, MX1, IL-6, IL-10, CCL20 and HBD-2)

- Histology (HE)

- Immunohistochemistry (CD1a, HLADR, CD8+, CD4+, CD14+, CD11c)

- Transdermal Analysis Patch (IL-8, IFN-*, IL-6, IL-10, CCL20 and HBD-2)

- Perfusion by Laser speckle contrast imaging (LSCI)

- Colorimetric

- Clinical evaluation (erythema grading scale)

- Photography (total body imaging); erythema index

- Thermography

- Skin microbiome

Secondary outcome

Tolerability / safety endpoints

- Vital signs

- 12-leads ECGs

- Local tolerance (Visual Analogue Scale (NRS) pruritus and pain)

- Circulating cytokines (IFN-*, IFN-*)

Study description

Background summary

Omiganan (OMN) is a novel, synthetic, cationic peptide. OMN appears to have in vitro activity against a wide variety of microorganisms such as gram-positive and gram-negative bacteria and fungi [1]. Recent evidence and in vitro models suggest that OMN also has pleiotropic effects regarding immune modulation. Cationic peptides are believed to support antiviral immune responses via enhancement of toll-like receptors (TLR) including TLR3, TLR7 and TLR9, and RIG-1/Mda5 signalling. The activation of TLRs and RIG-1/Mda5 induces interferon responses. Additionally, in vitro models indicate a strong induction of interferon responses enhanced by TLR3, RIG-1/Mda5 stimulation. This interferon response is strongly activated in the presence of a TLR 7 trigger, which also suggests to investigate the combined application of OMN with a TLR 7 agonist in humans. On the other hand, omiganan may exert immunosuppressive effects, as evidenced by an omiganan-dependent inhibition of the release of certain pro-inflammatory cytokines following in vitro innate immune challenges of primary human immune cells.
The mechanism of action of imiquimod (IMQ) is based on the specific binding to TLR-7 and TLR-8, thereby activating central transcription factors which induce the secretion of pro-inflammatory cytokines including interferons, interleukins and tumor necrosis factor alpha (TNF- a) which leads to inflammation and immune activation.
In a recent study (CHDR1430 Part A), a challenge model to temporarily induce local skin inflammation with IMQ (Aldara® cream) in healthy volunteers was developed. The top-line results of this study showed mild to moderate reversible skin inflammation in terms of erythema, perfusion and biopsy biomarkers when 5mg IMQ was applied once daily under occlusion to tape stripped skin for 2 days.
This healthy volunteer study has been designed based on the observed OMN effects in in vitro studies in primary human immune cells (CHDR1426, CHDR14522), and the observed IMQ effects on human skin in a recent clinical (CHDR1430A). The study objectives are (1) to investigate the immunomodulatory effects of topically applied OMN in furthermore untreated skin, (2) to investigate immuno-suppressive effects of OMN on IMQ-induced inflammatory responses of the skin, and (3) to study whether OMN enhances antiviral effects

in the skin induced by IMQ. Moreover, safety and tolerability will be assessed.

Study objective

Primary Objective

To explore the pharmacodynamics effects of topically applied OMN on
o Tape-stripped skin of healthy volunteers
o Tape-stripped and IMQ-primed skin of healthy volunteers
o Tape-stripped skin prior to IMQ application

Secondary Objectives
* To assess safety and tolerability of topically applied OMN in combination with IMQ

Study design

Randomized, evaluator-blinded, vehicle-controlled, dose- ranging study.

Study burden and risks

OMN: The nonclinical studies conducted to date on omiganan indicate that there were no unexpected adverse events following topical administration to rats. The risks associated with the topical administration of omiganan to humans have been identified in over 2500 subjects for the indications of various indications including treatment of the inflammatory lesions of rosacea, treatment of acne, treatment of atopic dermatitis 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.

IMQ: The risks associated with the topical application of IMQ have been identified in healthy volunteers as well as patients with various indications for treatment, such as BCC, AK and genital warts. Treatment appears to be safe, reversible and reasonably tolerated, with local skin reactions including erythema, oedema, vesicles, erosions/ulcerations, weeping/exudate, flaking/scaling/dryness and scabbing/crusting as main side effect. Since psoriasis exacerbations due to IMQ treatment have been described, psoriasis patients as well as patients with other auto-immune diseases and skin diseases are excluded to participate in this study to minimize potential risk(s).

Previous in vitro experiments with the application of IMQ to OMN primed human PBMCs led to an increase in antiviral biomarkers (IFN*, IFN*, IFN*). No human

data is available yet. Although systemic exposure is not expected with this limited treatment area, circulating IFN*, IFN* and IFN* will be measured at multiple time points. A dense visiting schedule will be used to monitor adverse events closely.

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. Healthy male and female subjects, 18 to 45 years of age, inclusive. Healthy status is defined by absence of evidence of any active or chronic disease following a detailed medical and surgical history, a complete physical examination including vital signs, 12-lead ECG, haematology, blood chemistry, and urinalysis.
2. Body mass index (BMI) between 18 and 30 kg/m2, inclusive, and with a minimum weight of 50 kg.

3. Fitzpatrick skin type I-III (Caucasian).
4. 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.
5. Able to participate and willing to give written informed consent and to comply with the study restrictions.

Exclusion criteria

1. Any disease associated with immune system impairment, including auto-immune diseases, HIV and transplantation patients
2. Family history of psoriasis
3. History of pathological scar formation (keloid, hypertrophic scar)
4. Have any current and / or recurrent pathologically, clinical significant relevant skin condition.
5. Previous use of imiquimod/ resiquimod/ gardiquimod
6. Known hypersensitivity to the (non)investigational drug, comparative drug, drugs of the same class, or any of their excipients.
7. Hypersensitivity for dermatological marker at screening
8. Requirement of immunosuppressive or immunomodulatory medication within 30 days prior to enrollment or planned to use during the course of the study.
9. Use of topical medication (prescription or over-the-counter [OTC]) within 30 days of study drug administration, or less than 5 half-lives (whichever is longer) in local treatment area
10. Tanning due to sunbathing, excessive sun exposure or a tanning booth within 3 weeks of enrollment.
11. Participation in an investigational drug or device study within 3 months prior to screening or more than 4 times a year.
12. Loss or donation of blood over 500 mL within three months prior to screening
13. Pregnant, a positive pregnancy test, intending to become pregnant, or breastfeeding

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	20-01-2017
Enrollment:	16
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Aldara 5% cream
Generic name:	imiquimod
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Omuiganan topical gel
Generic name:	Omiganan

Ethics review

Approved WMO Date:	21-12-2016
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	09-01-2017
Application type:	First submission
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	EUCTR2016-004702-34-NL
CCMO	NL60037.056.16