Anti-inflammatory drugs in TLR7 topical challenge model

No registrations found.

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

Summary

ID

NL-OMON28349

Source
NTR

Brief title
CHDR1912

Health condition

Dermatological challenge model, skin inflammation model

Sponsors and support

Primary sponsor: CHDR
Source(s) of monetary or material Support: CHDR

Intervention

Outcome measures

Primary outcome

Tolerability / safety endpoints
• Adverse events (AEs)
• Vital signs
• 12-leads ECGs

• Local tolerance (erythema grading scale, numeric rating scale (NRS) pruritus and pain)

Pharmacodynamic endpoints
Non-invasive measures:
• Perfusion by Laser speckle contrast imaging (LSCI)
• Erythema by Antera 3D camera
• Erythema by clinical evaluation (erythema grading scale)
• Optical Coherence Topography (OCT)
• 2D photography by ATBM for photo documentation only

Invasive measures:
• Suction blister exudates, including but not limited to
o Cytokines and chemokines
o Flow cytometry (neutrophils, monocytes/macrophages, CD4+ lymphocytes, CD8+ lymphocytes, CD56+ lymphocytes, CDlc dendritic cells)
• Skin punch biopsies
o Local biomarkers, including but not limited to: IL-8, IFN-α, IL-1β, IFN-ɣ, MXA, MX1, IL-6, IL-10, CCL20 and HBD-2
o Immunohistochemistry:CD1a, HLADR, CD8+, CD4+, CD14+, CD11c
o Histology (HE)

Secondary outcome

N.A.

Study description

Background summary

Inflammation is a response to damaged tissue and/or pathogens resulting in a release of cytokines and subsequent cellular activation. Although inflammation is in principle a healthy process, in some cases an excessive and/or poorly regulated inflammatory response can be harmful to the host, which is the case in many inflammatory disorders.
Toll-like receptors belong to the family of pattern recognition receptors (PRRs). These highly conserved receptors recognize pathogen-associated molecular patterns (PAMPs) and danger associated molecular patterns (DAMPs). Upon recognition PRRs induce the activation of a strong inflammatory response and thereby kick starting the innate immune response. Toll-like receptor 7 (TLR7) is an intracellular, endosomal TLR and is able to recognize single stranded (ss)RNA from viruses and the class of
imidazoquinolone drugs such as imiquimod (IMQ). The agonistic activity of IMQ on the TLR7 receptor causes activation of the central transcription factor, nuclear factor-kB and inducing secretion of pro inflammatory cytokines such as tumor necrosis factor alpha (TNF-α), interferon gamma (IFN-ɣ), IFN-α, interleukin(IL)-6, IL-1a, IL-1b, IL-8, IL-12, IL-17, IL-22, IL-23 granulocyte macrophage colony-stimulating factor, and granulocyte colony-stimulating factor

(innate immunity). All cytokine elevations and
local effects have been reported to be reversible. Imiquimod has shown to exhibit tumoricidal and anti-viral effects both in vitro and in vivo (Hanna et al, 2016). Aldara (imiquimod 5%) cream is an immune response modifier for topical administration and is currently on the market for (pre)malignant and HPV-induced skin lesions (see SPC Aldara). The safety and efficacy of imiquimod in immunosuppressed patients have not been established.

Study objective

Primary Objectives
• To assess the pharmacodynamic effects of prednisolone on the IMQ-induced inflammatory response
• To assess safety & tolerability of topical IMQ in combination with prednisolone

Secondary Objectives
• To explore pharmacodynamic biomarkers determined in blister exudate compared to skin punch biopsies in IMQ-induced inflammation

Study design

Baseline till EOS

Intervention

Imiquimod and Prednisolone

Contacts

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Eligibility criteria

Inclusion criteria

1. Healthy male or 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, hematology, blood chemistry, blood serology and urinalysis. In the case of uncertain or questionable results, tests performed during screening may be repeated before randomization to confirm eligibility or judged to be clinically irrelevant for healthy subjects;
2. Body mass index (BMI) between 18 and 30 kg/m2 and a maximum weight of 100 kg, inclusive;
3. Fitzpatrick skin type I-II (Caucasian);
4. Subjects and their partners of childbearing potential must use effective contraception for the duration of the study;
5. Able and willing to give written informed consent and to comply with the study restrictions.

Exclusion criteria

1. Any vaccination within the last 3 months;
2. Family history of psoriasis;
3. History of pathological scar formation (keloid, hypertrophic scar);
4. Have any current and / or recurrent pathologically, clinical significant skin condition at the treatment area (i.e. atopic dermatitis);
5. Previous use of Aldara (IMQ cream) 3 weeks prior to the baseline visit
6. Known hypersensitivity to the (non)investigational 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. Any (medical) condition that would, in the opinion of the investigator, potentially compromise the safety or compliance of the patient or may preclude the patient’s successful completion of the clinical trial.
14. Latent Diabetes Mellitus
15. Volunteers with clinically relevant infections

Study design

Design

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

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-01-2020
Enrollment:	24
Type:	Anticipated

IPD sharing statement

Plan to share IPD: No

Plan description
N.A.

Ethics review

Positive opinion

Date:	26-02-2020
Application type:	First submission

Study registrations

Followed up by the following (possibly more current) registration

ID: 55304
Bron: ToetsingOnline
Titel:

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

No registrations found.

In other registers

Register	ID
NTR-new	NL8391
CCMO	NL71422.056.19
OMON	NL-OMON55304

Study results

Summary results
N.A.