A single-arm, observational study to explore and characterize wound healing after skin punch biopsies in healthy volunteers

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Primary objective* To characterize and monitor wound healing after a standardized, induced skin trauma Secondary objectives* To evaluate safety and tolerability of biopsy-induced skin trauma

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Epidermal and dermal conditions
Study type	Observational invasive

Summary

ID

NL-OMON44210

Source
ToetsingOnline

Brief title
Wound healing in healthy volunteers

Condition

- Epidermal and dermal conditions

Synonym
Wound healing

Research involving
Human

Sponsors and support

Primary sponsor: Centre for Human Drug Research

Source(s) of monetary or material Support: Cutanea Life Sciences and CHDR research budget

Intervention

Keyword: Wound healing

Outcome measures

Primary outcome

Endpoints

* Biopsy biomarkers:

o Histology with hematoxylin and eosin (HE) staining

o Immunohistochemistry with wound healing related biomarkers (e.g. CD31,

collagen I, collagen III, aSMA, fibronectin)

o RNA sequencing (RNA-seq) or qRT-PCR for wound healing related biomarkers

(e.g. VEGF*, TGF*1, TGF*2, TGF*3, PDGF, CTGF, TNF, IL-1B, IL-4, GM-CSF, IL-6,

IL-10, MMP1, MMP3, OSM, LOX)

* Local skin biomarkers for wound healing related biomarkers (e.g. VEGF-A,

TNF*, IL-8, TLSP, MMP-3, IL-4) by transdermal analysis patch (TAP)

* Clinical imaging (e.g. 2D and 3D photography, thermography, laser speckle

contrast imaging (LSCI), trans epidermal water loss (TEWL), colorimetry)

* Clinical evaluation (erythema grading scale, Red-Yellow-Black (RYB) wound

assessment scale, the Patient and Observer Scar Assessment Scale (POSAS))

* Skin microbiome (healthy and biopsy lesions)

Secondary outcome

Tolerability / safety endpoints

* Adverse events (AEs)

* Local tolerance (erythema grading scale, RYB wound assessment scale, NRS

pruritus and pain, POSAS)

Study description

Background summary

The skin plays a critical role in protection where it acts as a barrier from damage and pathogens between the external and internal environments (Dreifke et al., 2015). Wounds compromise its protective role by disrupting the function and the normal structure of the skin and the underlying soft tissue. As a response to injury wound healing occurs in order to rapidly restore the defect. This process involves activation of keratinocytes, fibroblasts, endothelial cells, macrophages, and platelets and consists of multiple phases including hemostasis, inflammation, migration and cellular proliferation, and maturation and remodeling (Armstrong and Meyr, 2017). A simplified schematic of the course of wound healing is depicted in Figure 2. Hemostasis occurs immediately after dermal injury. The inflammation phase is characterized by cellular recruitment and increased vascular permeability. The epithelization phase is achieved by proliferation of basal cells and migration of epithelial cells. The last phase is known as the maturation and remodeling phase where collagen cross-linking and remodeling, wound contraction, and repigmentation takes place. Due to the broad involvement of various cell types, extracellular matrix and many reactive molecules each phase in wound healing produces characteristic changes within the tissue. A deficiency in any part of the process can lead to delayed wound healing, abnormal scar formation or chronic wounds.
To study wound healing in healthy volunteers a challenge model with skin punch biopsies has been described in literature previously (Greaves et al., 2014, Greaves et al., 2015, Illigens and Gibbons, 2013, Ud-Din et al., 2012). However, the characterization of this model was not performed comprehensively since advanced analysis of biopsies were omitted. Furthermore, analyses performed in previous studies only partially described wound healing processes either by insufficient time points for characterization or scarce simultaneous evaluations of multiple wound healing modalities.
The overall aim of this study is to develop a standardized model to temporarily and locally induce a skin trauma to investigate wound healing and monitor wound closure. This clinical model will enable future application as proof-of-pharmacology and proof-of concept studies as well as drug profiling in early drug development programs. More specifically, the objective of the trial is to explore and characterize the induction of well-defined skin trauma and natural wound healing process over the course of the different phases using a battery of dermatological assessments after skin punch biopsies in healthy volunteers. Furthermore, safety and tolerability will be assessed.

Characterization and monitoring of wound healing effects following skin punch biopsies will be performed by means of biophysical, biochemical, imaging, clinical parameters and subject reported outcomes.

Study objective

Primary objective
* To characterize and monitor wound healing after a standardized, induced skin trauma

Secondary objectives
* To evaluate safety and tolerability of biopsy-induced skin trauma

Study design

This is an observational, single center, single arm study.

Study burden and risks

Small skin punch biopsies are frequently performed in both clinical care and clinical research. Skin biopsies with 3 mm and 4 mm are considered minimally invasive since the wound surface is limited and the wound care is commonly not involves wound suture. The induced wounds heal quick and do not cause tremendous scaring. All subjects are excluded with a high potential for hypertrophic scaring.
Therefore, the risks associated with study participation are considered minimal.

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

Eligible subjects must meet all of the following inclusion criteria at screening:
1. Healthy subjects, 18 to 30 years of age (inclusive). The health status is verified by absence of evidence of any clinical significant active or uncontrolled chronic disease following a detailed medical history, a complete physical examination including vital signs, blood sampling of hematology, chemistry, and virology, urinalysis, urine drug and cotinine testing, and alcohol breath testing. 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, inclusive
3. Fitzpatrick Skin type I-II (Caucasian type).
4. Eligible lower back to perform biopsies (no excessive hair growth, no local skin disorder)
5. Willing to give written informed consent and willing and able to comply with the study protocol.

Exclusion criteria

Eligible subjects must meet none of the following exclusion criteria at screening:
1. History of pathological scar formation (keloid, hypertrophic scars)
2. Any form of body modification of the lower back hindering biopsy collection of unaltered skin (e.g. tattoos, piercings, implants)
3. Any disease associated with immune system impairment, including auto-immune diseases, HIV and transplantation patients.
4. Requirement of immunosuppressive or immunomodulatory medication, including glucocorticoids, non-steroid anti-inflammatory drugs (NSAIDs), and chemotherapeutic drugs within 30 days prior to enrollment or planned to use during the course of the study.
5. Have any current and / or recurrent pathologically, clinical significant relevant skin condition.

6. Use of topical medication (prescription or over-the-counter (OTC)) within 30 days of the start of the study in local treatment area.
7. Pregnant, a positive pregnancy test, intending to become pregnant, or breastfeeding.
8. Current smoker and/or regular user of other nicotine-containing products (e.g., patches).
9. Average consumption of more than 14 units of alcohol per week
10. Tanning due to sunbathing, excessive sun exposure or a tanning booth within 3 weeks of enrollment or planned to do so during the course of the study
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 subject or may preclude the subjects* successful completion of the clinical trial.

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Other

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	26-10-2017
Enrollment:	18
Type:	Actual

Ethics review

Approved WMO

Date:	09-10-2017
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
CCMO	NL63280.056.17