Efficacy analysis of several drugs in a humanized mouse model of psoriasis

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Autoimmune disorders
Study type	Observational invasive

Summary

ID

NL-OMON37202

Source
ToetsingOnline

Brief title
Pre-clinical efficacy of several drugs in psoriasis

Condition

- Autoimmune disorders
- Epidermal and dermal conditions

Synonym
flaking disease, Psoriasis

Research involving
Human

Sponsors and support

Primary sponsor: TNO
Source(s) of monetary or material Support: Farmaceutische industrie

Intervention

Keyword: Efficacy, Mouse, Psoriasis

Outcome measures

Primary outcome

Effect on the psoriatic process is tested by histology and immuno-histochemical

techniques in the transplanted

biopsies. Main read-out is epidermal thickness.

Secondary outcome

RNA will be isolated from the biopsies and analyzed on important gene

transcripts that appear to play a role in the development of psoriasis.

Secretion of inflammatory mediators by cells from patients. Markers on cultured

cells from psoriasis patients. Additionally, effects of the compounds will be

evaluated on the immune cells derived from blood of the patients (in vitro) ,

this in parallel to the in vivo mouse study.

Possibly also inflammatory cells in the skin tissue will be evaluated

Study description

Background summary

Psoriasis is a highly prevalent disease with great impact on the quality of
life of the patients. Current treatments are far
from ideal. The development of new compounds requires validation in an animal
model, however, many differences
exist between the skin of most animals and humans. TNO Life Sciences has
acquired
expertise in the past year in transplanting human psoriasis skin onto a mouse.
Thereby, we are able to perform
preclinical testing of compounds for psoriasis. Non-laesional skin is
transplanted onto a mouse and after engraftment

injection with autologous T-cells synchronizes the psoriatic process.
Scientific background information can be read in
Appendix 3. Since the study involves pre-clinical testing, patients will not experience a direct benefit from participation.

Study objective

In this study, the efficacy of different type drugs, on the development of the psoriatic process in the humanized mouse model for psoriasis, will be evaluated. These different, registered drugs intervene at different levels of the psoriatic process. By comparing these drugs in one study, insight can be obtained concerning differences in pathways and the sensitivity of different patients/ biopsies to the different drugs. To gain in depth insight , beside immunohistochemical evaluation also RNA will be isolated from the biopsies and analyzed on important gene transcripts that appear to play a role in the development of psoriasis.
Additionally, effects of the compounds will be evaluated on the immune cells derived from blood of the patients (in vitro) , this in parallel to the in vivo mouse study.

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Study design

A pharmaceutical company has asked TNO to test several drugs for psoriasis in our humanized mouse
model of psoriasis. Besides animal welfare approval, we also need medical ethical clearance for obtaining skin
biopsies and blood from psoriasis patients. The skin will be transplanted onto mice after which autologous T-cells
(isolated from the blood of patients) will be injected into the graft to synchronize development of psoriasis. As indicated
in the study protocol (Appendix 1), 4 skin punch biopsies will be obtained from non-lesional skin as well as 6 vials of
blood (ca. 10 ml each).

Study burden and risks

TNO has arranged insurance for the patients participating in this study. However, medical risks are very low. A week
after obtaining skin and blood samples, the stitches will be removed at the research center (PT&R) and a check will
take place. With the consent of the patient, the medical practitioner of each patient will be notified about the
participation.

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

Psoriasis patients: Adults (m/f) with a mild form of psoriasis vulgaris (PASI score of maximal 12). Patients are allowed to use local corticosteroids or ointments to prevent dry skin (Appendix 2).

Exclusion criteria

These patients have not received light therapy or another form of systemic treatments (methotrexate, cyclosporin A, anti-TNF treatments). Gender or age of the adults are not exclusion criteria (Appendix 2)

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	17-10-2012
Enrollment:	20
Type:	Actual

Ethics review

Approved WMO Date:	25-10-2012
Application type:	First submission
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	27-03-2013
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)

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	NL41235.028.12