PLEASE NOTE: *This trial has been registered retrospectively.*

Trial Description

Title

Histological and immunohistochemical examination of acute and chronic scratch lesions, prurigo nodularis, lichen simplex and brachioradial pruritus.

Trial Acronym

(SST-Pr-14-2008)

URL of the trial

[---]*

Brief Summary in Lay Language

Itch (pruritus) is defined as an unpleasant sensation of the skin that leads to scratching. The scratch reflex and its effects on the skin have yet to be sufficiently investigated. In addition to scratching, patients indicate rubbing, pinching, and pricking, etc. that can clinically lead to different patterns on the skin. Erosions, excoriations, crusts, scars and papules or nodules develop. Long-term scratching causes extensive lichenification (lichen simplex), prurigo nodularis, notalgia paresthetica or lichen amyloidosis.
In this project, we want to morphologically (i.e. with histological, immunohistological and molecular biological methods) examine the scratch patterns. We plan to histologically examine a large quantity of skin biopsies (n=600), in particular from patients who have been diagnosed with chronic pruritus (n=500), or brachioradial pruritus (n=100). We would like to conduct immunohistochemical tests on a smaller quantity of biopsies (per 50 representative biopsies of pruritus, prurigo and brachioradial pruritus). For comparison, normal skin biopsies should also be examined.
Molecular biological examinations are planned for a smaller quantity of biopsies. Every 20-50 patients with an inflammatory skin disease (e.g. atopic dermatitis, psoriasis, allergic contact dermatitis) and test subjects with normal skin should be examined in order to determine to what extent a special receptor (κ-opiod receptor), which would be suitable for a topical therapy, is present in the skin (Amendment 1 from 31.07.2011; positive vote from Münster Ethics Committee on 02.08.2011). In a second step, molecular biological methods should be applied to itchy, inflammatory diseases (e.g. neurodermatitis, prurigo nodularis, every 30 biopsies) to search for another receptor that has a role in triggering itch (Amendment 2 from 19.01.2012; positive vote from Münster Ethics Committee von 24.02.2012). In a further sub-project, itch is examined in liver diseases (Amendment 3a from 04.09.2012; positive vote from Münster Ethics Committee von 05.10.2012) and itchy diseases of the immune system that also affect the skin (Amendment 3b from 09.01.2014; positive vote from Münster Ethics Committee on 04.04.2014) by utilizing the same methods on 30 patients.

Brief Summary in Scientific Language

To date, the histological criteria of acute and chronic scratch lesions have not been clearly defined. However, these are of importance for differentiating between primary dermatoses and secondary changes in dermatohistological diagnostics. It is speculated that scratch lesions contribute to a peripheral sensitization of the symptom. Despite this, knowledge of exact histopathological and molecular biological changes in scratch lesions remains incomplete. We would like to carry out this project, based on a broad-based diagnostic and biopsy quantity, in order to contribute to histological appraisals and identify new, potential therapy targets for chronic pruritus.
Histological criteria should be compiled, in detail, by means of routine hematoxylin and eosin sections available through the tissue bank (n=600; patients with a diagnosis of chronic pruritus [n=500] or brachioradial pruritus [n=100]) and defined in correlation with the clinical data from patient health records (age, gender, skin status, dermatosis), acute and chronic scratch lesions criteria, prurigo (prurigo simplex subacute, prurigo nodularis) and lichen simplex. Immunohistochemical staining is performed on every 50 representative biopsies of pruritus, prurigo and brachioradial pruritus. Neuroreceptors (histamine receptor, vanilloid receptor, cannabinoid receptor, opioid receptor, interleukin-31 receptor, endothelin receptor, neurokinin receptor, gastrin releasing peptide receptor) and neuropeptides (substance P, calcitonin gene-related peptide, NGF) should be stained (with peroxidase or immunofluorescence). If changes are seen, a RT-PCR or western blot of the tissue is performed in order to confirm them on a molecular biological level. 10 normal skin biopsies should be stained for comparison. All biopsies are taken from the tissue bank.
Furthermore, dermatoses should be more closely examined in regards to the κ-opioid receptor expression (Amendment 1 from 31.07.2011). Biopsies are taken from every 20 to 50 patients with scratch lesions, or pruritus in atopic dermatitis, psoriasis, allergic contact dermatitis, irritant contact dermatitis, prurigo nodularis, lichen planus, urticaria, mycosis fungoides and sezáry disease, as well as test subjects with normal skin, and submitted for immunohistochemical staining and quantitative real-time PCR of the κ-opioid receptor. Blood is drawn from 5 test subjects and 5 patients with atopic dermatitis in order to perform a FACS analysis. The nuclear inflammation cells are then examined for their receptor expression and reaction to KOR agonists. Surface markers are also examined, such as anti-CD3, CD45, CD8, CD25 and FoxP3.
Because the neurokinin-1 receptor has proven to be an important therapy target, its expression in the skin will be more closely examined in a further subproject (Amendment 2 from 19.01.2012). The goal of the examination is to examine the receptor expression for every 30 patients with prurigo nodularis, neurodermatitis, chronic pruritus of different genesis and itching psoriasis and compare it with that of normal skin. This occurs by means of skin biopsy removal and quantitative real-time PCR, western blot and immunohistochemistry.
Cholestatic pruritus rarely causes scratch lesions and is well-suited for comparison with results from the previous substudy. It has already been proven that there are increased levels of autotaxin and its product, lysophosphatidic acid, present in the blood of patients with itchy liver diseases. In this subproject, ATX and LPA expression in itchy, scratched skin will be examined, and morphological results correlated with data from previous tests (Amendment 3a from 04.09.2012). Likewise, blood is drawn in order to determine the level of autotaxin, and genomic DNA isolated and submitted for sequence analysis in order to associate possible changes in certain genes with the presence of chronic pruritus. In addition to the sampling collective to Amendment 3a, the same tests are performed on 30 patients with itchy autoimmune dermatoses. As a control group for patients with cholestatic pruritus, skin biopsies and serum from 30 healthy tests subjects matched by gender, age and localization are examined (Amendment 3b from 09.01.2014).

Organizational Data

- DRKS-ID: **DRKS00009779**
- Date of Registration in DRKS: **2016/03/10**
- Date of Registration in Partner Registry or other Primary Registry: **[---]***
- Investigator Sponsored/Initiated Trial (IST/IIT): **yes**
- Ethics Approval/Approval of the Ethics Committee: **Approved**
- (leading) Ethics Committee Nr.: **2008-235-f-S , Ethik-Kommission der Ärztekammer Westfalen-Lippe und der med. Fakultät der Westfälischen Wilhelms-Universität Münster**

Secondary IDs

Health condition or Problem studied

- ICD10: **L29.9 - Pruritus, unspecified**
- ICD10: **L28.1 - Prurigo nodularis**

Interventions/Observational Groups

- Arm 1: **With skin biopsies from patients with scratch lesions from chronic pruritus, pruritic dermatoses, cholestatic pruritus and autoimmune dermatoses, histological criteria are identified and the distribution (immunohistochemistry), or expression (qRT-PCR, western blot), of neuroreceptors (the κ-opioid and neurokinin-1 receptors, in particular, but also receptores for histamine, capsaicin, cannabinoids, interleukin 31, endothelin, gastrin releasing peptide) and neuropeptides (substance P, calcitonin-gene related peptide, NGF) determined. A comparison is, to some extent, made with serum tests.**

Characteristics

- Study Type: **Non-interventional**
- Study Type Non-Interventional: **Other**
- Allocation: **Single arm study**
- Blinding: **[---]***

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- Who is blinded: **[---]***
- Control: **Uncontrolled/Single arm**
- Purpose: **Basic research/physiological study**
- Assignment: **Single (group)**
- Phase: **N/A**
- Off-label use (Zulassungsüberschreitende Anwendung eines Arzneimittels): **N/A**

Primary Outcome

Definition of the morphological criteria of scratch lesions with histological tests of skin biopsies.

Secondary Outcome

Testing for the distribution and expression of neuroreceptors and neuropeptides in itchy skin with immunohistochemistry and molecular biological methods.

Countries of recruitment

- DE **Germany**

Locations of Recruitment

- University Medical Center **Klinik für Hautkrankheiten, Münster**

Recruitment

- Planned/Actual: **Actual**
- (Anticipated or Actual) Date of First Enrollment: **2008/07/01**
- Target Sample Size: **600**
- Monocenter/Multicenter trial: **Monocenter trial**
- National/International: **National**

Inclusion Criteria

- Gender: **Both, male and female**
- Minimum Age: **18 Years**
- Maximum Age: **no maximum age**

Additional Inclusion Criteria

Pruritus

Exclusion criteria

below 18 years

Addresses

- **Primary Sponsor**

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Sources of Monetary or Material Support

- **Institutional budget, no external funding (budget of sponsor/PI)**

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Status

- Recruitment Status: **Recruiting ongoing**
- Study Closing (LPLV): **[---]***

Trial Publications, Results and other documents

** This entry means the parameter is not applicable or has not been set.*
**** This entry means that data is not displayed due to insufficient data privacy clearing.*