

# Deep phenotyping of vulvar (pre)malignant disease.

No registrations found.

<b>Ethical review</b>	Positive opinion
<b>Status</b>	Pending
<b>Health condition type</b>	-
<b>Study type</b>	Interventional

## Summary

### ID

NL-OMON23864

### Source

Nationaal Trial Register

### Brief title

CHDR2007

### Health condition

vulvar (pre)malignancies

## Sponsors and support

**Primary sponsor:** CHDR

**Source(s) of monetary or material Support:** CHDR

## Intervention

## Outcome measures

### Primary outcome

- Punch biopsies: histology (e.g. H&E and HPV typing), IHC (e.g. p16 and p53), mRNA extraction
- Vulvar pH\*
- Hormonal status (FSH, LS, estrogen)
- DermaToolbox:

- 2D photography\* (photo documentation)
- 3D photography\* (lesion dimensions)\ - Dermoscopy\* (erythema + roughness scores)
- Optical Coherence Tomography\* (skin morphology, skin layer thickness, blood perfusion)
- Confocal Microscopy\* (skin morphology)
- Ultrasonography\* (skin morphology, skin layer thickness, tumour penetration up to 4cm)
- Trans Epidermal Water Loss\* (skin barrier function)
- Clinical scores (e.g. Günthert, RECIST, PROVOKE)
- Patient reported outcomes\* (this may include, but is not limited to: NRS pruritus, NRS burning sensation, NRS pain, sleeplessness QoL, patient satisfaction scores of imaging tools)

## Secondary outcome

- Vulvar, vaginal and anal swabs\* for microbiome

# Study description

## Background summary

A wide spectrum of benign and (pre)malignant lesions may occur in the anogenital region. For example, lichen sclerosis (LS) is a chronic inflammatory dermatitis with a predilection for the anogenital area. This disease can cause severe atrophy in this area and lead to deformities of the vulvar structures. It is mainly a pruriginous condition but can also be asymptomatic. The median age at time of LS diagnosis is around 65 years and the prevalence is increasing with age up to 1:30 women. Most important, LS is associated with an enormous morbidity and an increased risk of vulvar premalignancy (dVIN) and subsequent cancer (4-6%).

The cornerstone of treatment for vulvar (pre)cancers is surgery. Surgical treatment in the vulvar area is frequently associated with significant morbidity due to damage to vital structures like urethra, vagina, clitoris and anus. Correct distinction between healthy and (pre)malignant tissue is one of the major challenges for the clinician. Incorrect identification of (pre)cancerous lesions results in re-excisions, recurrences, metastases and worse prognosis. This underlines the high unmet medical need for clinicians to better discriminate vulvar (pre)cancers.

In addition, most clinical trials within the vulvar cancer field make use of clinical outcomes, as physician-evaluated scores, in the assessment of drug efficacy. These outcomes can give a crude estimation of the disease “severity” and potential improvement during the clinical trials. However, these clinical endpoints have disadvantages as limited objectivity due to a possible response quantification bias by the scoring physician, potential inter-rater variability and lack of sensitivity needed to quantify smaller effects of a novel drug. Unfortunately, there is little research on the mechanisms underlying the development of and the response to treatment in vulvar (pre)cancers. Therefore, more objective endpoints are needed to support unbiased objective evaluation of drug efficacy in this field.

In this study a multi-modal and in-depth approach will be used, which consist of different

measurement methods and imaging techniques to acquire non-physician based disease-related outcomes of vulvar (pre)malignancies. For example, invasive punch biopsy will be compared to different non-invasive techniques such as 2D/3D photography, dermoscopy, optical coherence tomography (OCT), ultrasonography and trans-epidermal waterloss (TEWL) (Figure 1). By integrating data from different domains such as biophysical, imaging, molecular, cellular and microbial, a so-called 'systems dermatology' approach is used. The biomarkers created by these different technologies will describe the pathophysiology in high detail and support a holistic view on vulvar disease and potential drug mechanisms. Therefore, a two-part study is proposed. Part 1: a non-interventional clinical study to characterize different vulvar conditions, including lichen sclerosus and (pre)cancerous lesions (HSIL), in comparison to healthy controls. Part 2: an interventional clinical study in vulvar lichen sclerosus (LS) patients treated with topical clobetasol, to observe whether different sampling methods and non-invasive imaging techniques can discriminate the responsiveness to change in disease activity. The results/endpoints from this study can be used in the future for research into new treatments for these different vulvar conditions. The results will be analysed and integrated with a novel machine learning approach.

## **Study objective**

The overall aim of this study is to evaluate objectively measured disease related characteristics in patients with different vulvar conditions compared to healthy volunteers.

## **Study design**

Screening day 1, observational phase day 1 and 2, follow up day 8 and day 22, EOS day 8 and day 36

## **Intervention**

Clobetasol propionate ointment

## **Contacts**

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# Eligibility criteria

## Inclusion criteria

1. Non-pregnant female subjects, 25-75 years of age (inclusive); in general, stable good health as per judgment of the investigator based upon the results of a medical history, physical examination (BMI  $\leq$  30) and vital signs.
2. BMI of  $\leq$  30
3. If female of childbearing potential, have a negative urine pregnancy test at Day 0.
4. Willing to give written informed consent and willing and able to comply with the study protocol.
5. Ability to communicate well with the investigator in the Dutch or English language.
6. Subject is willing to undergo vulvar biopsies.
7. Subject is willing to refrain from washing (including bathing, swimming, showering and excessive sweating) the vulva counting from midnight of every study visit day.
8. Subject is willing to refrain from application of products (e.g. ointments, crème or wash) on the vulva 24 hours prior to every study visit day.
9. Subject is willing to refrain from sexual intercourse less than 24 hours prior to every study visit.
10. Subject is willing to refrain from shaving, waxing or other hair removing treatments in the perineal area in the 24 hours prior to every study visit.
11. Willing to refrain from any active treatment for vulvar HSIL and LS as from 14 days prior to Day 0.

Eligible HSIL patients must meet all of the following inclusion criteria at screening:

12. At least one sharply marginated lesion (plaque) that can be accurately measured (using RECIST criteria), in at least one dimension with a smallest diameter of  $\geq$ 15 mm, with confirmed HSIL diagnosis by histologic confirmation. This histologic diagnosis does not necessarily have to be performed close to inclusion.

Eligible LS patients must meet all of the following inclusion criteria at screening:

13. Clinically and/or histologically diagnosed with LS and under topical treatment with topical corticosteroids or willing to start topical steroid treatment during study participation.

Eligible VSCC patients must meet all of the following inclusion criteria at screening:

14. Histologically confirmed primary or local recurrent VSCC.

## Exclusion criteria

1. Significant, uncontrolled or unstable disease in any organ system as per judgment of the investigator (regardless of association with the immunosuppressing disorder/therapy),

- including but not limited to: psychiatric, neurologic, cardiovascular, pulmonary, gastrointestinal, hepatic, renal, endocrine, hematologic or respiratory disease.
2. History of immunological abnormality (e.g., immune suppression) that may interfere with study objectives, in the opinion of the investigator.
  3. Known infection requiring (topical or oral) antibiotic therapy within 28 days prior to Day 0;
  4. The use of any oral/systemic medication (e.g. immunomodulatory, immunosuppressive, acetylsalicylic acid) within 28 days prior to Day 0, if the investigator judges that it may interfere with the study objectives. The use of paracetamol (up to 4 g/day) is allowed;
  5. Pregnant, a positive pregnancy test, intending to become pregnant, or breastfeeding;
  6. Self-reported: (a) immunocompromised state, (b) sexually transmitted disease, (c) AIDS and/or (d) hepatitis.
  7. Have any current and / or recurrent clinically significant or subject reported skin condition in the vulvar area other than the (absence of) vulvar disease wherefore subject is included in the study.

Eligible vulvar patients must meet none of the following exclusion criteria at screening:

8. Have any current relevant (inflammatory) skin infections in the treatment area other than the observational disease (vulvar LS, vulvar HSIL or VSCC), inclusively, but not limited to atopic dermatitis, herpes, candidiasis or psoriasis.
9. Have used or received any topical vulvar HSIL treatment, laser therapy or surgery in the anogenital area within 28 days prior to Day 0
10. Have used or received any topical corticosteroids or other topical immune suppressive treatment for LS within 14 days prior to Day 0
11. Have used or received chemo-or radiotherapy or surgery in the anogenital area within 3 months prior to enrolment.

## Study design

### Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	N/A , unknown

### Recruitment

NL	
Recruitment status:	Pending
Start date (anticipated):	01-02-2021

Enrollment: 40  
Type: Anticipated

## IPD sharing statement

**Plan to share IPD:** No

### Plan description

N.A.

## Ethics review

Positive opinion  
Date: 25-01-2021  
Application type: First submission

## Study registrations

### Followed up by the following (possibly more current) registration

ID: 54913  
Bron: ToetsingOnline  
Titel:

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

No registrations found.

## In other registers

Register	ID
NTR-new	NL9388
CCMO	NL73964.058.20
OMON	NL-OMON54913

## Study results

### Summary results

N.A.