

# Trial of treatment and follow-up of vaginal intraepithelial neoplasia (VAIN)

<b>Submission date</b> 04/03/2013	<b>Recruitment status</b> No longer recruiting	<input type="checkbox"/> Prospectively registered
		<input type="checkbox"/> Protocol
<b>Registration date</b> 15/04/2013	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan
		<input checked="" type="checkbox"/> Results
<b>Last Edited</b> 11/09/2017	<b>Condition category</b> Urological and Genital Diseases	<input type="checkbox"/> Individual participant data

## Plain English summary of protocol

### Background and study aims

Human papillomavirus (HPV) can cause cervical, vaginal and vulvar dysplasias (abnormal developments) which usually are diagnosed with a Pap smear. The majority of dysplasias caused by HPV will spontaneously regress, but a prolonged infection (continuing for years) can lead to cancer. Vaginal dysplasias (vaginal intraepithelial neoplasia, VAIN, grades 1-3) are usually treated with laser ablation or surgically with partial vaginal resection. The dysplasias are very commonly long-lasting and treatment often needs to be repeated several times every six months. The treatment can be very challenging due to commonly observed multifocal lesions. Mild dysplasias (VAIN 1) can be followed up to two years prior to treatment, because spontaneous regression commonly happens. It has also been proposed that taking punch biopsies promotes spontaneous regression, because it may stimulate immune response. Topical imiquimod is used for treatment of genital warts (condyloma). Genital warts are benign lesions caused by certain types of HPV. Imiquimod acts as an immunomodulator and it promotes the body's immune response. Imiquimod has previously been studied in the treatment of other genital lesions caused by HPV such as vulvar, vaginal and cervical dysplasias and the results have been promising. Vaginally administered imiquimod has been found to be quite well tolerated. Possible side effects include a burning local sensation, lower abdominal pain or cold like symptoms and fever. We are conducting a study to compare different treatment options for VAIN.

### Who can participate?

We are recruiting patients who are referred to or are already being treated at Helsinki University Central Hospitals Womens clinic for VAIN1 that has persisted over two years or recently diagnosed VAIN 2-3. Patients need to be over 18 years of age. We exclude patients who are pregnant or breastfeeding, premenopausal patients without reliable contraception, patients who are simultaneously in need for treatment for a cervical dysplasia, have a known allergy to imiquimod, have difficulty understanding Finnish or English, are HIV positive or have been diagnosed with vaginal carcinoma.

### What does the study involve?

Patients referred to colposcopy (the procedure during which a cervix is examined using a colposcope) for VAIN will be enrolled in the study after informed consent. Patients will be randomly allocated to one of three groups: follow-up, laser treatment or treatment with topical

imiquimod (self-administered 12.5 mg dose 1-2 times a week for 2 months). During colposcopy routine tests include a Pap smear and punch biopsies of detected lesions, additional testing will be done to test for high risk HPV types (hrHPV). Follow-up at the colposcopy clinic will happen 4, 8 and 16 weeks after the primary visit. If VAIN 2-3 persists, patients will be referred to other treatment options and have a control colposcopy at 24 weeks.

What are the possible benefits and risks of participating?

Benefits of participating include a more intensive follow-up scheme than usual and some additional testing. Patients may benefit from alternative treatment options than the current standard treatment. The results of additional testing are available to the patient upon request. Participating in the study is thought to have minimal risks for the patient. Patients in the imiquimod group might experience side effects from the medication, but the dosage can be halved if necessary. The study period is short (4 months) when taking into consideration the risk of the dysplasia progressing and thus participating in the study will not postpone significantly treatment if treatment method needs to be changed at the end of the study period.

Where is the study run from?

The study is run from and performed at the Womens clinic of Helsinki University Central Hospital (HUCH), Finland.

When is the study starting and how long is it expected to run?

December 2012 to May 2015.

Who is funding the study?

Helsinki University Central Hospital (Finland).

Who is the main contact?

Dr Annika Riska  
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## Contact information

**Type(s)**

Scientific

**Contact name**

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## Additional identifiers

Clinical Trials Information System (CTIS)

2012-005377-31

**Protocol serial number**

3108

## **Study information**

**Scientific Title**

Randomized trial of treatment and follow-up of vaginal intraepithelial neoplasia (VAIN)

**Study objectives**

The aim is to evaluate the effectiveness, tolerability and success rates of different treatment options for VAIN with laser treatment or topical imiquimod. We will also evaluate the so called biopsy effect meaning the possible effect that taking punch biopsies has on promoting spontaneous healing.

**Ethics approval required**

Old ethics approval format

**Ethics approval(s)**

University of Helsinki Institutional Review Board, 19/12/2012, ref: 385/13/03/03/2012

**Study design**

Randomized controlled three-arm trial

**Primary study design**

Interventional

**Study type(s)**

Treatment

**Health condition(s) or problem(s) studied**

Vaginal intraepithelial neoplasia (VAIN)

**Interventions**

Group A: Follow-up with colposcopy, Pap smear, punch biopsy and hrHPV test 0, 4, 8 and 16 weeks.

Group B: Laser treatment and follow-up with colposcopy, punch biopsy and hrHPV test 4, 8 and 16 weeks.

Group C: Topical imiquimod treatment and follow-up with colposcopy, punch biopsy and hrHPV test 4, 8 and 16 weeks. First two treatment weeks patients in the imiquimod group will self-administer 12.5 mg of imiquimod vaginally in a single dose. During study weeks three to eight they will apply 12.5 mg of imiquimod twice a week 3-4 days apart.

Patients from all study groups will be referred to laser treatment, surgical treatment or other treatment options after 16 weeks if VAIN2-3 persists or has progressed. These patients will have an additional control colposcopy at 24 weeks.

**Intervention Type**

Drug

**Phase**

Not Applicable

**Drug/device/biological/vaccine name(s)**

imiquimod

**Primary outcome(s)**

Histological regression to VAIN1 or less within 4 weeks of the end of treatment (week 16) will be considered a positive outcome.

**Key secondary outcome(s)**

1. Complete histological regression
2. HPV-negativity (week 24)
3. Good tolerability of the treatment

**Completion date**

15/09/2015

**Eligibility****Key inclusion criteria**

1. A biopsy-confirmed VAIN1 that has persisted for two years or biopsy-confirmed VAIN2-3
2. Previously laser or surgically treated VAIN, when previous treatment has occurred over 1 month prior
3. Immune compromised patients (i.e. patients with rheumatoid arthritis, scleroderma, etc.) who frequently have VAIN
4. Patients of legal age (18 years old and above)

**Participant type(s)**

Patient

**Healthy volunteers allowed**

No

**Age group**

Adult

**Lower age limit**

18 years

**Sex**

Female

**Key exclusion criteria**

1. Vaginal carcinoma
2. Pregnancy or breast-feeding
3. Lack of reliable contraception in premenopausal patients
4. Known allergy to imiquimod

5. Language difficulties (patients who do not speak sufficient Finnish or English)
6. Simultaneous need for Loop Electrosurgical Excision Procedure (LEEP)
7. HIV positive

**Date of first enrolment**

19/12/2012

**Date of final enrolment**

01/05/2015

## Locations

**Countries of recruitment**

Finland

**Study participating centre**

BO 610

Helsinki

Finland

00290

## Sponsor information

**Organisation**

Helsinki University Central Hospital (Finland)

**ROR**

<https://ror.org/02e8hzh44>

## Funder(s)

**Funder type**

Hospital/treatment centre

**Funder Name**

Helsinki University Central Hospital (Finland)

## Results and Publications

Individual participant data (IPD) sharing plan

## IPD sharing plan summary

Not provided at time of registration

## Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">Results article</a>	results	15/11/2016		Yes	No