

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

Submission date 04/03/2013	Recruitment status No longer recruiting	☐ Prospectively registered
		☐ Protocol
Registration date 15/04/2013	Overall study status Completed	☐ Statistical analysis plan
		☒ Results
Last Edited 11/09/2017	Condition category Urological and Genital Diseases	☐ 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 Women's 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?

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Contact information

Type(s)

Scientific

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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/02e8hzhf44>

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?
Results article	results	15/11/2016		Yes	No