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

Submission date
04/03/2013

Recruitment status
No longer recruiting

Registration date
15/04/2013

Overall study status
Completed

Last Edited
11/09/2017

Condition category
Urological and Genital Diseases

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] 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 bodys 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 ofthree 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

EudraCT/CTIS number

2012-005377-31

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
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

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details below to request a patient information sheet (Finnish and English).

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

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

Overall study start date
19/12/2012

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

Age group
Adult

Lower age limit
18 Years

Sex
Female

Target number of participants
30

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)

Sponsor details

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Sponsor type
Hospital/treatment centre

Website
http://www.hus.fi/

ROR
https://ror.org/02e8hzf44

Funder(s)

Funder type
Hospital/treatment centre

Funder Name
Helsinki University Central Hospital (Finland)

Results and Publications

Publication and dissemination plan
To be confirmed at a later date

Intention to publish date
31/12/2015

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