Preventing overtreatment of CIN using methylation markers

No registrations found.

Ethical review	Positive opinion
Status	Pending
Health condition type	-
Study type	Observational non invasive

Summary

ID

NL-OMON29301

Source
Nationaal Trial Register

Brief title
CONCERVE

Health condition

Cervical intraepithelial neoplasia
Overtreatment
Methylation markers
Regression

Cervicale intraepitheliale neoplasie
Overbehandeling
Methylerings markers
Regressie

Sponsors and support

Primary sponsor: VU medical center
Source(s) of monetary or material Support: ZonMw

Intervention

Outcome measures

Primary outcome

The primary study endpoint is (non-) regression at the end of the study based on histology of the cervical exit biopsy. All cervical biopsies will be examined by a gynaeco-pathologist and classified as no CIN, CIN1, CIN2, CIN3 or cervical carcinoma. Regression is defined as CIN1 or less on the exit biopsy based on morphology. Non-regression is defined as CIN2+ on the exit biopsy based on morphology.

Secondary outcome

It has been shown that HPV-clearance precedes regression of cervical lesions by an average of 3 months. Therefore, the secondary study endpoint is defined as HPV clearance (double negative hrHPV test at two consecutive time points). HPV DNA detection will be done with the clinically validated HPV-Risk assay, a multiplex real-time PCR-based assay designed for the clinical detection of high-risk HPV DNA of 15 (probably) high-risk HPV types (i.e. HPV16, -18, -31, -33, -35, -39, -45, -51, -52, -56, -58, -59, -66, -67, and -68). This assay detects HPV 16 and 18 in separate channels, and the other HPV types as a pool.

Study description

Background summary

Current cytology-based cervical screening programmes serve to detect and treat high-grade precursor lesions (CIN2/3) to prevent cervical cancer. However, the diagnostic-treatment trajectory is associated with considerable overtreatment since CIN2/3 lesions, particularly in young women, have a high spontaneous regression rate. Pathologists are unable to differentiate between CIN2/3 lesions with a low short-term progression risk to cervical cancer (productive lesions), not in need of immediate treatment, and those with a high short-term progression risk (transforming lesions) that need immediate treatment. Individual cancer risk prediction of CIN2/3 is therefore essential to reduce overtreatment. Recently, it has been shown that DNA methylation markers can differentiate between productive and transforming CIN2/3. Here, we aim to validate prospectively that testing for the methylation status of a CIN2/3 predicts (non-) regression leading to prevention of overtreatment.

Study objective

Analysis of methylation status can predict which CIN2/3 lesions will regress and which not, determining the need of immediate treatment versus active surveillance.

Study design

Baseline, 6, 12, 18, 24 months

Intervention

Standard therapy for CIN2/3 lesions consists of excision of the lesion by either LLETZ or cold knife conisation. In this study, treatment consists of a watchful waiting policy. Participants will be monitored by an intense follow-up schedule consisting of 6-monthly visits to the colposcopy clinic for 2 years. During these visits, cervical cytology, hrHPV testing, methylation marker analysis and colposcopic evaluation of the cervix will be performed.

Control:
Women not included in the study population and who will receive standard excisional therapy for
their CIN2/3 lesion will be asked to participate in a reference group. This standard therapy consists of
a LLETZ or cold knife conisation and will be performed according to national guidelines. By including a
reference population in our study, we aim to assess the clinical ‘cutoff’ for lesion size that gynaecologists use in their decision to treat patients and not to include them in the study protocol. One
hundred subjects will be included in this group.
Women participating in the reference group will be asked to use the Evalyn brush to self-collect a
cervico-vaginal specimen. Furthermore, a cervical scrape will be collected by the gynaecologist.
Sample collection will be done prior to treatment, so that no extra visits or gynaecological examinations will be needed.

Contacts

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Eligibility criteria

Inclusion criteria

In order to be eligible to participate in this study, a subject must meet all of the following criteria:

- CIN2 or CIN3 on a cervical punch biopsy

- CIN covering 50% or less of the visible cervix

- Female aged 18-55 years

Exclusion criteria

A potential subject who meets any of the following criteria will be excluded from participation in this study:

- History of cervical pathology

- Transformation zone is not visible at colposcopy

- Prenatal diethylstilboestrol exposure

- Concomitant cancer

- Insufficient Dutch or English language skills

Study design

Design

Study type: Observational non invasive

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

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-12-2016
Enrollment:	200
Type:	Anticipated

IPD sharing statement

Plan to share IPD: Undecided

Ethics review

Positive opinion

Date:	31-08-2016
Application type:	First submission

Study registrations

Followed up by the following (possibly more current) registration

ID: 45770
Bron: ToetsingOnline
Titel:

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

No registrations found.

In other registers

Register	ID
NTR-new	NL5794
NTR-old	NTR6069
CCMO	NL56187.029.16
OMON	NL-OMON45770

Study results