TOPical Imiquimod treatment of high-grade Cervical intraepithelial neoplasia, a multicenter, open-label, non-randomized, controlled study (TOPIC-3 study)

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This study aims to investigate the treatment efficacy, side-effects and quality of life associated with imiquimod treatment of high-grade CIN lesions in a selected population of patients who prefer imiquimod treatment instead of LLETZ. The study…

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Reproductive neoplasms female benign
Study type	Interventional

Summary

ID

NL-OMON47108

Source
ToetsingOnline

Brief title
Imiquimod treatment of CIN lesions

Condition

- Reproductive neoplasms female benign

Synonym
CIN2-3, premalignant lesion of the cervix

Research involving
Human

Sponsors and support

Primary sponsor: Medisch Universitair Ziekenhuis Maastricht
Source(s) of monetary or material Support: Ministerie van OC&W,MEDA Pharma

Intervention

Keyword: Cervical intraepithelial neoplasia, Imiquimod, Predictive biomarkers, Treatment

Outcome measures

Primary outcome

1. Treatment efficacy of imiquimod 5% cream for the treatment of CIN2-3 lesions, compared to LLETZ treatment, in selected populations. Treatment efficacy for the imiquimod group is defined as regression to CIN 1 or less at 20 weeks follow-up. Treatment efficacy for the standard treatment group is defined as no need for additional treatment within 6 months after LLETZ treatment.

2. Identification of predictive biomarkers for treatment efficacy of imiquimod in the individual patient, based on biomarkers reflecting host, virus and cellular factors.

Secondary outcome

- To assess the incidence and severity of side effects of imiquimod therapy, compared to LLETZ treatment.

- To assess histological disease recurrence within 24 months follow-up, for both treatment groups.

- To assess Quality of life (QoL) before, during and after treatment for both treatment groups.

Study description

Background summary

Cervical Intraepithelial Neoplasia (CIN) is the premalignant condition of cervical cancer. The standard treatment of histologically confirmed CIN2-3 changes is surgical excision by large loop excision of the transformation zone (LLETZ), with potential complications, such as hemorrhage, infection and preterm birth in subsequent pregnancies. For this reason, non-invasive therapies are needed. Imiquimod cream has been studied as a non-invasive treatment alternative in high-grade CIN, but evidence on treatment efficacy is limited and evidence on disease recurrence and quality of life during and after treatment is lacking. One RCT has been performed and shows that treatment of high-grade CIN with vaginal imiquimod cream leads to disease regression in 73%. Side-effects were generally mild, but common. A recent survey among gynecologists and a patient preference study indicate that imiquimod treatment of high-grade CIN is mainly preferred by a selected population of women with a future pregnancy wish. These women accept a lower treatment efficacy and higher rates of side-effects from imiquimod treatment in order to prevent future preterm birth caused by LLETZ treatment. Ideally, those women with a high probability of successful treatment would be selected.

Study objective

This study aims to investigate the treatment efficacy, side-effects and quality of life associated with imiquimod treatment of high-grade CIN lesions in a selected population of patients who prefer imiquimod treatment instead of LLETZ. The study also aims to identify predictive biomarkers for the clinical response to imiquimod treatment, in order to select patients in which good treatment response is expected.

Study design

Multicenter, open-label, non-randomized controlled intervention study.

Intervention

Patients are allocated to one of two treatment groups according to their preference:
1. Imiquimod treatment. Patients in this group are treated by a 16-week regime of imiquimod 5% cream. A control colposcopy with diagnostic biopsies will be performed after 10 weeks to rule out disease progression. A final colposcopy with diagnostic biopsies will be performed after 20 weeks to evaluate disease efficacy.

2. Standard treatment. LLETZ will be performed on patients in this group.

Study burden and risks

The burden associated with participation includes:
- a questionnaire concerning demographic and behavioral factors for all patients
- contraception in the imiquimod group
- two pregnancy tests in the imiquimod group for sexually active patients
- use of medication with potential side-effects in the imiquimod group
- additional consultations in the imiquimod group (1x for start treatment, 4x telephone consultation, 1x hospital visit, 1x additional colposcopy with biopsies)
- documentation of medication use and side effects in the imiquimod group
- documentation of side-effects in the LLETZ group
- quality of life questionnaires at three points in time for all patients

A LLETZ procedure may not be necessary for these participants, when imiquimod treatment is succesful. This may prevent complications, of which we consider the reduced risk of premature birth as the most important. The risk of disease progression in the imiquimod arm is minimalized by the study protocol.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

- de novo CIN2 or CIN3 lesion, histologically confirmed by diagnostic biopsy
- age of 18 years or older

Exclusion criteria

- previous histologically confirmed high-grade CIN (CIN 2*3)
- PAP 4 cytology as indication for the current baseline colposcopy
- concomitant vulvar and/or vaginal intraepithelial neoplasia
- previous cervical malignancy
- current malignant disease
- immunodeficiency (including HIV/AIDS and immunodepressive medication)
- pregnancy or lactation
- legal incapability
- insufficient knowledge of the Dutch language

Study design

Design

Study type:	Interventional
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL
Recruitment status: Recruitment stopped

Start date (anticipated):	07-11-2016
Enrollment:	120
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Aldara
Generic name:	Imiquimod
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	05-09-2016
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	20-09-2016
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	18-01-2017
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	08-06-2017
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	14-06-2017
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

Approved WMO Date:	03-07-2017
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	13-12-2017
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	04-10-2018
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	17-10-2018
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

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

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2016-002096-96-NL
CCMO	NL57849.068.16

Study results

Date completed:	09-02-2023
Actual enrolment:	123