TOPical Imiquimod treatment of high-grade Cervical intraepithelial neoplasia (TOPIC trial): a randomized controlled trial

Published: 21-05-2014
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To investigate the effectiveness of imiquimod 5% cream for the treatment of CIN2-3 lesions, compared to LLETZ treatment and to assess long-term disease recurrence, side effects and quality of life associated with different treatment modalities.

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

Summary

ID

NL-OMON41566

Source
ToetsingOnline

Brief title
Imiquimod treatment of CIN lesions.

Condition

- Reproductive neoplasms female benign

Synonym
CIN 2/3, high grade cervical intraepithelial neoplasia

Research involving
Human

Sponsors and support

Primary sponsor: Medisch Universitair Ziekenhuis Maastricht

Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: "cervical intraepithelial neoplasm", "immunotherapie", "treatment'

Outcome measures

Primary outcome

The main endpoint of the study is regression-or-not of CIN2 or CIN 3 lesions after imiquimod or conservative management, defined as regression to CIN 1 or less, at 20 weeks follow-up and adequate treatment of high-grade CIN by LLETZ, defined as no need for additional treatment within 6 months.

Secondary outcome

1. Side effects of imiquimod therapy and LLETZ therapy as scored by the Common Terminology Criteria for Adverse Events guidelines.

2. Disease recurrence at 6, 12 and 24 months follow-up, defined as abnormal cervical cytology for all treatment roups.

3. Quality of life (QoL) before, during and after treatment, assessed by the following QoL questionnaires at 0 and 20 weeks and after 1 year:

a. Medical Outcomes Study 36-Item Short-Form General Health Survey (RAND 36), to assess generic health-related quality of life

b. European Organization for Research and Treatment of Cancer (EORTC) quality-of-life questionnaire: QLQ-C30, to assess cancer-specific health-related quality of life

c. European Organization for Research and Treatment of Cancer (EORTC) quality-of-life questionnaire: QLQ-CX24, to assess cervical cancer specific

quality of life, including sexual functioning

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, with potential complications, such as hemorrhage, infection and preterm birth in subsequent pregnancies.
For this reason, adjuvant non-invasive therapies are needed. Imiquimod (non-invasive immunomodulator) is effective in the treatment of HPV related vulvar intraepithelial neoplasia (VIN). VIN and CIN have a comparable pathophysiology, and imiquimod may be effective as well in CIN. However, in case of CIN, few studies are available and results are not consistent.

Study objective

To investigate the effectiveness of imiquimod 5% cream for the treatment of CIN2-3 lesions, compared to LLETZ treatment and to assess long-term disease recurrence, side effects and quality of life associated with different treatment modalities.

Study design

Single-centre, single blinded randomized controlled intervention trial

Intervention

Patients will be randomized into one of two groups:
1. Imiquimod treatment. Patients in this group are treated by a 16-week regime of imiquimod 5% cream.
2. Standard treatment. LLETZ will be performed on patients in this group.
A colposcopy will be performed after 10 weeks for the first group. In case of regression or stable disease, the treatment will be continued for another 10 weeks. In case of progression, LLETZ will be performed. Re-evaluation will be performed after another 10 weeks, by colposcopy with biopsies. LLETZ wil be performed in case of persistent or progressive disease.

Study burden and risks

The burden associated with participation includes a questionnaire concerning demographic and behavioural factors and two control colposcopies for subjects

in the imiquimod group. Subjects allocated to the imiquimod arm will have cervical application of imiquimod. A LLETZ procedure may not be necessary for participants of the study when a CIN2/3 lesion regresses spontaneously or during imiquimod treatment. This may prevent complications, of which we consider the reduced risk of premature birth as the most important. A small risk of disease progression during the study cannot be ruled out.

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

- immuno-compromised women,
- pregnant of lactating women,
- legally incapable women
- previous histologically confirmed high grade CIN (CIN 2-3)

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Single blinded (masking used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	09-02-2015
Enrollment:	140
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:	21-05-2014
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	09-09-2014
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	12-12-2014
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	06-02-2015
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	10-06-2015
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	02-09-2015
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	09-10-2015
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	06-01-2016
Application type:	Amendment

Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Not approved Date:	25-04-2016
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	EUCTR2013-001260-34-NL
ClinicalTrials.gov	NCT02329171
CCMO	NL44336.068.13

Study results

Date completed:	09-05-2016
Actual enrolment:	6

Summary results
Trial ended prematurely