# A randomised, double-blind, placebo-controlled study to evaluate the efficacy of imiquimod 5% in women with Vulvar Intraepithelial Neoplasia (VIN) 2 and 3.

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Imiquimod, an immunomodulator, has been shown safe and effective in the treatment of external genital warts caused by low risk human papillomavirus (HPV). Therefore, it is hypothesized that this topical treatment may also be effective against...

| | |
|---|---|
| **Ethische beoordeling** | Positief advies |
| **Status** | Werving gestopt |
| **Type aandoening** | - |
| **Onderzoekstype** | Interventie onderzoek |

## Samenvatting

### ID

NL-OMON20043

**Bron**
NTR

**Verkorte titel**
N/A

**Aandoening**

VIN is a premalignant disease of the vulvar skin from which an invasive carcinoma may develop. It affects mainly young women, and causes severe and longlasting symptoms, such as pruritis, vulvar pain and sexual dysfunction. The disease is often multifocal on the vulva, and strongly related to infection with HPV. Standard therapy nowadays comprises surgical removal of all visible lesions. However, recurrence rates are high.

### Ondersteuning

**Primaire sponsor:** University and governmental budget (90%), and a small unrestricted research grand from 3M Nederland (10%) and studymedication with randomizationcode.

## Onderzoeksproduct en/of interventie

## Uitkomstmaten

### Primaire uitkomstmaten

Reduction in lesion size.

# Toelichting onderzoek

### Achtergrond van het onderzoek

VIN is a skin disease causing many severe and long-lasting symptoms, such as pruritis, vulvodynia and sexual dysfunction. The incidence has increased in the last decade and patients are affected at a younger age than before. Until now, the choice of therapy for high grade VIN has been dominated by the premalignant nature of the disease. Standard therapy comprises surgical removal of all visible lesions to relieve symptoms and prevent the development of invasive disease. For several reasons treatment results are unsatisfying:

1. surgical intervention is invasive to the patient and may result in mutilation of the vulva;

2. recurrence rates are high;

3. progression to invasive disease is not influenced by radical excision;

4. surgery does not interfere with HPV, the viral cause of VIN.

Since we found promising results on the treatment of VIN with imiquimod in a pilot study, and others described similar positive results in small numbers of patients as well, we wanted to investigate the effectiveness of imiquimod in high grade VIN in a randomised controlled trial.

### Doel van het onderzoek

Imiquimod, an immunomodulator, has been shown safe and effective in the treatment of external genital warts caused by low risk human papillomavirus (HPV). Therefore, it is hypothesized that this topical treatment may also be effective against different HPV types, and thus encourage regression of dysplastic vulvar lesions caused by high risk HPV.

### Onderzoeksopzet

N/A

**Onderzoeksproduct en/of interventie**

After qualifying for study participation patients are randomly assigned to receive either 250mg of imiquimod 5% cream (Aldara, 3M Pharmaceuticals, St Paul, MN, USA) or 250mg of placebo cream. Dosing will take place twice a week in the evening for a period of 16 weeks.

A clinical assessment will take place every four weeks during treatment, and four weeks after final treatment. To investigate long-term effects and to exclude recurrence of VIN final assessments will take place after 7 and 12 months.

A formalin fixed biopsy is taken for histological verification of VIN 2/3 within three months before the start of the study, together with a second biopsy from the same lesion frozen in liquid nitrogen for HPV DNA testing. At 20 weeks a post-treatment biopsy is taken at exactly the same spot as the first biopsy to evaluate the histological effect, and again a frozen sample is taken for detection of HPV DNA. If a recurrence is suspected at 12 months a biopsy is taken again. In case of persistent or residual lesions after one year, the patient is offered treatment with imiquimod.

# Contactpersonen

## Publiek

The Netherlands Cancer Institute, Department of Gynecology, Plesmanlaan 121

M. Beurden, van
Amsterdam 1066 CX
The Netherlands
+31 (0)20 512 2975

## Wetenschappelijk

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Amsterdam 1066 CX
The Netherlands
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# Deelname eisen

### Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

1. Histologically proven, multifocal VIN 2 or 3 without invasion;

2. age of 18 and older;

3. reliable method of contraception throughout the study.

### Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

1. Pregnancy;

2. (micro-)invasive carcinoma;

3. history of vulvar cancer;

4. unifocal lesion;

5. any other treatment for VIN or anogenital warts within one month of start of trial;

6. hypersensitivity to any components of the cream;

7. history of psoriasis or other inflammatory dermatosis of the vulva;

8. immunodeficiency;

9. insufficient command of the Dutch or English language.

## Onderzoeksopzet

### Opzet

| | |
|---|---|
| Type: | Interventie onderzoek |
| Onderzoeksmodel: | Parallel |
| Toewijzing: | Gerandomiseerd |
| Blindering: | Dubbelblind |
| Controle: | Placebo |

## Deelname

Nederland

| | |
|---|---|
| Status: | Werving gestopt |
| (Verwachte) startdatum: | 26-04-2001 |
| Aantal proefpersonen: | 52 |
| Type: | Werkelijke startdatum |

# Ethische beoordeling

Positief advies

| | |
|---|---|
| Datum: | 17-09-2006 |
| Soort: | Eerste indiening |

# Registraties

## Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

## Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

## In overige registers

| Register | ID |
|---|---|
| NTR-new | NL723 |
| NTR-old | NTR733 |
| Ander register | : N/A |
| ISRCTN | ISRCTN11290871 |

# Resultaten

### Samenvatting resultaten

N Engl J Med. 2008 Apr 3;358(14):1465-73.