Prospective randomised controlled study on imiquimod 5% cream as pre-treatment of Mohs micrographic surgery for primary large nodular basal cell carcinoma in the face.

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Objectives1. Reduction of defect size after MMS with a pre-treatment with imiquimod 5% cream2. Reduction of tumour size of large nodular facial BCC, after pre-treatment with imiquimod 5% cream.3. Improvement of cosmetic results.4. Histological...

Ethical review	Approved WMO
Status	Pending
Health condition type	Skin neoplasms malignant and unspecified
Study type	Interventional

Summary

ID

NL-OMON31041

Source
ToetsingOnline

Brief title
Prospectief randomised study on imiquimod as pre-treatment of MMS

Condition

- Skin neoplasms malignant and unspecified

Synonym
basal cell carcinoma, skin cancer

Research involving
Human

Sponsors and support

Primary sponsor: Catharina-ziekenhuis
Source(s) of monetary or material Support: wetenschappelijk fonds?

Intervention

Keyword: Basal cell carcinoma (BCC), Imiquimod, Mohs, randomised

Outcome measures

Primary outcome

Defect sizes: Sizes are measured (in mm2), between group differences are calculated.

Secondary outcome

Tumour sizes: Sizes are measured, between group differences are calculated (imiquimod versus control group).

In addition sizes pre and post imiquimod treatment (in the imiquimod group) will be compared.

Increase in area from baseline lesion to post-MMS defects are calculated and compared between both groups.

Reconstruction time will be measered in both groups and the between group difference will be noted.

Cost analysis:

Between group differences for total costs will be compared. These costs will be related to decrease in defect size and cosmetic result.

Cosmetic outcome:

Outcomes of the visual analog scale will be compared for both groups.

Quality of life: A questionnaire will be used to compare both treatments.

Before treatment, 4 weeks and 3 months after treatment.

Study description

Background summary

Basal cell carcinoma (BCC) is the most common malignancy of the skin (1). While the mortality rate due to this tumour is insignificant, an increasing group of especially younger patients are concerned about the cosmetic outcome of the treatment of a facial tumour. Various therapeutic modalities exist (1). In most cases surgical excision will take place. Mohs micrographic surgery (MMS) is an advanced technique, which is used mainly for BCC in the face and with high risk for recurrence, in the H-zone or > 2 cm (2). The size of the defect after excision of the tumour can significantly be reduced by using MMS, compared to the standard surgical excision. The cosmetic outcome is therefore overall better. In addition treatment of primary tumours does have a better cosmetic outcome compared to recurrent tumours (3). MMS has the lowest recurrence rate in the treatment of BCC (2). It is however, a time consuming and therefore costs are higher (3).
New non-surgical treatments for BCC are investigated, such as imiquimod 5% cream (imiquimod). Imiquimod is an immune respons modifier, it induces cytokines which stimulate a cell-mediated immunerespons (4). Imiquimod 5% cream has been demonstrated to be safe and effective in the treatment of anogenital warts (5).
Studies show that imiquimod has a beneficial effect on small superficial and small nodular BCCs, total or partial clearance is obtained (5-9).
Imiquimod could be used for BCC as an additional treatment before surgery, and not only serve as a monotherapy. It could be an excellent pre-treatment for MMS for larger nodular BCC. Pre-treatment with imiquimod 5% cream could reduce tumour size and result in a smaller defect after MMS, and therefore result in a better cosmetic outcome. Furthermore, it could reduce the number of Mohs rounds needed to clear the tumour completely and therefore reduce the costs of this treatment.

In other words; when imiquimod cream and MMS are combined, the chance on a better outcome is increased. Imiquimod reduces tumour size and defect size. MMS

provides radicality, so that risk of recurrence is low. These factors all provide a better cosmetic outcome. While BCC grows very slowly, a delay of 3 months between diagnosis and treatment is accepted.

Study objective

Objectives
1. Reduction of defect size after MMS with a pre-treatment with imiquimod 5% cream
2. Reduction of tumour size of large nodular facial BCC, after pre-treatment with imiquimod 5% cream.
3. Improvement of cosmetic results.
4. Histological evaluation of apoptosis by using caspase 3 and evaluation of the upregulation of FasR to determine the sensitivity of the BCC for apoptosis.
5. Calculation of cost-effectiveness.
6. Comparing quality of life between groups.
7. Recurrence rates.

Study design

Study design:
Prospective randomised controlled study.
Treatment with imiquimod cream for 4 weeks. 6 Weeks after treatment MMS will be performed.
The control group will only undergo MMS.
Follow-up 12 months.
The study will take place in The Catharina Hospital Eindhoven

Intervention

Product:
Imiquimod 5% cream (Aldara®) applied locally on the skin, on the target tumour and 1 cm around the tumour. The cream has to be applied at night and left for approximately 8 hours.
It has to be applied once daily, 5 days a week, for 4 weeks.
No other local treatment modality is allowed on the target area during the study, in both groups.

Study burden and risks

Adverse events that have been reported are mainly mild local skin reactions; these include erythema, itching, pain, erosions, and excoriations (5-7). Multiple studies report less adverse events when using the lower frequency dosing regimens (5-8,14,16). When reviewing literature, it appears that 87% of the patients reports at least one local skin reaction, some patients need a rest period if the local reactions are severe. 2% Of the patients stopped

treatment prematurely because of local skin reactions (17). In the trial described by Schulze et al, 2 of 166 patients stopped therapy due to adverse events. In one patient bleeding occurred in the treatment area and the other patient develop a bacterial skin infection. It is not clear if the bleeding occurred due to the treatment, BCC do bleed easily, spontaneously (16).
Systemic adverse events have been studied. No clinical or laboratory (blood and urine) changes were observed (6,7,9). Subjective systemic adverse events were mentioned in the study of Beutner et al, mainly fatigue, headache and fever. Temperatures were measured and no fevers were noted (5).
In previous large controlled trials about imiquimod cream for anogenital warts, no differences in frequency or severity of systemic adverse events were seen between the imiquimod group and the placebo group (5).

Possible benefits: Reduction of tumour size, decrease of defect, improvement cosmetic result.

Contacts

Public
Catharina-ziekenhuis

Michelangelolaan 2
5602 ZA Eindhoven
NL
Scientific
Catharina-ziekenhuis

Michelangelolaan 2
5602 ZA Eindhoven
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age

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

Inclusion criteria

Patients > 18 yrs
Nodular/ nodular and partially superficial basal cell carcinoma in the face
Diameter 1-5 cm

Exclusion criteria

pregnant women
women who breastfeed
Recurrent BCC
BCC with agressive growth pattern
BCC within 1 cm from the eyes, lips or mucosa of the nose
Another skin cancer within 5 cm of the target tumor
Former treatment of BCC in the target area
Allergy for imiquimod cream or substances

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-05-2007
Enrollment:	80
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Aldara
Generic name:	imiquimod 5% cream
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	30-07-2007
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

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	EUCTR2007-000622-42-NL
CCMO	NL16478.060.07