Topical Vitamin D3, Diclofenac or a combination of both to treat Basal Cell Carcinoma

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Primary Objective: To determine whether topical application of Calcitriol (Silkis) 3 µg/g, Diclofenac 10% or a combination of both can lead to a 40% histological reduction (*)/increase (*) of expression of the following antibodies: Ki67 (*), BCL2…

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

Summary

ID

NL-OMON36360

Source
ToetsingOnline

Brief title
Topical treatment basal cell carcinoma

Condition

- Skin neoplasms malignant and unspecified

Synonym
basal cell carcinoma, non-melanoma skin cancer

Research involving
Human

Sponsors and support

Primary sponsor: Medisch Universitair Ziekenhuis Maastricht
Source(s) of monetary or material Support: KWF kankerbestrijding

Intervention

Keyword: Basal cell carcinoma, Diclofenac, Topical, Vitamin D3

Outcome measures

Primary outcome

A significant reduction or increase (=40%) in expression of the different antibodies tumor tissue of the biopsy and the therapeutic excission will be tested. The intensity of the staining will be taken into account.

The following antibodies will be tested:

• Ki67

• *-catenin

• BCL2

• Caspase 3

• Cox2

• LC3b

• Hif1α

• sFRP4

• sFRP5

Secondary outcome

* Macroscopic tumour changes

* Toleration of therapy

* Patient satisfaction

Both tolerance and satisfaction will be asses by diaries and questionnaires.

Study description

Background summary

Basal cell carcinoma (BCC) is the most frequent malignant tumor in Caucasians and the incidence is still increasing with 3-8% each year.
Since BCCs generally occur on sun-exposed areas of the skin, the rice in incidence is mainly explained by the increasing exposure to (intermittent) ultraviolet radiation. Surgical excision is still the standard treatment for (micro) nodular BCCs. The costs as well as the increased workload are stressing the health care system even further and posing BCC an important health care problem. Since half of the BCCs arise primarily on the face & (bald) head and treatment by surgical excision may result in a disfiguring scar, patients often experience a dramatic decrease of their quality of life. Hence, there is an urgent medical and societal need for a simple and cheap (targeted) treatment, preferably to be performed by the patients themselves. This treatment must be safe and effective. Such treatment is not available yet.
BCC tumorigenesis is complex and must be multifactorial. Genetic alterations of multiple components of the Sonic Hedgehog (SHH) pathway are involved in sporadic BCC pathogenesis; inactivating mutations in Patched-1 (PTCH1) and activating mutations of Smoothened (SMO) and Suppressor of Fused (SU(FU)). With this knowledge, inhibition of the SHH pathway by a SMO antagonist was successfully administered, however treatment resulted only in partial clinical response of BCC. Recently, involvement of the Wingless (Wnt) pathway has been proven to be essential in BCC tumorigenic response. Moreover, a recent study of our own department provides the first evidence that epigenetic alterations, particularly promoter hypermethylation, influence both the SHH and Wnt pathway (own data, not published), which can serve as therapeutic targets. Both non-steroidal anti-inflammatory drugs (NSAIDS) and vitamin derivatives are able to directly or indirectly target the Wnt pathway. Furthermore, vitamin D3 is able to inhibit Smoothened (SMO) in vitro, which results in inhibition of the SHH pathway. Although in vivo studies are lacking, we assume that topical application of these drugs may inhibit BCC growth and/or may cure BCC and thus might provide very promising future perspectives. Calcitriol and NSAIDs ointments are both already available for other indications and save in use. Eventually, our approach may result in a systematic approach to BCC, targeting both genetic and epigenetic changes to treat and/or prevent further tumour growth.

Study objective

Primary Objective:

To determine whether topical application of Calcitriol (Silkis) 3 µg/g, Diclofenac 10% or a combination of both can lead to a 40% histological reduction (*)/increase (*) of expression of the following antibodies: Ki67 (*), BCL2 (*), Caspase 3 (*) and Cox2 (*) (proliferation and apoptosis), LC3B (*) (autophagy), HIF1α (*) (hypoxia), β-catenin (*), sFRP4 (*) and sFRP5 (*) (Wnt pathway activity).

Secondary Objectives:
To asses macroscopic tumour changes, toleration of the therapy and patient satisfaction.

Study design

open-label, singel-blinded, randomized-controlled intervention trial.

Intervention

Application of 3u/g Calicitriol, Diclofenac 3% or a combination of both.
Patients should apply the crème(s) twice daily on the tumor untill 1 cm around it and subsequently cover it with a plaster (Tegaderm).

Study burden and risks

Patients participating should apply the study crème twice daily during 8 weeks at the tumour and subsequently cover it. This will take the patients 5 minutes a day. As part of the study, patients should visit the hospital once extra for a controlvisit. This takes about 15 minutes. Apart from this, all patients will recieve regular care as exists for BCC care.
Side effects of the crèmes are hardly to be expected. Side effects that may occur are redness and skin irritation, but can easily be controlled. In case of an allergic reaction for one of the ingredients, treatment for this patient will be stopped. Previous studies showed that local application of vitamin D as well as Diclofenac is safe and does not lead to therapeutic plasma levels. The benefit for the patients is that the tumor may possibly shrink, resulting in a smaller scar due to the surgery.
Largest benefit will be made for future patients if it turned out that these new therapies are effective.

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

Minimum age 18 years
Primary basal cell carcinoma > 4 mm, histologically confirmed
(Micro) nodular or superficial histological subtype
Comorbidities may not interfere with study treatment
Capable to understand instructions

Exclusion criteria

Age under 18 years
Tumors located at the H-zone of the face
Deficient histological conformation
Proven or suspected malignancy of other organs
Not capable of comprehending instructions
Incompetent
Use of oral NSAIDs during the trial period or within 30 days before starting therapy
Use of oral vitamin D (containing) supplements during the trial period or within 30 days before starting therapy

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Other
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-11-2011
Enrollment:	128
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Silkis
Generic name:	Calcitriol
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Solaraze
Generic name:	Diclofenac diethylammonium

Ethics review

Approved WMO

Date:	24-11-2010
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

Approved WMO

Date:	18-07-2011
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	17-10-2011
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	EUCTR2010-022410-11-NL
CCMO	NL33606.068.10
Other	nog niet bekend