Topical sinecatechins ointment in treatment of primary superficial Basal Cell Carcinoma: a double blind, randomized, placebo-controlled trial.

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Primary Objective: To determine whether topical sinecatechins 10% (Veregen®) ointment application can lead to a histological clearance (efficacy) of a superficial basal cell carcinoma.
Secondary Objective(s): To assess compliance and adverse...

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

Summary

ID

NL-OMON40522

Source
ToetsingOnline

Brief title
Green tea ointment trial.

Condition

- Skin neoplasms malignant and unspecified

Synonym
skincancer, Superficial basal cell carcinoma

Research involving
Human

Sponsors and support

Primary sponsor: Medisch Universitair Ziekenhuis Maastricht

Source(s) of monetary or material Support: Farmaceutische Industrie: Will-Pharma,Medigene AG (Munchen, Duitsland),Will-Pharma (Zwanenburg, Nederland)

Intervention

Keyword: Basal cell carcinoma, Sinecatechins, Superficial, Treatment

Outcome measures

Primary outcome

The main study parameter is histological clearance of the target tumour (efficacy). This will be analysed by comparing the proportion of patients with complete histological clearance in the treatment group to placebo group assessed by two independent blinded dermato-pathologists.

Secondary outcome

Compliance, number of local skin reactions, adverse events and serious adverse events and histological effects of treatment with sinecatechins 10% ointment versus placebo.

Study description

Background summary

Basal cell carcinoma (BCC) is the most frequently occurring nonmelanoma skin cancer in Caucasians, representing approximately 80% of cases. Incidence rates for men and women in the Netherlands are 165 and 157 per 100,000 person-years respectively and are still rising 3-10% annually. In 2009, the lifetime risk for developing a first histologically confirmed BCC for men was approximately 1 in 5 (21%) and for women it was 1 in 6 (18%).
A simplified classification of BCC includes the following three histological subtypes: nodular (40,6), superficial (30,7%) and infiltrative BCC (28,7%). Superficial BCCs (sBCCs) differ from the other subtypes as they tend to appear at a younger age, usually occur on the trunk and are often multiple. This subtype has the fastest growing incidence.
A characteristic feature of BCCs is their low risk to metastasize, though if untreated they may induce considerable functional and cosmetic morbidity as

they are locally invasive. Surgery is the first treatment of choice for BCC. However due to the rising incidence and the extensive workload this entails, a non-invasive topical treatment is often chosen for sBCC as they grow down from the epidermis into the superficial dermis and therefore are easily accessible for topical treatment. Photodynamic therapy (PDT), imiquimod cream or 5-fluorouracil cream are available topical treatments for sBCC however their tumour free survival rates are not equal to the higher tumour free survival rates of surgical treatment. Next to the efficacy, the now available topical treatments are associated with local skin reactions at the treatment site, mainly erythema and erosion (imiquimod cream and 5-fluorouracil cream) or pain and burning sensation (PDT). This creates the need for additional or alternative non-invasive topical treatments.

The main exogenous predisposing risk factor of BCC is ultraviolet light exposure. However BCC tumourigenesis is multifactorial. The vast majority of BCCs occur sporadically. Approximately 90% of sporadic BCCs have identifiable mutations in at least one allele of the patched 1 (PTCH1) gene, an inhibitor of the Hedgehog (Hh) signalling pathway. This relieves the inhibition of smoothened (SMO) by PTCH1 and SMO sends signals through a series of interacting proteins, including suppressor of fused (SUFU), resulting in activation of the downstream Gli family of transcription factors, leading to proliferation.
A recent study presents convincing evidence that canonical Wingless-type MMTV integration site (Wnt) signalling pathway is essential for a tumorigenic response to deregulated Hh signalling in skin. Several earlier studies also report a link between the Hh and Wnt pathways in BCC. The canonical Wnt pathway regulates the ability of the *-catenin protein to accumulate and enter the nucleus, where it interacts with proteins and converts them into transcriptional activators, leading to proliferation.
The tumour suppressor gene p53, which controls the intrinsic pro-apoptotic pathway, is mutated in 40% of sporadic BCCs.

The active constituents of green tea are promising because of their supposed anti-BCC-carcinogenesis effects as described by several epidemiological, cell culture and animal studies. The so-called polyphenols known as catechins are the active constituents of green tea and the catechin epigallocatechin-3-gallate (EGCG) is the major and most active catechin. EGCG is thought to have a cytotoxic effect on skin cancer cells and has the availability of inhibition of cell growth and induction of apoptosis. It is also suggested that EGCG plays a role in inactivation of *-catenin signalling, an important component of the WNT pathway.
Sinecatechins 10% ointment (Veregen®) is a standardized extract of green tea leaves of the species Camellia sinensis, containing mainly green tea polyphenols, particularly catechins (more than 85%). The lead catechin in sinecatechins ointment is EGCG. It is approved by the US Food and Drug Administration (FDA) for genital warts in adults.
There are no clinical trials on human subjects with topical EGCG on sBCC yet. With this trial we are the first to try to validate the anti-carcinogenic

potentials of topical EGCG in humans with sBCC. We assess the effectiveness of sinecatechins 10% (Veregen®) versus placebo for the topical treatment of sBCCs.

Study objective

Primary Objective: To determine whether topical sinecatechins 10% (Veregen®) ointment application can lead to a histological clearance (efficacy) of a superficial basal cell carcinoma.

Secondary Objective(s): To assess compliance and adverse reactions (safety). To assess histological effects with additional immunohistochemic stains; Bcl-2 (anti-apoptosis), Ki67 (proliferation).

Study design

Clinical double blind, randomized, placebo-controlled intervention trial

Intervention

21 patients with sinecatechins 10% ointment twice daily for six weeks
21 patients with placebo twice daily for six weeks

Study burden and risks

First visit, punch biopsy, telephonic consultation and surgical excision are part of regular care of superficial basal cell carcinoma. Treatment with sinecatechins ointment or placebo, inclusion visit and two control visits are part of the study.

A potential risk when participating in this study is an allergy for one of the components of the sinecatechins 10% ointment or placebo.
Local skin reactions at application site represent a special safety issue for topically applied treatments. Therefore we will evaluate and describe local skin reactions separately from other adverse events. Local skin reactions can be easily controlled and therefore are acceptable for the subjects. We do not expect any other risks.

Contacts

Public
Medisch Universitair Ziekenhuis Maastricht

P. Debeyelaan 25
Maastricht 6229 HX

NL
Scientific
Medisch Universitair Ziekenhuis Maastricht

P. Debeyelaan 25
Maastricht 6229 HX
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

- Adults aged 18 years or older
- Primary histological proven superficial basal cell carcinoma * 4mm and * 20mm in diameter
- Comorbidities may not interfere with study treatment (evaluated by investigator)
- Capable to understand instructions

Exclusion criteria

- Recurrent sBCC (previous treatment)
- Breast-feeding or pregnant women
- Serious comorbidities
- Use of immunosuppressive medication during the trial period or within 30 days before enrolment
- Patients with genetic skin cancer disorders
- Tumour located in the H zone (high-risk area of face) or scalp (see protocol picture 1)

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	17-11-2014
Enrollment:	42
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Veregen 10% ointment
Generic name:	Sinecatechins 10% ointment
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	13-01-2014
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	23-04-2014
Application type:	First submission

Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	31-07-2014
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	12-08-2014
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	EUCTR2013-005439-26-NL
ClinicalTrials.gov	NCT02029352
CCMO	NL47392.068.13

Study results

Date completed:	24-05-2016
Actual enrolment:	42