Treatment of superficial basal cell carcinoma by topical photodynamic therapy with fractionated 5-aminolevulinic acid 20% versus two stage topical photodynamic therapy with methylaminolevulinate

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To compare effectiveness, costs and patient preferences in the treatment of sBCC with fractionated 5-ALA 20% PDT versus MAL PDT in 2 sessions.

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

Summary

ID

NL-OMON50578

Source
ToetsingOnline

Brief title
Fractionated 5-ALA 20% PDT vs two stage MAL PDT in sBCC

Condition

- Skin neoplasms malignant and unspecified

Synonym
Basal cell carcinoma, skin cancer

Research involving
Human

Sponsors and support

Primary sponsor: Medisch Universitair Ziekenhuis Maastricht
Source(s) of monetary or material Support: Ministerie van OC&W,Stichting Annadal;Maastricht Universitair Medisch Centrum

Intervention

Keyword: 5-aminolevulinic acid, Methylaminolevulinate, Photodynamic therapy, Superficial basal cell carcinoma

Outcome measures

Primary outcome

Treatment failure 5 years after treatment of sBCC with fractionated 5-ALA 20%

PDT versus MAL PDT in 2 sessions.

Secondary outcome

Degree of pain during treatment, side-effects of treatments, patient

preferences and health care costs of treatment with fractionated 5-ALA 20% PDT

versus MAL PDT in 2 sessions.

Study description

Background summary

Basal cell carcinoma throughout the world
Skin cancer is the most common cancer, with basal cell carcinoma (BCC) being the most common form of all skin cancers. There are 44.000 new BCCs each year, and it's incidence is still rising. Of all types of BCC, superficial basal cell carcinoma (sBCC), is the histopathologic subtype with the fastest growing incidence, especially on the trunk in younger patients.It is a common health problem and although there is no chance of metastasis it can lead to more aggressive forms of BCC with the ability to cause serious local destruction.

Treatment options
The DBC (diagnose behandel combinatie) cost price, the amount received for diagnostic and treatment of one BCC, for surgical excision is partly free negotiable between each hospital and health insurances. Only the DBC cost price

of patients whose health insurance has no contract with the hospital is public for everyone. This leads to around 18 million euro (based on a cost price of 400.00 euro for 44.000 new BCCs per year) that is yearly spent on the surgical treatment of BCC in the Netherlands and cost will only increase in future with the growing incidence.
For most BCC subtypes the only effective treatment is surgery but for sBCC other non-invasive treatments like photodynamic therapy (PDT) are suitable. It is well accepted in today*s dermatologic practice that surgical excision can be considered as over-treatment for sBCC. PDT is superior to surgical excision in primary sBCC of any size in low-risk sites. As a consequence unnecessary anaesthesia and incisions are avoided thereby preventing side-effects, such as scars, haematomas or functional disruption, and healthy tissue is preserved. Both 5-aminolevulinic acid (5-ALA) and the more lipophilic methylaminolevulinate (MAL) can be used as a precursor of the photosensitiser. These agents generate an excess of protoporphyrin IX in metabolic active cells, which are illuminated by a specific light source leading to release of reactive oxygen radicals in tissue. The result is apoptosis and necrosis of tumour cells. MAL is a worldwide registered agent for the use of topical PDT in sBCC while 5-ALA is not registered in the European Union. In the Netherlands both fractionated 5-ALA 20% and MAL PDT in 2 sessions are used as treatment for sBCC. Although there are studies showing the effectiveness of both treatment regimens, the effectiveness, costs and patient preferences have never been studied in a prospective randomised trial.

Developments in treatment: photodynamic therapy
PDT has become increasingly implemented in standard care for sBCC in the last years. Nowadays, in the Maastricht University Medical Centre, about 60% of patients are treated with PDT. Similar situations are found in the Erasmus MC Rotterdam and the Vie Curi Medical Centre Venlo. On national level, around two thirds of patients are treated with MAL PDT in 2 sessions and one third with fractionated 5-ALA 20% PDT. Because MAL was first marketed and registered as a treatment option for premalignant and superficial malignancies most hospitals in the Netherlands use this topical agent. However, there is no evidence which of the 2 agents is more (cost-)effective and/ or preferred by patients. 5-ALA 20% PDT versus MAL PDT

There are only a few randomised controlled studies on treatment of the most common skin cancer. Choice of PDT treatment with fractionated 5-ALA 20% or MAL in 2 sessions often depends on the experience and choice of the physician or the availability of the precursor in a hospital. World-wide, most studies are performed with MAL and it has been accepted as the standard of care in PDT. However, according to the literature, the effectiveness in terms of clearance rates is in different studies lower for MAL in two sessions compared to fractionated 5-ALA 20% PDT: 79% versus 97% intention to treat (ITT) after one year in sBCC. Contra dictionary, MAL has the theoretical benefit of being more and faster absorbed in the cell than 5-ALA 20% and, thereby, should generate a higher production of protoporphyrin IX. In addition MAL has higher selectivity

for tumour cells, inducing fewer side-effects in normal tissue. This discrepancy between theoretical working mechanism and clearance rates needs further clinical research of the effectiveness of both treatments.
PDT is a hospital administered treatment modality during which patients have to come to the hospital one day (fractionated 5-ALA 20%) or two days one week apart (MAL in 2 sessions). Patient compliance could be higher with fractionated 5-ALA 20% than with MAL in 2 sessions because patients have to visit the hospital a second time. At some parts of the body patients experience a variable burning pain sensation during PDT which might influence completing the treatment. Kuijpers et al. found no significant differences in pain scores between ALA-PDT in 2 sessions and MAL-PDT in 2 sessions. We expect 5-ALA 20% PDT to have more side-effects in our study as patients are treated twice on the same day.
Furthermore it is important to take into consideration the differences in patient acceptability costs (see *economic evaluation*). A well-designed superiority study comparing the two topical PDT treatment modalities: fractionated 5-ALA 20% (superior) and MAL in 2 sessions will provide the answers needed to establish the position of the two modalities in the treatment of patients with sBCC. Our hypothesis is that 5-ALA 20% is as more effective than MAL PDT with the same potential side-effects. Patients* compliance might be higher in the 5-ALA 20% group treated on one day and health care costs can be reduced by using 5-ALA 20% instead of the more expensive MAL cream. The conclusions from the proposed study can serve as a basis for updating guidelines for the treatment of sBCC to catch up with recent developments in clinical practice.

Study objective

To compare effectiveness, costs and patient preferences in the treatment of sBCC with fractionated 5-ALA 20% PDT versus MAL PDT in 2 sessions.

Study design

Clinical, prospective, randomized, single-blinded multicenter study

Intervention

- 81 patients with fractionated 5-ALA 20% PDT on the same day (2 hour free interval)
- 81 patients with MAL PDT in 2 sessions (1 week interval)

Study burden and risks

There is no burden for patients with sBCC. The will be treated according to regular care like physical examination, photography, punch biopsy and PDT

treatment.

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

Minimal age of 18 years
Histological proven sBCC
Primary sBCC (no previous treatment)
Being able to understand instructions

Exclusion criteria

Age under 18 years
No histological proven sBCC
Recurrent sBCC (previously treated)
Not able to understand instructions
Concomitant disease requiring systematic immunosuppressive treatment
Genetic skin cancer disorders
Pregnant women
Breastfeeding women
Porphyria
Allergy for photosensitizer components

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Masking:	Single blinded (masking used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	30-08-2013
Enrollment:	162
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	5-aminolevulinic acid hydrochloride 20% gel
Generic name:	5-aminolevulinic acid hydrochloride 20% gel
Product type:	Medicine
Brand name:	Metvix 160 mg/g creme
Generic name:	Methyl aminolevulinate (as hydrochloride)

Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	27-09-2012
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	31-01-2013
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	12-06-2014
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	07-07-2014
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	13-12-2016
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	18-05-2020
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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	EUCTR2011-005809-77-NL
ClinicalTrials.gov	NCT01491711
CCMO	NL39661.078.12

Study results

Results posted: 08-03-2022

First publication
08-03-2022