Topical Ingenol mebutate versus 5% 5-fluorouracil versus 5% Imiquimod versus photodynamic therapy in treatment of actinic keratosis: a multi-center randomized efficacy and cost-effectiveness study

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Determine which treatment is the most effective treatment in terms of lesion reduction, costs and patient satisfaction when comparing topical treatment with photodynamic therapy (PDT), 5% 5-fluorouracil (5-FU) cream, 5% Imiquimod (IMI) cream and...

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

Summary

ID

NL-OMON50427

Source
ToetsingOnline

Brief title
IM vs 5% 5-FU vs 5% IMI vs PDT in treatment of AK

Condition

- Skin neoplasms malignant and unspecified

Synonym
actinic keratosis, solar keratosis

Research involving

Human

Sponsors and support

Primary sponsor: Medisch Universitair Ziekenhuis Maastricht
Source(s) of monetary or material Support: ZonMw;goed gebruik geneesmiddelen

Intervention

Keyword: 5-fluorouracil, Actinic keratosis, cost-effectiveness, efficacy, imiquimod, ingenol mebutate, photodynamic therapy

Outcome measures

Primary outcome

Primary outcome measure: treatment success, i.e. the proportion of patients

with *75% lesion reduction in the number of AK lesions counted at baseline in

the treatment area 12 months post final treatment (* 75% patient clearance at

12 months).

Secondary outcome

- Treatment failure: proportion of participants with <75% reduction in number

of AK lesions after 3 and 12 months post final treatment compared to baseline

(<75% patient clearance at 3 and 12 months).

- Treatment success at 3 months post-treatment: proportion of participants with

75% reduction in number of AK lesions at 3 months post final treatment (75%

patient clearance at 3 months).

- Decrease in number AK from baseline per patient, at 3 and 12 months post

final treatment.

- Complete lesion clearance: proportion of lesions with 100% clearance in all

treated patients at 3 and 12 months post final treatment.

- Investigator Global Improvement Indices (IGII) at 3 and 12 months post final

treatment.

- Number of new lesions at 3 and 12 months post final treatment.

- Healthcare/treatment costs

- Side effects

- Patient satisfaction

- Cosmetic outcome

- Treatment compliance, defined as the number of applied treatments as

percentage of the number of prescribed treatments.

- Proportion of patients who develop a SCC in the treatment area during study

follow-up and long-term follow-up.

Study description

Background summary

Skin cancer is the most common cancer in Caucasians and therefore a major public health issue. Its incidence is increasing rapidly. Actinic keratosis (AK) is the most prevalent precancerous chronic skin condition. It can transform into squamous cell carcinoma (SCC). AK*s generally arise in a skin area that has diffuse precancerous damage, a phenomenon called field cancerization. Because of its precancerous character, it is advised to treat AK and herewith prevent development into SCC. The most frequently used field-directed treatments in the Netherlands are photodynamic therapy (PDT), topical 5% f-fluorouracil (5% 5-FU) and topical 5% Imiquimod (5% IMI). Lately another topical product is approved by Dutch healthcare insurances: Ingenol mebutate (IM). Up to date, which treatment the patient will receive, does not rely on evidence-based-medicine, but generally on the preference of the physician. Current national and international guidelines state no clear recommendations for the best choice of therapy. The aim of this study is to investigate what is the most effective field-directed treatment for AK

Study objective

Determine which treatment is the most effective treatment in terms of lesion reduction, costs and patient satisfaction when comparing topical treatment with

photodynamic therapy (PDT), 5% 5-fluorouracil (5-FU) cream, 5% Imiquimod (IMI) cream and ingenol mebutate (IM) gel, in treatment of actinic keratosis (AK)

Study design

Multi-centre randomised controled single blind clinical phase IV trial

Intervention

5% Imiquimod versus 5% 5-fluorouracil versus Ingenol mebutate versus MAL-photodynamic therapy

Study burden and risks

During and post treatment patients will be asked to answer a short questionnaire regarding side effects, experience of the treatment and satisfaction. For the long-term follow-up, one extra visit is necessary.

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

- Patients older than 18 years
- Female in child bearing potential should be using contraceptive measures, during and till 3 months post-treatment
- Fitzpatrick skintype I-IV
- Clinically confirmed diagnosis of AK
- One joint area of minimal 25 cm2 and maximal 100 cm2 of AK
- Minimum of 5 AK lesions within the joint area
- AK Olsen grade I-III
- Location: head/neck area

Exclusion criteria

- Received any kind of treatment for AK in the past 3 months, except for cryosurgery outside the treatment area.
- (N)MSC in target area
- Immuno-comprised status
- Use of immunosuppressant drugs in the past 3 months and / or at time of treatment (inhalation corticosteroids / nasal corticosteroids are permitted)
- Porphyria
- Not able to give informed consent
- Allergy to study drugs or peanut/nut/soy products
- Pregnant and breastfeeding women
- Genetic skin cancer disorders
- No understanding of dutch language

Study design

Design

Study phase:	4
Study type:	Interventional

Masking:	Single blinded (masking used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	11-12-2014
Enrollment:	624
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Aldara
Generic name:	Imiquimod
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Efudix
Generic name:	5-fluorouracil
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Metvix
Generic name:	Methylaminolevulinic acid
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Picato
Generic name:	Ingenol mebutate
Registration:	Yes - NL intended use

Ethics review

Approved WMO

Date:	30-09-2014
Application type:	First submission

Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	10-11-2014
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	09-01-2015
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	03-03-2015
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	25-03-2016
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	03-04-2019
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	06-05-2019
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

ID: 22756
Source: Nationaal Trial Register
Title:

In other registers

Register	ID
EudraCT	EUCTR2014-003691-23-NL
CCMO	NL50621.068.14
OMON	NL-OMON22756

Study results

Date completed:	19-07-2018
Actual enrolment:	624