Multi-centre, randomized, investigator-blind, intra-individual active and vehicle-controlled study, comparing Metvix® Natural Daylight Photodynamic Therapy versus Metvix® conventional Photodynamic Therapy in subjects with actinic keratosis

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Primary efficacy objective:To show the non-inferior efficacy of Metvix® Natural Day Light Photo Dynamic Therapy (NDL-PDT) versus Metvix® conventional Photo Dynamic Therapy (c-PDT) in Subjects with mild and moderate AKs at Week 12 in terms of percent...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Cutaneous neoplasms benign
Study type	Interventional

Summary

ID

NL-OMON38765

Source
ToetsingOnline

Brief title
Study of Metvix® NDL-PDT vs c-PDT in subjects with actinic keratosis

Condition

- Cutaneous neoplasms benign

Synonym
Actinic (solar) Keratoses. Sunspot

Research involving
Human

Sponsors and support

Primary sponsor: Galderma
Source(s) of monetary or material Support: Pharmaceutical Industry: Galderma R&D

Intervention

Keyword: Actinic Keratosis, Natural daylight, Photodynamic therapy

Outcome measures

Primary outcome

The primary efficacy endpoint is the lesion complete response rate, defined as

the percentage of pre-existing and treated lesions at baseline that were

assessed as clear at Week 12.

Secondary outcome

Secondary efficacy endpoints

- Lesion complete response rate for mild lesions only.

- Subject-side complete response rate defined as the percentage of subjects

with all treated lesions clear in the corresponding TA, at Week 12.

- change in lesion severity

- number of new lesion

Primary Safety endpoint

- subject's self assessment of pain at baseline post-PDT procedures

Secondary Safety endpoint

- Incidence and severity of Adverse Events

- skin aspect of lesion in complete response

Other endpoint: weather and light asessment

Study description

Background summary

Actinic keratoses are common cutaneous lesions. They are hyperkeratotic lesions on skin. These cutaneous lesions are superficial. They are due to ultra-violet radiations which damage and disturb the skin cell cycle.
Actinic keratoses are found in high number on areas typically exposed to sun such as face, scalp, arms, neck, and hands. It is a condition of elderly people, with fair skin, mainly men, with outdoors activites during their life.
With ageing of population and growing outdoors leazure activities, the incidence of actinic keratosis is increasing. The reported prevalence is between 11% et 60% depending on world region.
The actinic keratoses are not a serious condition but tey are pre-cancerous lesions requested to be treated due to their risk of transformation into squamous cell carcinoma (non melanoma skin cancer).
Several treatment are available on market, topical, surgical, cryotherapya nd oral. In addition to high efficacy, the preference of patients and physicians patient goes to treatment less painful, well tolerated, not inducing scra, allowing to treat large area at the same time.
The photo-dynamic therapy is tretrecommended as first line treatment for actinic keratoses. It is very efficient allowing treatment of large areas with an excellent cosmesis. This treatment consist of the application of a topical photosentizer then activated by a light source.
The Metvix® is a topical treatment indicated for mild and moderate actinic keratoses. Following application, it penetrates into the skin. It has a high selectivity for neoplasic celles where hit preferably accumulates and transforms into Protoporphyrine IX. Under red light (lamp), a reaction leads to transformation into free radicals causing apoptosis and necrosis of noplasic cells.
Metvix ®photodynamic therapy is attractive but could be consider lenghtly as it request an pplication under occlusion for 3 hours. Some patienst have reported this treatment as painful.
Recently, some clinical studies have showed that Metvix® can be activated with natural daylight, the protoporphyrine IX absorbing several peaks in visible light (505, 540, 580 et 630 nanometers). The Metvix® activatad by the natural daylight shows a similar efficacy when compared to Metvix® activated by red light (lamp) for mild and moderate actinic keratoses. Moreover, the treatment

with natural daylight is reported as less painful for patients, protoporphyrine IX activation being immediate right after its production versus after 3 hours accumulation for activation by red light (lamp).
The aim of this European study multicentric is to confirmed that Metvix® activated by natural daylight has a similar efficacy and is less painful in comparizon to Metvix® activated by red light (lamp) in patients with mild and moderate actinic keratoses.
Moreover to assess sensitivity of the method Metvix® activated by natural daylight , a comparative arm Metvix® placebo activated by red light (lamp) will be tested (ratio 1:6) in this study.
This is a randomised, controlled, intraindividual (right/left) comparative study.
The investigator in charge of assessment will be blinded of treatment received.
A tird party, referenced as procedure operator will be in charge of treatment and ilumination.
This is a multicentric study, including approximately 5 countries in Europe and 15 sites.
120 patients will be enrolled, above 18 years, with symetrical areas in terms of actinic keratoses mild and moderate, on the face or on the scalp and meeting eligibility criteria.
The patients will receive Metvix® activated by the natural daylight on right or left face/scalp and Metvix® activated by red light on contralateral side.

Study objective

Primary efficacy objective:
To show the non-inferior efficacy of Metvix® Natural Day Light Photo Dynamic Therapy (NDL-PDT) versus Metvix® conventional Photo Dynamic Therapy (c-PDT) in Subjects with mild and moderate AKs at Week 12 in terms of percent reduction in lesions count.

Primary safety objective:
To compare the Subject's self-assessment of pain of Metvix® NDL-PDT with that of Metvix® c-PDT.

Study design

This study will be conducted as a multi-centre, randomized, investigator-blind, active and vehicle-controlled, intra-individual study.

This study will compare Metvix* NDL-PDT to Metvix* c-PDT (Group 1).

In addition this study will include a Metvix® NDL-PDT arm versus Metvix® vehicle cream c PDT (Placebo) to assess the sensitivity of the trial (Group 2).

Intervention

The patients will be followed during 12 weeks and will have 3 visits. They will be treated at their first visit and will be assessed at 1 and 12 weeks by the investigator. Subjects will also be requested to complete questionnaires.

Study burden and risks

This clinical study is performed with a product within the indication approved on the market. Related adverse event are known and well described in the SmPC. Basically the possible reactions are due to the toxic effects of the Metvix® activation by the light (photodynamic therapy).
Based on the 3 studies published by Wiegell et al, and on the preliminary results of the Galderma study RD.03.SPR.29102, the use of NDL- PDT is expected to improve the tolerability of the treatment (less pain during illumination) and simplify the use of Metvix® while maintaining a similar efficacy compared to the c- PDT.

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

- Male or female, who is at least 18 years of age or older,
- Clinical diagnosis of mild (Grade 1) and/or moderate (Grade 2) AKs on the face or the scalp on treated areas (TAs) according to Olsen et al scale (1991). (e.g.: thin and/or non-hyperkeratotic AKs),
- Subject with two symmetrical TAs (either two half scalps or two half faces excluding ears, chin, bridge of the nose, eyelids and lips inside the vermillion border): no more than a twofold difference in terms of total number of lesions between the two TAs
- TA comparable in terms of size: 6 by 16 cm at a maximum
- A minimum of 5 AKs (either mild, moderate or both) per TA
- No more than two lesions difference in number of moderate AKs between the two TAs.
- Female of non-childbearing potential, OR female of childbearing potential with a negative urine pregnancy test (UPT).
- If female of childbearing potential, they should:
- have been strictly abstinent 1 month prior to Baseline and agrees to remain abstinent for the duration of the clinical trial,
- and/or agree to use a highly effective and approved contraceptive method(s) during the duration of the clinical trial (bilateral tubal ligation OR combined oral contraceptives (oestrogens and progesterone) or implanted or injectable contraceptives with a stable dose for at least 1 month prior to Baseline OR vasectomized partner for at least 3 months prior to Baseline OR hormonal intra uterine device (IUD) inserted at least 1 month prior to Baseline.

Exclusion criteria

- Subject with clinical diagnosis of at least one severe (Grade 3) AK on TAs according to Olsen et al (1991) scale (e.g. hyperkeratotic AKs),
- Subject with pigmented AK on the TAs,
- Immuno-compromised Subject for idiopathic, disease specific or therapeutic reasons;
- Subject with porphyria,
- Subject with clinical diagnosis of other skin disease (including non-melanoma skin cancer) on the TAs which, in the opinion of the investigator, might interfere with the interpretation of the clinical results,
- Subject with systemic diseases that, in the opinion of the investigator might interfere with the interpretation of the clinical results,
- History of hypersensitivity to nut products (e.g. peanut and almond oil) or soya,
- Subject with a known past history of skin cancer in the TAs
- Past history of skin melanoma
- The Subject has received, applied or taken the following treatments or Procedures within the specified time frame prior to the Baseline visit:
Topical treatment(s) on TAs:
5-Fluorouracil, diclofenac, imiquimod, retinoids, ingenol mebutat (Pep-005) : Duration 12

weeks
Surgical: elliptical excision, excision and reconstructive surgery, Mohs* micrographic surgery, chemical peels/chemosurgery, cryosurgery, dermabrasion: Duration 12 weeks
PDT: Duration 12 weeks
Laser: Duration 12 weeks
Electrocoagulation: Duration 12 weeks
Radiotherapy and UV radiation therapy: Duration 12 weeks
Investigative therapies for Actinic Keratoses: Duration 12 weeks
Alpha-hydroxy acid, salicylic acid ointment, urea: Duration 2 weeks
Systemic treatment(s)
Systemic retinoids: Duration 12 weeks
Immunosuppressive drugs (such as glucocorticoids, cytostatic, antibodies, drugs acting on immunophilins, interferon, opioids , TNF binding proteins, Mycophenolate, small biologics agents):Duration 12 weeks

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Other
Allocation:	Randomized controlled trial
Masking:	Single blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	18-09-2013
Enrollment:	24
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Metvix®

Generic name:	methyl aminolevulinate (as hydrochloride)
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	24-04-2013
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	27-08-2013
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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	EUCTR2013-000973-54-NL
CCMO	NL44221.091.13