Safety and Efficacy of BL 5010 in Removal of Lesions in Patients with Seborrheic Keratosis

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This study is being conducted to provide a preliminary assessment of whether BL-5010 sloughs off SK lesions and has an acceptable safety profile (including no or minimal dermal irritation following the application at the site of the SK lesion)....

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

Summary

ID

NL-OMON33988

Source
ToetsingOnline

Brief title
NA

Condition

- Cutaneous neoplasms benign

Synonym
skin lesions, wart-like spots

Research involving
Human

Sponsors and support

Primary sponsor: BioLineRx Ltd
Source(s) of monetary or material Support: BioLine Rx

Intervention

Keyword: efficacy, Phase 1, safety, seborrheic keratosis

Outcome measures

Primary outcome

To assess whether BL-5010 is safe for use in patients with seborrheic keratosis

(SK)

Secondary outcome

To assess whether BL-5010 induces dermal irritation at the site of the

application of BL-5010

To determine whether BL-5010 completely removes the SK index lesion after one

or two applications of BL-5010

To assess the cosmetic outcome as assessed by the investigator and the patient

at the site of the sloughed-off index lesion

To determine the feasibility of histological examinations of the sloughed-off

index lesion

Study description

Background summary

TCA has been widely used as a peeling agent for the treatment of a number of hyperkeratotic lesions, including seborrheic keratosis, actinic keratosis, solar lentigines, and the signs of photoaging (Chun, 2004). TCA causes coagulative necrosis of cells through extensive protein denaturation and resultant structural cell death. Histologically, TCA peel results in the eradication of solar elastosis, which is replaced by a thickened, homogenized band of dermal collagen, which is complemented by cytologic and architectural normalization of the epidermis.
Formic acid is a caustic acid used in the treatment of common warts and in removal of nits from the scalp (Bhat, 2001). The exact mechanism of action of

formic acid is not known. It probably acts in a manner similar to formalin, which destroys tissue by dehydration. After applying formic acid to warts, the wart becomes slightly whitish in color and the superficial layer peels off, indicating a keratolytic effect.
The anticipated method of action of combined TCA and FA is believed to cause in-situ, in vivo fixation, preservation, and mummification of the lesion by cross linking of the molecules and proteins thus causing slough off of the lesion and potentially enables histolopathological examination and diagnosis. In most cases this result will probably be achieved by a single application of BL-5010, although some lesions may require two applications.
A practitioner applied a mixture of TCA, FA, and water to benign skin lesions of patients and reported the following results. Twenty-seven patients with a total of 55 lesions were treated. Most of the lesions were intradermal nevi (IDN). All of the lesions sloughed off successfully. Ninety three (51/55) lesions sloughed off after a single application of the mixture of TCA, FA, and water. Six (11%) cases of hypopigmentation, 1 (2%) case of hyperpigmentation, and 3 (5%) cases of superficial scarring occurred at the site of the index lesion. Histopathological diagnosis could be performed on all sloughed off lesions except for one that was lost.

BL-5010 is a new, liquid preparation with a proposed indication for the topical treatment of benign lesions of the skin, such as Seborrheic Keratosis. Seborrheic Keratosis (SK) occurs commonly in the older population and frequently causes discomfort or is considered to be cosmetically disturbing. Such lesions can be painful and also tend to become injured and sometimes bleed and/or become infected.
At present, skin lesions that are not suspected to be malignant are treated by methods such as cryotherapy, laser therapy, or electro-cauterization. Such treatment often leads to complications that include pain, bleeding and discharge, as well as infection, blistering, and hematoma. Such complications often necessitate the application of localized antibiotics as well as bandaging, are liable to cause further discomfort to the individual treated, the healing process is liable to be slow and prolonged, and may lead to scarring. Furthermore, cryotherapy, laser therapy, and electro-cauterization destroy the treated skin region making histopathological diagnosis of the skin lesions impossible.
BL-5010 is intended as a convenient treatment for removal of benign lesions of the skin such as SK, which does not necessitate any antiseptic precautions or local anesthesia. In addition the use of BL-5010 is intended to enable histolopathological examination and diagnosis of the lesion, which is not achievable with the use of cryotherapy, laser therapy or electro cauterization.

Study objective

This study is being conducted to provide a preliminary assessment of whether BL-5010 sloughs off SK lesions and has an acceptable safety profile (including no or minimal dermal irritation following the application at the site of the SK

lesion). Furthermore, if BL-5010 does slough off lesions, the cosmetic outcome should be evaluated and, there is a need to provide data as to whether the sloughed-off lesions can be used for histopathological diagnosis.

Study design

This will be an open-label, single-arm, safety and feasibility study of topical application of BL-5010 to be conducted in up to 60 patients with seborrheic keratosis. Patients will be enrolled into the study in stages. For the first two stages, continued enrollment in the next stage will require approval by an independent medical safety officer (IMSO). Two patients will be enrolled in the first stage and, if the IMSO approves continued patient enrollment into the study, an additional eight patients will be enrolled in the second stage. If the IMSO approves continued patient enrollment into the study after the first 10 patients, 15 additional patients will be enrolled in the third stage. When 25 patients have been enrolled and have completed treatment with one or two applications of BL-5010, an interim descriptive analysis will be conducted. Based on the results of the interim analysis the sponsor may either continue to enroll another 35 patients (total of 60 patients) in a fourth stage or terminate the study.

Intervention

Each patient will receive up to two topical administrations of BL-5010 to one SK lesion. The investigator will apply a titrated dose of BL 5010 to the one SK lesion.

Study burden and risks

A burning sensation and dermal irritation at the site of application and possible other local AE's. Following treatment slight changes in color, redness or swelling at the site of application may be noticed. All acids have an irritant effect on mucous membranes and therefore it should be avoided to have contact of BL-5010 with eyes and mucous membranes e.g. lips, nostrils and ears. In case of a brown skin caused by UV radiation, the skin may be subject to changes in pigmentation (skin colour). Similarly, exposure to UV after treatment may lead to post-inflammatory hypopigmentation (loss of skin colour) or hyperpigmentation (darkening of the skin).
Keloid formation at the site of application may happen at a later stage after completion of the study.

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 will be included in the study if they:
1. Are male or post menopausal female Caucasian patients between 18 to 85 years of age who can provide and have signed a written informed consent, and understand and comply with the requirements of the protocol
2. Have at least one SK lesion on the face (except for the first ten patients), scalp (only lesions that are not located within the hairline), trunk, or extremities that is 2.5 to 5 mm at its widest diameter and is not near the eye, nose, or mouth (e.g., investigator judges that the distance between the index lesion and either the eye, nose, or mouth is far enough to prevent BL 5010 causing irritation

Exclusion criteria

Patients will be excluded from the study if they have or meet any of the following criteria:
1. Have no individual SK lesions >2.5 mm that are not separated by at least 2 cm
2. Have no individual SK lesion but have only *collision lesions*

3. Have a history of keloid formation following surgical removal of skin lesions or other forms of dermal injury
4. Have any type of infection (e.g., methicillin-resistant staphylococcus aureus infection, etc.)
5. Are immunocomprised including all transplant patients or patients receiving any chemotherapy
6. Have a known diagnosis of Hepatitis B or C, or HIV
7. Have clinically significant unstable medical problems such as diabetes mellitus, clinically concerning cardiac arrhythmias, arteriosclerotic heart disease, renal insufficiency or failure, history of malignant melanoma, or history of cancer (excluding basal cell carcinoma) within the past 5 years prior to Screening
8. Have a clinically significant laboratory test in the 30-day interval prior to Screening such as a hemoglobin level below 10 gm/dL or an AST or ALT level greater than three times the upper limit of normal, etc.
9. Have been hospitalized for any medical condition within one month prior to Screening
10. Have used illicit drugs of abuse or have a history of alcohol abuse in the 3-month interval prior to Screening
11. Have been exposed to an investigational drug or device within 30 days prior to Screening or is scheduled to receive another investigational drug or device during either the Treatment Phase or Follow-up Evaluation
12. Have taken within the past 6 months or are currently taking any immunomodulatory drugs (e.g., ciclosporine, tacrolimus, etc.), biologic drugs (e.g., infliximab, Enbrel, etc.), or immunosuppressive drugs (e.g., azathioprine, corticosteroids, etc.) unless they have consented to an acceptable washout as follows:
• Systemic treatments (steroids, immune suppressants, etc.) - 1 month washout
• Exposure to ultra-violet light - 1 month washout
• Topical treatments (topical steroids, etc.) - 2 week washout
13. Are fertile men who are not willing to use an acceptable form of contraception. Where male patients have a female partner of childbearing potential, the female partner should use two different but effective forms of contraception.;Acceptable forms of effective contraception include:
• a. Established use of oral, injected or implanted hormonal methods of contraception
• b. Placement of an intrauterine device (IUD) or intrauterine system (IUS)
• c. Barrier methods of contraception: Condom or Occlusive cap (diaphragm or cervical/vault caps) with spermicidal foam/gel/film/cream/suppository
• d. Male sterilisation (with the appropriate post-vasectomy documentation of the absence of sperm in the ejaculate)
• e. True abstinence: When this is in line with the preferred and usual lifestyle of the patient;Males should use a barrier method during and for 3 months after their last dose of study drug, unless they are sterilized, in which case a period of 7 days can be applied.;For inclusion into the study female patients must:
• be postmenopausal for at least 1 year, OR
• have had a bilateral oopherectomy and/or hysterectomy, OR
• have had a bilateral tubal ligation or otherwise be incapable of pregnancy;The following lesions cannot be used as the *index lesion*:
1. Actinic keratosis, warts, condylomata acuminatum, or molluscum contagiosum
2. Skin lesions such as dysplastic nevi, Spitz nevi, etc.

3. Scalp lesions within the hairline

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	29-10-2009
Enrollment:	30
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	BL-5010
Generic name:	nvt

Ethics review

Approved WMO Date:	08-01-2009
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	27-08-2009
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Approved WMO Date:	09-11-2009
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	30-12-2009
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	21-01-2010
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	EUCTR2008-006890-34-NL
CCMO	NL25870.078.08