A Phase 2, Randomized, Vehicle-Controlled, Double-Blind, Proof-of-Concept Study to Evaluate Efficacy and Safety of Topical Ionic Contra-viral Therapy (ICVT) Comprised of Digoxin and Furosemide in Cutaneous Warts

Published: 21-11-2014
Last updated: 21-04-2024

Primary objective: • To assess efficacy of CLS003 in reduction of wart area after six weeks of treatment when applied to cutaneous warts (common or plantar)• To evaluate the activity of the ionic contra-viral therapy CLS003, in a HPV biomarker after...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Epidermal and dermal conditions
Study type	Interventional

Summary

ID

NL-OMON41194

Source
ToetsingOnline

Brief title
Efficacy and safety of ICVT in healthy volunteers with warts

Condition

- Epidermal and dermal conditions

Synonym
Cutaneous warts

Research involving

Human

Sponsors and support

Primary sponsor: Centre for Human Drug Research
Source(s) of monetary or material Support: Cutanea Life Sciences

Intervention

Keyword: Efficacy, Ionic Contra Viral Therapy, Safety, Warts

Outcome measures

Primary outcome

Pharmacodynamic / efficacy endpoints

Pharmacodynamic effects of CLS003 will be assessed at the time points indicated

in the Visit and

Assessment Schedule (Table 1) by

• Morphological wart assessment on-site;

• Wart size and morphology assessment by standardized clinical photography;

• HPV viral load assessment of target lesions by quantitative PCR including HPV

genotyping in swabs and biopsies.

• Percent reduction in wart area at Week 6 to baseline

• Percent reduction in wart area at follow-up Weeks 10 and 14 to baseline

• Change in the HPV viral load (nominal, natural log transformed, and natural

log of viral load per DNA copies) as determined by qPCR at Weeks 0, 2,4,6, 10

and 14 to baseline

• Mean HPV viral load (nominal, natural log transformed, and natural log of

viral load per DNA copies)at treatment weeks and overall

• Percent clearance of warts

Secondary outcome

Tolerability / safety endpoints

Adverse events (AE) will be collected throughout the study, at every study

visit. Vital signs will be collected at baseline and weeks 1, 4, 6, 10 and 14.

Plasma digoxin levels will be determined by therapeutic drug monitoring (TDM)

at week 2, week 4 and week 6. ECGs will be performed at screening and week 14

(EOS).

Study description

Background summary

Cutanea Life Sciences (CLS) is investigating various formulations with digoxin and furosemide as a potential treatment for HPV infections of skin and other similar tissue. The anti-viral activity of digoxin and furosemide has been demonstrated in several in-vitro studies conducted by CLS. Both drugs prompted antiviral effects by extracellular K+; these effects were most potent when digoxin and furosemide were used in combination.
This new approach, described as Ionic Contra-Viral Therapy (ICVT), is suggested to be most effective via local application. One potential viral target of ICVT is human papillomavirus (HPV) in associated cutaneous and mucosal lesions. While there are multiple potential clinical indications, this first study will focus on cutaneous warts.
Current clinical treatments for HPV infections mainly involve lesion destruction. The usual first line treatments are wart paints containing salicylic acid and / or lactic acid and cryotherapy, usually with liquid nitrogen. However, current available treatments are considered unsatisfactory and there is an unmet need to develop drugs with greater efficacy and specificity.
Specifically, the ionic properties of digoxin and furosemide were noted to inhibit the K+ influx on which DNA viruses rely for replication. These drugs interact with the cell membrane ion co-transporters Na+/K+-ATPase and Na+-K+-2Cl- co-transporter-1. This controlled depletion of cellular K+ has the potential to broaden the spectrum of antiviral activity.
This study is intended to utilize an efficient biomarker and pharmacokinetic study design to assess safety and to evaluate ICVT as a

potential treatment for HPV-associated conditions in a small group of healthy subjects as a pilot study. Because clinical outcomes
(i.e. clearance of the lesion) often require lengthy treatment / observation periods the study design will utilize measurements of HPV
viral load as a biomarker of anti-viral effect.

Study objective

Primary objective:
• To assess efficacy of CLS003 in reduction of wart area after six weeks of treatment when applied to cutaneous warts (common or plantar)
• To evaluate the activity of the ionic contra-viral therapy CLS003, in a HPV biomarker after six weeks of treatment, and after four and eight weeks of post-treatment follow-up, when applied to cutaneous warts (common or plantar), as assessed by:
o Changes from pretreatment in wart area
o Clinical assessments of the wart morphology
o Changes from pre-treatment in the exploratory HPV quantitative biomarker
• To evaluate the changes in wart dimensions and morphology relative to the specific HPV genotypes, and HPV viral load at pre-treatment (baseline)

Secondary objective:
• To evaluate the safety and tolerability of CLS003 when applied to cutaneous warts for up to six weeks

Study design

This is a A Phase 2, Randomized, Vehicle-Controlled, Double-Blind, Proof-of-Concept Study to Evaluate Efficacy and Safety of Topical Ionic Contra-viral Therapy (ICVT) Comprised of Digoxin and Furosemide in Cutaneous Warts.

Intervention

Subjects will administer a gel containing a dose of 10-25mg per wart. De gel will contain either 0.125% furosemide (w/w), 0,125% digoxin (w/w), a combination of digoxin 0.125% (w/w) and furosemide 0.125% (w/w) or solely the vehicle.

Study burden and risks

CLS003 has been investigated in a prior phase I study conducted in twelfth (12) healthy volunteers with cutaneous warts. Subjects were treated on 7 consequetive days. Plasma levels of furosemide en digoxin were below the limit of quantification, indicating that CLS iss only marginally absorbed. CLS was well tolerated and no serious adverse events occured. The most common reported

treatment emergent adverse events were all mild in severity and included headache, application site erythema and application site pruritus.

CLS003 seems to be a quite safe product and subtherapeutic doses will be administered. Nevertheless, we have implemented the following precautionary measures;
• Subjects who have any current and / or recurrent pathologically relevant skin infections/illness in the treatment area other than common warts (with the exception of herpes simplex virus labialis) are excluded from study participation;
• Subjects who have any current uncontrolled infection will be excluded from study participation;
• Subjects with a known sensitivity to any of the investigational product ingredients, including digoxin and furosemide are excluded from study participation;
Thus, in this study the subjects will only receive sub-therapeutic doses of test product and the subjects will be screened thoroughly prior to study enrolment.

Contacts

Public
Centre for Human Drug Research

Zernikedreef 8
Leiden 2333CL
NL
Scientific
Centre for Human Drug Research

Zernikedreef 8
Leiden 2333CL
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1.Healthy subjects (male, non-pregnant female), 18 to 65 years of age, inclusive. (Healthy status is defined by absence of evidence of any active or chronic disease following a detailed medical and surgical history, a complete physical examination including vital signs,12-lead ECG, haematology, blood chemistry, and urinalysis.);;2.Body mass index (BMI) between 18 and 30 kg/m2, inclusive;;3.Fitzpatrick skin type I-II-III-IV;;4.Capable of tolerating treatment;;5.Free of clinical significant systemic or dermatologic disorder, which, in the opinion of the investigator, will interfere with the study results or increase the risk of Adverse Events;6. Have at least 2 (non-subungual) common warts or at least 2 (non-subungual) plantar warts on non-genital, non-facial skin of which at least 2 are 3mm in diameter in their longest dimensions on the plane of the skin ;7.If female of childbearing potential, have a negative urine pregnancy test at Screening/Day 1, and is willing to use effective contraception during the study (i.e. oral, implanted, injectable, IUD, diaphragm, condom, tubal ligation, abstinence, or are in a monogamous relationship with a partner who has had a vasectomy);;8.Able to participate and willing to give written informed consent and to comply with the study restrictions;;9.Ability to communicate well with the investigator in the Dutch language;;10.Free of any clinical significant systemic or dermatologic disorder, which, in the opinion of the investigator, will interfere with the study results or increase the risk of Adverse Events;;11.Willing to refrain from using cosmetics or other topical products in the treatment area, or prohibited medications for the duration of the study;;12.Agree not to use any wart-removing product (prescription or over-the-counter) other than the study product during the course of the study

Exclusion criteria

Eligible subjects must meet none of the following exclusion criteria:;1.Any clinically significant abnormality as determined by medical history taking and physical examinations obtained during the screening visit that in the opinion of the investigator would interfere with the study objectives or compromise subject safety;;2.For women: a positive pregnancy test and/or nursing at screening or women who plan to become pregnant or are breastfeeding.;3.A positive test for drugs of abuse at screening;;4.History of alcohol or illicit drug abuse (alcohol abuse defined as alcohol consumption > 28 units/week);;5.Positive test results for Hepatitis B, Hepatitis C or HIV;;6.Have used salicylic acid or any other over-the-counter wart-removing product in the treatment area within 30 days prior to enrolment;;7.Have received cryotherapy in the treatment area within 60 days prior to enrolment;;8.Have required systemic intake of immunosuppressive or immunomodulatory medication (including oral or parenteral corticosteroids) within 30 days prior to enrolment or

during the course of the study. Routine use of inhaled or intranasal corticosteroids during the study is allowed; ;9.Have any current and / or recurrent pathologically relevant skin infections in the treatment area other than common warts (with the exception of herpes simplex virus labialis);;10.Have a known sensitivity to any of the investigational product ingredients, including digoxin and furosemide;;11.Clinically relevant abnormal laboratory results, ECG, vital signs, or physical findings at screening that in the opinion of the investigator would interfere with the study objectives or compromise subject safety;;12.Participation in an investigational drug or device study within 3 months prior to screening or more than 4 times in the past year;;13.Any psychological conditions which, in the opinion of the investigator, might create undue risk to the subject or interfere with the subject's ability to comply with the protocol;;14.Not having a general practitioner;;15.Not willing to accept information transfer which concerns participation in the study, or information regarding health, like laboratory results, findings at anamnesis or physical examination and eventual adverse events to and from his general practitioner;;16.Not willing to give permission to have the general practitioner to be notified upon participation in this study;

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):	29-12-2014
Enrollment:	80
Type:	Actual

Ethics review

Approved WMO Date:	21-11-2014
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	26-11-2014
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

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	EUCTR2014-003688-39-NL
CCMO	NL50718.056.14