Clinical trial results:
A phase 2, randomized, vehicle-controlled, double-blind study to explore the efficacy, pharmacodynamics and safety of topical ionic contra-viral therapy (ICVT) comprised of digoxin and furosemide in HPV-induced genital lesions of immunocompromised and immunocompetent patients.

Summary

EudraCT number	2016-000870-39
Trial protocol	NL
Global end of trial date	30 October 2018

Results information

Result version number	v1 (current)
This version publication date	24 September 2022
First version publication date	24 September 2022
Summary attachment (see zip file)	M3. CHDR1607_CSR Summary_6Jun2019 (M3. CHDR1607_CSR Summary_6Jun2019.pdf)

Trial information

Trial identification

Sponsor protocol code	CHDR1607

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-
Other trial identifiers	ToetsingOnline: NL57025.056.17

Notes:

Sponsors

Sponsor organisation name	Cutanea Life Sciences
Sponsor organisation address	1500 Liberty Ridge Drive, Suite 3000, Wayne, United States, PA 19087
Public contact	J. Burggraaf, Centre for Human Drug Research, +31 715246400, clintrials@chdr.nl
Scientific contact	J. Burggraaf, Centre for Human Drug Research, +31 715246400, clintrials@chdr.nl

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	06 June 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	30 October 2018
Global end of trial reached?	Yes
Global end of trial date	30 October 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

- To explore the pharmacodynamics of the ionic contra-viral therapy CLS003 in immunocompromised and immunocompetent patients with benign and premalignant HPV-induced genital lesions.
- To evaluate clinical efficacy of CLS003 compared to vehicle in immunocompromised and immunocompetent patients with benign and premalignant HPV-induced genital lesions

Protection of trial subjects:

CLS003 consists of a combination of the active substances digoxin and furosemide. The cardiac glycoside digoxin and the loop diuretic furosemide are currently market registered drugs for various indications e.g. heart failure / atrium fibrillation and hypertension, respectively. The formulations on the market comprise oral and parenteral route of administration leading to high systemic exposure to both drugs. Consequently, there is a vast amount of pre-clinical and clinical experience with these mechanisms of action. Therefore, drugs of this class can be administered safely to healthy volunteers and patients with a topical formulation. Potential beneficial effects on AGWs and vulvar HSIL are to be explored in this study. Therefore, providing the protocol is adhered to, careful observation and medical management will minimize any associated risk in this study.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 August 2017
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Netherlands: 24
Worldwide total number of subjects	24
EEA total number of subjects	24

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23	0

months)	
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	23
From 65 to 84 years	1
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients will be enrolled into the study following satisfactory completion of a screening visit where eligibility for the study will be checked. Patients will be recruited via media advertisement and via referring gynaecologists and dermatologists.

Pre-assignment

Screening details:

Within 5 weeks prior to study baseline visit (Day 0), patients will undergo a medical screening. Screening will be performed in a fasting state (≥4 hours), and consists of medical history, physical examination, Fitzpatrick skin type classification, 12-lead ECG, vital signs, weight, height, heartrate, blood sampling and urinalysis.

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Carer, Assessor, Data analyst

Arms

Are arms mutually exclusive?	Yes
Arm title	Active drugs

Arm description: -

Arm type	Experimental
Investigational medicinal product name	CLS003 - ICVT topical formulation containing digoxin (0.125%) and furosemide (0.125%)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Gel
Routes of administration	Topical

Dosage and administration details:

ICVT topical formulation containing digoxin (0.125% w/w) and furosemide (0.125%). 0.3mL of gel (approximately 200 mg) applied topically once daily for 6 weeks. (approximately 200 mg).

Arm title	Placebo

Arm description: -

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Gel
Routes of administration	Topical

Dosage and administration details:

Approximately 200 mg/ 0,3ml of vehicle will be applied on all visible lesions.

Number of subjects in period 1	Active drugs	Placebo
Started	18	6
Completed	18	6

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial (overall period)

Reporting group description: -

Reporting group values	Overall trial (overall period)	Total	
Number of subjects	24	24	
Age categorical Units: Subjects			
Adults (18-64 years)	23	23	
From 65-84 years	1	1	
Gender categorical Units: Subjects			
Female	5	5	
Male	19	19	

End points

End points reporting groups

Reporting group title	Active drugs
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Primary: Wart count

End point title	Wart count[1]
End point description:	
End point type	Primary
End point timeframe:	
The warts were counted at every study visit.	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: For results and analysis see attached document.

End point values	Active drugs	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18	6		
Units: number	18	6		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Adverse events (AE) will be collected throughout the study, at every study visit.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	19.1

Reporting groups	
Reporting group title	Active drugs
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Serious adverse events	Active drugs	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 18 (0.00%)	0 / 6 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Active drugs	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 18 (38.89%)	4 / 6 (66.67%)	
Vascular disorders			
Rectal haemorrhage			
subjects affected / exposed	0 / 18 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 18 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
General disorders and administration site conditions			
Application site discomfort			

subjects affected / exposed	6 / 18 (33.33%)	3 / 6 (50.00%)	
occurrences (all)	6	3	
Influenza like illness			
subjects affected / exposed	1 / 18 (5.56%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Reproductive system and breast disorders			
Genital discharge			
subjects affected / exposed	1 / 18 (5.56%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Skin and subcutaneous tissue disorders			
Chronic spontaneous urticaria			
subjects affected / exposed	1 / 18 (5.56%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Psychiatric disorders			
Depressed mood			
subjects affected / exposed	0 / 18 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 18 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	1 / 18 (5.56%)	0 / 6 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported