Clinical trial results:
A randomized, placebo-controlled, evaluator-blinded, study to assess the anti-inflammatory effects of topical erythromycin and clindamycin in patients with inflammatory facial acne

Summary

EudraCT number	2017-003105-18
Trial protocol	NL
Global end of trial date	08 May 2019

Results information

Result version number	v1 (current)
This version publication date	25 March 2022
First version publication date	25 March 2022
Summary attachment (see zip file)	M3. CHDR1732_CSR_24Dec2019 (M3. CHDR1732_CSR_24Dec2019 (2).pdf)

Trial information

Trial identification

Sponsor protocol code	CHDR1732

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Centre for Human Drug Research
Sponsor organisation address	Zernikedreef 8, Leiden, Netherlands, 2333 CL
Public contact	Principal Investigator, Centre for Human Drug Research, +31 715246400, clintrials@chdr.nl
Scientific contact	Principal Investigator, 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	24 December 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	08 May 2019
Global end of trial reached?	Yes
Global end of trial date	08 May 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Objectives
- To evaluate the effects of topically applied erythromycin and clindamycin in patients with facial AV
- To explore skin and faecal microbiota in patients with AV;
- To evaluate the effects of topically applied erythromycin and clindamycin on skin and faecal microbiota;

Protection of trial subjects:

Erythromycin gel and clindamycin lotion have been on the market for over 30 years. They are both known to be safe and well tolerated. For the facial skin punch biopsies the following points were considered in the risk analysis: 1. A small biopsy of 2mm is minimally invasive (smallest possible diameter for maximal, efficient determination of biomarkers and primary study objective) 2. Patients with a Caucasian skin type (Fitzpatrick I and II) have lower chances for postinflammatory hyperpigmentation and hypertrophic scarring or keloid. Patients with a darker skin type will be excluded 3. Patients with positive history of pathological scar formation will be excluded 4. Acne patients have an irregular phenotype of the skin. Very small scars on less visible locations are not prominently apparent (hairline, jawline, lower cheek) 5. Healing of minimal biopsies resolves usually within 6-9 months without sequelae 6. Patients gave separate consent on the ICF for the biopsies, and declared to be informed about the risks and temporary cosmetic burden In conclusion, the investigators and dermatologist assessed the risk minimal for the patient and deemed this necessary to perform to answer the primary objective.

Background therapy: -

Evidence for comparator:

No comparator was used.

Actual start date of recruitment	21 December 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: 30
Worldwide total number of subjects	30
EEA total number of subjects	30

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 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	30
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

21-Dec-2017 - 20-Mar-2019

Pre-assignment

Screening details:

Inclusion criteria: Healthy male and female subjects, 18 to 45 years of age. Mild to moderate inflammatory acne vulgaris on the face and present for at least 6 months
Exclusion criteria: Severe acne where systemic treatment is needed. Use of any topical (anti-acne) medication. History of pathological scar formation.

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Single blind
Roles blinded	Assessor[1]

Blinding implementation details:

Only the assessor was blinded.

Arms

Are arms mutually exclusive?	Yes
Arm title	Erythromycin

Arm description:

Erythromycin 4% topical gel formulation

Arm type	Experimental
Investigational medicinal product name	Erythromycin 4% topical gel formulation
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Gel
Routes of administration	Topical

Dosage and administration details:

BID facial application for 4 weeks.

Arm title	Clindamycin

Arm description:

Clindamycin 1% topical lotion formulation

Arm type	Experimental
Investigational medicinal product name	Clindamycin 1% topical lotion formulation
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cutaneous liquid
Routes of administration	Topical

Dosage and administration details:

BID facial application for 4 weeks.

Arm title	Placebo

Arm description:

70 % topical ethanol solution

Arm type	Placebo

Investigational medicinal product name	70 % topical ethanol solution
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cutaneous/oromucosal solution
Routes of administration	Topical

Dosage and administration details:

BID facial application for 4 weeks.

Notes:

[1] - The roles blinded appear inconsistent with a simple blinded trial.

Justification: Only the assessor was blinded.

Number of subjects in period 1	Erythromycin	Clindamycin	Placebo
Started	10	10	10
Completed	10	10	10

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	30	30	
Age categorical Units: Subjects			
Adults (18-64 years)	30	30	
Gender categorical Units: Subjects			
Female	14	14	
Male	16	16	

End points

End points reporting groups

Reporting group title	Erythromycin
Reporting group description:	
Erythromycin 4% topical gel formulation	
Reporting group title	Clindamycin
Reporting group description:	
Clindamycin 1% topical lotion formulation	
Reporting group title	Placebo
Reporting group description:	
70 % topical ethanol solution	

Primary: Change in Investigator Global Assessment Acne (IGA)

End point title	Change in Investigator Global Assessment Acne (IGA)[1]

End point description:

Acne severity will be assessed at screening and every study visit by the Investigator Global Assessment for facial acne (clear, almost clear, mild, moderate, severe, very severe). This will be done by a treatment blinded evaluator.

End point type	Primary

End point timeframe:

Day 0, day 7, day 14, day 21, day 28 and day 42

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: See uploaded CSR for endpoints and analyses.

End point values	Erythromycin	Clindamycin	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10	10	10	
Units: Number of participants				
Mild	9	7	6	
Moderate	1	4	4	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Signing of informed consent form until end of study.	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	21.1
Reporting groups	
Reporting group title	Erythromycin
Reporting group description: Subjects treated with erythromycin	
Reporting group title	Clindamycine
Reporting group description: Subjects treated with clindamycine	
Reporting group title	Placebo
Reporting group description: Subjects treated with placebo	

Serious adverse events	Erythromycin	Clindamycine	Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Concussion			
alternative dictionary used: MedDRA 18			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Erythromycin	Clindamycine	Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 10 (70.00%)	6 / 10 (60.00%)	7 / 10 (70.00%)
Nervous system disorders			

Migraine			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	2 / 10 (20.00%)
occurrences (all)	0	0	4
headache			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
General disorders and administration site conditions			
Application site dysaesthesia			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Influenza like illness			
subjects affected / exposed	1 / 10 (10.00%)	2 / 10 (20.00%)	3 / 10 (30.00%)
occurrences (all)	1	2	3
Fatigue			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	1 / 10 (10.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	1	1	0
Asthma			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Reproductive system and breast disorders			
Dysmenorrhoea			
subjects affected / exposed	1 / 10 (10.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	1	1	0
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Toothache			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Abdominal pain upper			

subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Skin and subcutaneous tissue disorders			
Skin abrasion			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Eczema eyelids			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	1 / 10 (10.00%)	2 / 10 (20.00%)	2 / 10 (20.00%)
occurrences (all)	1	2	2
Gastroenteritis			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
22 February 2018	-Screening period extended from 14 days to 21 days -Comedo extraction for P. acnes culture is added -Faeces questionnaire added

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported