Clinical trial results:
Effect of CD07805/47 gel in subjects presenting with flushing related to erythematotelangiectatic or papulopustular rosacea

Summary

EudraCT number	2013-005083-26
Trial protocol	DE
Global end of trial date	30 June 2014

Results information

Result version number	v1 (current)
This version publication date	20 February 2016
First version publication date	20 February 2016

Trial information

Trial identification

Sponsor protocol code	RD.03.SPR.40225E

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02300129
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Galderma R&D SNC
Sponsor organisation address	Les Templiers, 2400 Route des Colles , Biot, France, 06410
Public contact	CTA Coordinator, Galderma R&D SNC, +33 (0)493-95-70-85, cta.coordinator@galderma.com
Scientific contact	CTA Coordinator, Galderma R&D SNC, +33 (0)493-95-70-85, cta.coordinator@galderma.com

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	12 February 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	30 June 2014
Global end of trial reached?	Yes
Global end of trial date	30 June 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

− to demonstrate objectively that CD07805/47 0.5% gel is able to prevent a flush induced by a specific trigger (hot water) in controlled condition;
− to demonstrate that CD07805/47 0.5% gel is able to prevent a flush whatever the trigger in everyday life condition;
− to investigate if reduction in redness is associated with a decrease in skin sensations such as heat, burning/stinging, skin tension and sweating;
− to demonstrate that such efficacy on transient redness and sensations takes place in both populations (rosacea type I and rosacea type II).

Protection of trial subjects:

All study participants were required to read and sign an Informed Consent Form.

Background therapy:

Not applicable

Evidence for comparator:

Not applicable

Actual start date of recruitment	14 April 2014
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	Germany: 34
Worldwide total number of subjects	34
EEA total number of subjects	34

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)	32
From 65 to 84 years	2
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants took part in the study at 1 investigative site in Germany from 14 April 2014 to 30 June 2014

Pre-assignment

Screening details:

A total of 46 subjects were screened, 34 were randomised for Period 1, and 32 participated in Period 2.

Period 1

Period 1 title	Flush model
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Investigator, Subject

Arms

Arm title	flush model

Arm description:

The period 1 (1 week) includes cross-over (first and third sessions) and split face design (second session). During this period, the study drugs are applied as follows:
placebo gel on both sides on face;
one side of the face treated with CD07805/47 0.5% gel and the other side with CD07805/47 placebo gel (allocation of treatment on each half-face is randomized)
CD07805/47 0.5% gel on both sides on face

Arm type	Experimental
Investigational medicinal product name	Brimonidine tartrate
Investigational medicinal product code	CD07805/47
Other name	
Pharmaceutical forms	Gel
Routes of administration	Cutaneous use

Dosage and administration details:

CD07805/47 0.5% gel

Investigational medicinal product name	CD07805/47 placebo Gel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Gel
Routes of administration	Cutaneous use

Dosage and administration details:

placebo gel

Number of subjects in period 1[1]	flush model
Started	33
Completed	32
Not completed	1
Consent withdrawn by subject	1

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: One subject was excluded from ITT (intent to treat) population because he didn't perform any efficacy assessment during the study so N=33 instead fo 34 subjects

Period 2

Period 2 title	Cross over
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	No
Arm title	CD07805/47 0.5% gel cross over

Arm description:

The period 2 (4 weeks) corresponds to a cross-over design. The CD07805/47 0.5% gel is applied once a day on the whole face and then the CD07805/47 placebo gel for the 2 following weeks or inversely according to randomisation

Arm type	Experimental
Investigational medicinal product name	Brimonidine tartrate
Investigational medicinal product code	CD07805/47
Other name	
Pharmaceutical forms	Gel
Routes of administration	Cutaneous use

Dosage and administration details:

CD07805 0.5% gel once a day during 2 weeks

Arm title	CD07805/47 Placebo gel cross-over

Arm description:

The period 2 (4 weeks) corresponds to a cross-over design. The CD07805/47 0.5% gel is applied once a day on the whole face and then the CD07805/47 placebo gel for the 2 following weeks or inversely according to randomization

Arm type	Placebo
Investigational medicinal product name	CD07805/47 Placebo gel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Gel
Routes of administration	Cutaneous use

Dosage and administration details:

placebo once a day during 2 weeks

Number of subjects in period 2	CD07805/47 0.5% gel cross over	CD07805/47 Placebo gel cross-over
Started	32	32
Completed	31	31
Not completed	1	1
Adverse event, non-fatal	1	1

Baseline characteristics

Reporting groups	
Reporting group title	Flush model

Reporting group description: -

Reporting group values	Flush model	Total	
Number of subjects	33	33	
Age categorical			
All subjects included in Period 1 (flush model)			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	31	31	
From 65-84 years	2	2	
85 years and over	0	0	
Age continuous			
Units: years			
arithmetic mean	50.2		
standard deviation	± 10.4	-	
Gender categorical			
Units: Subjects			
Female	2	2	
Male	31	31	

End points

End points reporting groups

Reporting group title	flush model

Reporting group description:

The period 1 (1 week) includes cross-over (first and third sessions) and split face design (second session). During this period, the study drugs are applied as follows:
placebo gel on both sides on face;
one side of the face treated with CD07805/47 0.5% gel and the other side with CD07805/47 placebo gel (allocation of treatment on each half-face is randomized)
CD07805/47 0.5% gel on both sides on face

Reporting group title	CD07805/47 0.5% gel cross over

Reporting group description:

The period 2 (4 weeks) corresponds to a cross-over design. The CD07805/47 0.5% gel is applied once a day on the whole face and then the CD07805/47 placebo gel for the 2 following weeks or inversely according to randomisation

Reporting group title	CD07805/47 Placebo gel cross-over

Reporting group description:

The period 2 (4 weeks) corresponds to a cross-over design. The CD07805/47 0.5% gel is applied once a day on the whole face and then the CD07805/47 placebo gel for the 2 following weeks or inversely according to randomization

Primary: total number of flushes for each 2-week period in Period 2

End point title	total number of flushes for each 2-week period in Period 2

End point description:

The primary efficacy endpoint of this study was the total number of flushes reported in the subject diary for each 2-week period in Period 2.

End point type	Primary

End point timeframe:

Day 22 Day 36/Early termination

End point values	CD07805/47 0.5% gel cross over	CD07805/47 Placebo gel cross-over		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31[1]	31[2]		
Units: flushes count				
arithmetic mean (standard deviation)	15.3 (± 12.1)	16.3 (± 14)		

Notes:

[1] - One subject was excluded from ITT (Intent to treat) population (no efficacy assessment performed)
[2] - One subject was excluded from ITT (Intent to treat) population (no efficacy assessment performed)

Statistical analyses

Statistical analysis title	CD07805/47 0.5% gel vs CD07805/47 Placebo gel

Statistical analysis description:

31 subjects were in this analysis based on 62 values

Comparison groups	CD07805/47 0.5% gel cross over v CD07805/47 Placebo gel cross-over

Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.742 [3]
Method	ANOVA

Notes:

[3] - P value associated to treatment effect in the model. Study design with a power of 80% and a type I error at 5 % (two-sided)
Analysis of variance including sequence, subject (sequence), period and treatment as factor in the model.

Adverse events

Adverse events information

Timeframe for reporting adverse events:

The collection of AEs is from the time that a subject signs the ICF to their final visit. Adverse event reporting additional description:

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	16.0

Reporting groups

Reporting group title	Split Face design Period 1
Reporting group description: -	
Reporting group title	Cross over design period 1
Reporting group description: -	
Reporting group title	Cross-over design Period 2

Reporting group description: -

Serious adverse events	Split Face design Period 1	Cross over design period 1	Cross-over design Period 2
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 33 (0.00%)	0 / 34 (0.00%)	0 / 32 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

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

Non-serious adverse events	Split Face design Period 1	Cross over design period 1	Cross-over design Period 2
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 33 (6.06%)	1 / 34 (2.94%)	5 / 32 (15.63%)
Nervous system disorders			
Headache	Additional description: non cutaneous adverse event		
subjects affected / exposed	0 / 33 (0.00%)	0 / 34 (0.00%)	1 / 32 (3.13%)
occurrences (all)	0	0	1
Eye disorders			
erythema of eyelid	Additional description: Adverse event not related to CD07805/47 0,5% gel		
subjects affected / exposed	0 / 33 (0.00%)	0 / 34 (0.00%)	1 / 32 (3.13%)
occurrences (all)	0	0	1
Gastrointestinal disorders			

Cheilitis	Additional description: Adverse event not related to CD07805 0.5% gel		
subjects affected / exposed	0 / 33 (0.00%)	0 / 34 (0.00%)	1 / 32 (3.13%)
occurrences (all)	0	0	1
Oral herpes	Additional description: Adverse event not related to CD07805/47 0.5% gel		
subjects affected / exposed	0 / 33 (0.00%)	0 / 34 (0.00%)	1 / 32 (3.13%)
occurrences (all)	0	0	1
Gastroenteritis	Additional description: Non cutaneous adverse event		
subjects affected / exposed	0 / 33 (0.00%)	0 / 34 (0.00%)	1 / 32 (3.13%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
erythema and skin tightness	Additional description: cutaneous adverse event related to CD07805/47 0.5% gel		
subjects affected / exposed	0 / 33 (0.00%)	1 / 34 (2.94%)	0 / 32 (0.00%)
occurrences (all)	0	2	0
erythema, papules and pruritus	Additional description: During the split face design period 1, cutaneous adverse events were related to CD07805 placebo gel During the cross over design period 2, adverse events of special interest were related to CD07805/47 0.5% gel leading to subject discontinuation		
subjects affected / exposed	2 / 33 (6.06%)	0 / 34 (0.00%)	1 / 32 (3.13%)
occurrences (all)	6	0	3

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

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

none reported

Notes: