Clinical trial results:
A Multi-Center, Randomized, Double-Blind, Parallel-Group Vehicle Controlled Study To Compare The Efficacy And Safety Of CD5789 50g/g Cream Versus Vehicle Cream In Subjects With Acne Vulgaris

Summary

EudraCT number	2016-002860-15
Trial protocol	DE CZ
Global end of trial date	14 November 2017

Results information

Result version number	v1 (current)
This version publication date	06 April 2019
First version publication date	06 April 2019
Summary attachment (see zip file)	Synopsis (RD.06.SRE.18251.pdf)

Trial information

Trial identification

Sponsor protocol code	RD.06.SPR.18251

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02566369
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Galderma S.A.
Sponsor organisation address	Avenue Gratta-Paille 2, Lausanne, Switzerland, 1018
Public contact	CTA Coordinator, Galderma S.A., +41 21 642 78 00, cta.coordinator@galderma.com
Scientific contact	CTA Coordinator, Galderma S.A., +41 21 642 78 00, cta.coordinator@galderma.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-001492-PIP01-13
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes
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	17 January 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	14 November 2017
Global end of trial reached?	Yes
Global end of trial date	14 November 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Multi-center, randomized, double blind, vehicle controlled study, to assess the efficacy and safety of CD5789 50 microgram/g cream in subjects 9 years of age and older with moderate acne vulgaris on face and trunk, when applied once daily for 12 weeks.

Protection of trial subjects:

All subjects were required to read and sign an informed consent. The subjects could withdraw from the treatment at any time and for any reason.

Background therapy:

Not applicable

Evidence for comparator:

Not applicable

Actual start date of recruitment	30 November 2015
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: 124
Country: Number of subjects enrolled	Hungary: 88
Country: Number of subjects enrolled	United States: 802
Country: Number of subjects enrolled	Canada: 139
Country: Number of subjects enrolled	Puerto Rico: 55
Worldwide total number of subjects	1208
EEA total number of subjects	212

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)	19
Adolescents (12-17 years)	573
Adults (18-64 years)	616
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 1208 subjects were enrolled and exposed to CD5789 50 microgram/g cream or vehicle cream for 12 weeks. A minimum of 14 days between Screening and Baseline visit (+/- 3 days). Study visits for Weeks 1,2,4,8 (+/- 3 days) and Week 12 (+/- 5 days).

Pre-assignment

Screening details:

Male or Female subjects, 9 years of age and older, with moderate acne vulgaris, with at least 20 inflammatory lesions and 25 non-inflammatory lesions for face, and , at least 20 inflammatory and 20-100
non-inflammatory on the trunk. No more than 1 nodule on the face and trunk. Inclusion criteria for trunk was optional for subjects ages 9 to 11.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	CD5789 50 microgram/g cream

Arm description: -

Arm type	Experimental
Investigational medicinal product name	CD5789 50 microgram/g cream
Investigational medicinal product code	CD5789
Other name	trifarotene
Pharmaceutical forms	Cream
Routes of administration	Cutaneous use

Dosage and administration details:

A thin layer of study product cream (one pump actuation) was applied to the face region: forehead, nose, chin, area between the nose and upper lip, and each cheek. Avoid application proximity in/close to eyes, angles of mouth, lips and mucous membranes.

A thin layer of study product cream (two pump actuations) was applied to the truncal region: right and left upper back, right and left shoulders and right and left anterior chest, self-reachable by the subject. Avoid application to axillary region, anterior and posterior neck.

Apply daily, in the evening, for 12 weeks, after washing the treated areas with preferred mild or soapless cleanser and allow to fully dry before applying study drug. The use of non comedogenic moisturizer was encouraged to be used as desired but respecting an interval of 1 hour (before and after) study drug application.

Arm title	Vehicle cream

Arm description: -

Arm type	Placebo
Investigational medicinal product name	Vehicle cream
Investigational medicinal product code	N/A
Other name	placebo
Pharmaceutical forms	Cream
Routes of administration	Cutaneous use

Dosage and administration details:

A thin layer of study product cream (one pump actuation) was applied to the face region: forehead,

nose, chin, area between the nose and upper lip, and each cheek. Avoid application proximity in/close to eyes, angles of mouth, lips and mucous membranes.

A thin layer of study product cream (two pump actuations) was applied to the truncal region: right and left upper back, right and left shoulders and right and left anterior chest, self-reachable by the subject. Avoid application to axillary region, anterior and posterior neck.

Apply daily, in the evening, for 12 weeks, after washing the treated areas with preferred mild or soapless cleanser and allow to fully dry before applying study drug. The use of non comedogenic moisturizer was encouraged to be used as desired but respecting an interval of 1 hour (before and after) study drug application.

Number of subjects in period 1	CD5789 50 microgram/g cream	Vehicle cream
Started	612	596
Completed	540	535
Not completed	72	61
Consent withdrawn by subject	39	32
Adverse event, non-fatal	14	1
Protocol violation	3	1
Other	2	1
Pregnancy	-	2
Lost to follow-up	13	23
Lack of efficacy	1	1

Baseline characteristics

Reporting groups	
Reporting group title	CD5789 50 microgram/g cream
Reporting group description: -	
Reporting group title	Vehicle cream
Reporting group description: -	

Reporting group values	CD5789 50 microgram/g cream	Vehicle cream	Total
Number of subjects	612	596	1208
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	10	9	19
Adolescents (12-17 years)	304	269	573
Adults (18-64 years)	298	318	616
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	19.6	19.3	
standard deviation	± 6.88	± 5.89	-
Gender categorical Units: Subjects			
Female	305	324	629
Male	307	272	579

End points

End points reporting groups	
Reporting group title	CD5789 50 microgram/g cream
Reporting group description: -	
Reporting group title	Vehicle cream
Reporting group description: -	

Primary: Absolute Change in Facial Inflammatory Lesion Count	
End point title	Absolute Change in Facial Inflammatory Lesion Count
End point description:	
End point type	Primary
End point timeframe:	
Baseline to Week 12	

End point values	CD5789 50 microgram/g cream	Vehicle cream		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	612	596		
Units: Absolute Change in Lesion Counts				
least squares mean (standard error)	-19.0 (± 0.50)	-15.4 (± 0.51)		

Statistical analyses

Statistical analysis title	Absolute Change in Inflammtory Lesion Count (Face)
Comparison groups	CD5789 50 microgram/g cream v Vehicle cream
Number of subjects included in analysis	1208
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Least Square Mean Difference
Point estimate	-3.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.9
upper limit	-2.2

Primary: Absolute Change in Facial Non Inflammatory Lesions

End point title	Absolute Change in Facial Non Inflammatory Lesions

End point description:

End point type	Primary

End point timeframe:

Baseline to Week 12

End point values	CD5789 50 microgram/g cream	Vehicle cream		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	612	596		
Units: Absolute Change in Lesion Counts				
least squares mean (standard error)	-25.0 (± 0.87)	-17.9 (± 0.87)		

Statistical analyses

Statistical analysis title	Absolute Change in Non-Inflammatory (Face)
Comparison groups	CD5789 50 microgram/g cream v Vehicle cream
Number of subjects included in analysis	1208
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Least Square Mean Difference
Point estimate	-7.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.4
upper limit	-4.8

Primary: IGA Success Rate (Face)

End point title	IGA Success Rate (Face)

End point description:

End point type	Primary

End point timeframe:

Baseline to Week 12

End point values	CD5789 50 microgram/g cream	Vehicle cream		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	612	596		
Units: Percentage				
number (not applicable)	29.4	19.5		

Statistical analyses

Statistical analysis title	IGA Success Rate
Comparison groups	CD5789 50 microgram/g cream v Vehicle cream
Number of subjects included in analysis	1208
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	9.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	4.8
upper limit	14.8
Variability estimate	Standard deviation

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline to Week 12

Adverse event reporting additional description:

Overall Summary of Treatment Emergent Adverse Events

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18.0

Reporting groups

Reporting group title	CD5789 50 microgram/g cream
Reporting group description: -	
Reporting group title	Vehicle cream
Reporting group description: -	

Serious adverse events	CD5789 50 microgram/g cream	Vehicle cream	
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 617 (0.65%)	2 / 591 (0.34%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Facial bones fracture			
subjects affected / exposed	1 / 617 (0.16%)	0 / 591 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Procedural dizziness			
subjects affected / exposed	1 / 617 (0.16%)	0 / 591 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congenital, familial and genetic disorders			
Hereditary angioedema			
subjects affected / exposed	0 / 617 (0.00%)	1 / 591 (0.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			

Urinary tract infection			
subjects affected / exposed	0 / 617 (0.00%)	1 / 591 (0.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Infectious mononucleosis			
subjects affected / exposed	1 / 617 (0.16%)	0 / 591 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	1 / 617 (0.16%)	0 / 591 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atypical pneumonia			
subjects affected / exposed	0 / 617 (0.00%)	1 / 591 (0.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	CD5789 50 microgram/g cream	Vehicle cream	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	209 / 617 (33.87%)	123 / 591 (20.81%)	
Injury, poisoning and procedural complications			
Sunburn			
subjects affected / exposed	27 / 617 (4.38%)	5 / 591 (0.85%)	
occurrences (all)	27	5	
Nervous system disorders			
Headache			
subjects affected / exposed	6 / 617 (0.97%)	12 / 591 (2.03%)	
occurrences (all)	6	12	
General disorders and administration site conditions			
Application site irritation			
subjects affected / exposed	66 / 617 (10.70%)	4 / 591 (0.68%)	
occurrences (all)	66	4	

Application site puritus			
subjects affected / exposed	24 / 617 (3.89%)	8 / 591 (1.35%)	
occurrences (all)	24	8	
Skin and subcutaneous tissue disorders			
Skin irritation			
subjects affected / exposed	8 / 617 (1.30%)	0 / 591 (0.00%)	
occurrences (all)	8	0	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	24 / 617 (3.89%)	27 / 591 (4.57%)	
occurrences (all)	24	27	
Upper respiratory tract infection			
subjects affected / exposed	10 / 617 (1.62%)	8 / 591 (1.35%)	
occurrences (all)	10	8	
Influenza			
subjects affected / exposed	6 / 617 (0.97%)	9 / 591 (1.52%)	
occurrences (all)	6	9	
Sinusitis			
subjects affected / exposed	6 / 617 (0.97%)	1 / 591 (0.17%)	
occurrences (all)	6	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
20 September 2016	Increase in the number of study centers to 120 centers due to slow recruitment
06 March 2017	1.Increased the number of study centers in order to meet study completion deadline: a. 40 new sites in US, Canada and Puerto Rico b. 18 new sites in Europe, Germany and Hungary 2.Extended recruitment duration to 23 months

Notes:

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.

Not applicable

Notes: