

**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	2015-002540-13
Trial protocol	HU ES CZ
Global end of trial date	12 May 2017

Results information

Result version number	v1 (current)
This version publication date	11 January 2020
First version publication date	11 January 2020
Summary attachment (see zip file)	Synopsis (RD.06.SRE.18252.pdf)

Trial information**Trial identification**

Sponsor protocol code	RD.06.SPR.18252
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02556788
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)	EMA-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	31 October 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	07 February 2017
Global end of trial reached?	Yes
Global end of trial date	12 May 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	23 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	Poland: 188
Country: Number of subjects enrolled	Romania: 129
Country: Number of subjects enrolled	Spain: 28
Country: Number of subjects enrolled	Czech Republic: 123
Country: Number of subjects enrolled	Hungary: 140
Country: Number of subjects enrolled	Russian Federation: 181
Country: Number of subjects enrolled	Ukraine: 145
Country: Number of subjects enrolled	United States: 278
Worldwide total number of subjects	1212
EEA total number of subjects	608

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)	15
Adolescents (12-17 years)	555
Adults (18-64 years)	642
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 1212 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 Trial (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:

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Number of subjects in period 1	CD5789 50 microgram/g cream	Vehicle cream
Started	602	610
Completed	558	573
Not completed	44	37
Consent withdrawn by subject	18	21
Adverse event, non-fatal	9	1
Protocol violation	4	1
Other	-	1
Pregnancy	1	1
Other reasons	3	-
Lost to follow-up	9	11
Lack of efficacy	-	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	602	610	1212
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)	9	6	15
Adolescents (12-17 years)	267	288	555
Adults (18-64 years)	326	316	642
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	19.6	19.9	
standard deviation	± 6.20	± 6.38	-
Gender categorical Units: Subjects			
Female	357	338	695
Male	245	272	517

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 Inflammatory Lesion Count (Face)

End point title	Absolute Change in Inflammatory Lesion Count (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	602	610		
Units: Absolute Change in Lesions				
least squares mean (standard error)	-24.2 (± 0.51)	-18.7 (± 0.51)		

Statistical analyses

Statistical analysis title	Change in Facial Inflammatory Lesion Counts
Comparison groups	CD5789 50 microgram/g cream v Vehicle cream
Number of subjects included in analysis	1212
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-5.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.9
upper limit	-4.3
Variability estimate	Standard deviation

Primary: Absolute Change in Non Inflammatory Lesions (Face)

End point title	Absolute Change in Non Inflammatory Lesions (Face)
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End point description:

End point type	Primary
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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	602	610		
Units: Absolute Change in Lesions				
least squares mean (standard error)	-30.1 (± 0.71)	-21.6 (± 0.71)		

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	1212
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-8.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.3
upper limit	-6.6
Variability estimate	Standard deviation

Primary: IGA Success Rate

End point title	IGA Success Rate
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End point description:

End point type	Primary
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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	602	610		
Units: Percentage				
number (not applicable)	42.3	25.7		

Statistical analyses

Statistical analysis title	IGA Success Rate
Comparison groups	CD5789 50 microgram/g cream v Vehicle cream
Number of subjects included in analysis	1212
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	16.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	11.3
upper limit	22
Variability estimate	Standard deviation

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline to Week 12

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	18.0
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Reporting groups

Reporting group title	Vehicle
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Reporting group description: -

Reporting group title	CD5789 50 microgram/gram
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Reporting group description: -

Serious adverse events	Vehicle	CD5789 50 microgram/gram	
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 609 (0.66%)	2 / 602 (0.33%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Ligament Sprain			
subjects affected / exposed ^[1]	1 / 1 (100.00%)	1 / 1 (100.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed ^[2]	1 / 1 (100.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Suicide Attempt			
subjects affected / exposed ^[3]	1 / 1 (100.00%)	1 / 1 (100.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Major Depression			

subjects affected / exposed ^[4]	0 / 1 (0.00%)	1 / 1 (100.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Sinusitis			
subjects affected / exposed ^[5]	1 / 1 (100.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis			
subjects affected / exposed ^[6]	1 / 1 (100.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.

Justification: This is correct as reported.

[2] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.

Justification: This is correct as reported.

[3] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.

Justification: This is correct as reported.

[4] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.

Justification: This is correct as reported.

[5] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.

Justification: This is correct as reported.

[6] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.

Justification: This is correct as reported.

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

Non-serious adverse events	Vehicle	CD5789 50 microgram/gram	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	21 / 609 (3.45%)	45 / 602 (7.48%)	
Investigations			
Blood bilirubin increased			
subjects affected / exposed ^[7]	1 / 1 (100.00%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Blood creatine increased			
subjects affected / exposed ^[8]	1 / 1 (100.00%)	0 / 1 (0.00%)	
occurrences (all)	1	0	

Injury, poisoning and procedural complications			
Sunburn			
subjects affected / exposed ^[9]	0 / 1 (0.00%)	2 / 2 (100.00%)	
occurrences (all)	0	2	
Drug administered at inappropriate site			
subjects affected / exposed ^[10]	0 / 1 (0.00%)	1 / 1 (100.00%)	
occurrences (all)	0	1	
Blood and lymphatic system disorders			
Lymphadenopathy			
subjects affected / exposed ^[11]	0 / 1 (0.00%)	1 / 1 (100.00%)	
occurrences (all)	0	1	
General disorders and administration site conditions			
Application site irritation			
subjects affected / exposed ^[12]	0 / 1 (0.00%)	15 / 15 (100.00%)	
occurrences (all)	0	15	
Application site pruritus			
subjects affected / exposed ^[13]	2 / 2 (100.00%)	5 / 5 (100.00%)	
occurrences (all)	2	5	
Application site pain			
subjects affected / exposed ^[14]	0 / 1 (0.00%)	4 / 4 (100.00%)	
occurrences (all)	0	4	
Application site dryness			
subjects affected / exposed ^[15]	0 / 1 (0.00%)	3 / 3 (100.00%)	
occurrences (all)	0	3	
Application site erosion			
subjects affected / exposed ^[16]	0 / 1 (0.00%)	1 / 1 (100.00%)	
occurrences (all)	0	1	
Application site erythema			
subjects affected / exposed ^[17]	0 / 1 (0.00%)	1 / 1 (100.00%)	
occurrences (all)	0	1	
Eye disorders			
Eyelid exfoliation			
subjects affected / exposed ^[18]	0 / 1 (0.00%)	1 / 1 (100.00%)	
occurrences (all)	0	1	
Eyelid oedema			

subjects affected / exposed ^[19] occurrences (all)	0 / 1 (0.00%) 0	1 / 1 (100.00%) 1	
Gastrointestinal disorders Cheilitis subjects affected / exposed ^[20] occurrences (all)	0 / 1 (0.00%) 0	1 / 1 (100.00%) 1	
Skin and subcutaneous tissue disorders Skin irritation subjects affected / exposed ^[21] occurrences (all) Skin fissures subjects affected / exposed ^[22] occurrences (all)	0 / 1 (0.00%) 0 0 / 1 (0.00%) 0	2 / 2 (100.00%) 2 1 / 1 (100.00%) 1	
Psychiatric disorders Insomnia subjects affected / exposed ^[23] occurrences (all)	0 / 1 (0.00%) 0	1 / 1 (100.00%) 1	
Infections and infestations Herpes simplex subjects affected / exposed ^[24] occurrences (all) Tinea versicolour subjects affected / exposed ^[25] occurrences (all) Oral herpes subjects affected / exposed ^[26] occurrences (all)	0 / 1 (0.00%) 0 0 / 1 (0.00%) 0 1 / 1 (100.00%) 1	1 / 1 (100.00%) 1 1 / 1 (100.00%) 1 0 / 1 (0.00%) 0	

Notes:

[7] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: This is correct as reported.

[8] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: This is correct as reported.

[9] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: This is correct as reported.

[10] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: This is correct as reported.

[11] - The number of subjects exposed to this adverse event is less than the total number of subjects

Justification: This is correct as reported.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
19 January 2017	Major changes included in the Protocol: 1. Increase in the number of investigational centers from 75 to 85 centers 2. Russian Minister of Health request to edit wording of inclusion criteria number 1 to better reflect the age groups. 3. Japan was removed from the region(s)/countries involved in the study
24 February 2017	Major changes included in the PIP: Due to the unexpected slow recruitment for subjects aged less 14 years old and 14 to 17 years old: a. Extension of study completion from October 2016 to August 2017; b. Modification of the agreed paediatric investigation plan to decrease the number of paediatric subjects enrollment. Request was accepted by the Pediatric Committee.

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: