



## Clinical trial results: A Long-Term Safety and Efficacy Study of CD5789 50g/g Cream in Subjects with Acne Vulgaris Summary

EudraCT number	2014-001755-23
Trial protocol	HU CZ
Global end of trial date	23 February 2017

### Results information

Result version number	v1 (current)
This version publication date	05 April 2019
First version publication date	05 April 2019
Summary attachment (see zip file)	Synopsis (RD.06.SRE.18250.pdf)

### Trial information

#### Trial identification

Sponsor protocol code	RD.06.SPR.18250
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#### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02189629
WHO universal trial number (UTN)	-

Notes:

### Sponsors

Sponsor organisation name	Galderma S.A.
Sponsor organisation address	Avenue de 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:

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**Results analysis stage**

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Analysis stage	Final
Date of interim/final analysis	13 April 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	23 February 2017
Global end of trial reached?	Yes
Global end of trial date	23 February 2017
Was the trial ended prematurely?	No

Notes:

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**General information about the trial**

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Main objective of the trial:

Open label study, non-comparative, to evaluate the safety of CD5789 50 microgram/g cream in subjects 9 years of age and older with moderate acne vulgaris on face and trunk. Efficacy was evaluated as a secondary endpoint.

Protection of trial subjects:

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

Background therapy:

Not applicable

Evidence for comparator:

Not applicable

Actual start date of recruitment	23 February 2015
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	12 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

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**Population of trial subjects**

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**Subjects enrolled per country**

Country: Number of subjects enrolled	Czech Republic: 104
Country: Number of subjects enrolled	Germany: 95
Country: Number of subjects enrolled	Hungary: 91
Country: Number of subjects enrolled	United States: 163
Worldwide total number of subjects	453
EEA total number of subjects	290

Notes:

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**Subjects enrolled per age group**

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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)	18
Adolescents (12-17 years)	268
Adults (18-64 years)	167
From 65 to 84 years	0
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details:

A total of 455 subjects were enrolled and 453 were exposed to CD5789 50 microgram/g cream for up to 52 weeks. A minimum of 14 days between Screening and Baseline visit ( +/- 3 days). Study visits for Weeks 1,2,4 and 8 (+/- 3 days). Study visits for Weeks 12,20,26,38, and 52 visits (+/- 5 days).

### Pre-assignment

Screening details:

Male or Female subjects, 9 years of age and older, with moderate acne vulgaris, at least 20 inflammatory lesions and 25 non-inflammatory lesions for the face, and , at least 20 inflammatory and 20 non-inflammatory lesion for 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	Non-randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

Open-label study

### Arms

<b>Arm title</b>	CD5789 50 microgram/gram
Arm description: -	
Arm type	open label
Investigational medicinal product name	Trifarotene
Investigational medicinal product code	CD5789
Other name	
Pharmaceutical forms	Cream
Routes of administration	Cutaneous use

Dosage and administration details:

a thin layer of CD5789 50 microgram/gram cream (one pump actuation) was applied to the face and trunk. Apply daily, in the evening, for 12 weeks, after washing the treated area with a mild cleanser and allow to dry before applying drug. Use of moisturizer was encouraged.

Number of subjects in period 1	CD5789 50 microgram/gram
Started	453
Completed	348
Not completed	105
Consent withdrawn by subject	51
Adverse event, non-fatal	16
Other	12
Pregnancy	1
Lost to follow-up	17
Lack of efficacy	4
Protocol deviation	4



## Baseline characteristics

### Reporting groups

Reporting group title	Overall Trial
Reporting group description: -	

Reporting group values	Overall Trial	Total	
Number of subjects	453	453	
Age categorical			
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)	18	18	
Adolescents (12-17 years)	268	268	
Adults (18-64 years)	167	167	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous			
Units: years			
arithmetic mean	18.3		
standard deviation	± 6.6	-	
Gender categorical			
Units: Subjects			
Female	226	226	
Male	227	227	

### Subject analysis sets

Subject analysis set title	Safety Population
Subject analysis set type	Safety analysis
Subject analysis set description:	
Defined as all subjects who applied the study drug at least once.	

Reporting group values	Safety Population		
Number of subjects	453		
Age categorical			
Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	0		
Children (2-11 years)	18		
Adolescents (12-17 years)	268		
Adults (18-64 years)	167		

From 65-84 years	0		
85 years and over	0		

  

Age continuous			
Units: years			
arithmetic mean	18.3		
standard deviation	± 6.6		
Gender categorical			
Units: Subjects			
Female	226		
Male	227		

## End points

### End points reporting groups

Reporting group title	CD5789 50 microgram/gram
Reporting group description: -	
Subject analysis set title	Safety Population
Subject analysis set type	Safety analysis
Subject analysis set description:	
Defined as all subjects who applied the study drug at least once.	

### Primary: Safety and Local Tolerability Assessments

End point title	Safety and Local Tolerability Assessments <sup>[1]</sup>
End point description:	
Local Tolerability Worst Post Baseline (Face)	
Local Tolerability Worst Post Baseline (Trunk)	
Treatment Emergent Adverse Events	
End point type	Primary
End point timeframe:	
Baseline to Week 52	

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: In this long-term safety study, all efficacy and safety data were analyzed descriptively.

<b>Attachments (see zip file)</b>	Face/Local Tolerability Worst Post Baseline- Face.docx
	Trunk/Local Tolerability Worst Post Baseline- Trunk.docx

### Statistical analyses

No statistical analyses for this end point

### Secondary: Efficacy

End point title	Efficacy
End point description:	
Success rate of IGA at each scheduled time point (face): subjects were considered a success at a particular visit if they had an IGA score of "Clear" (0) or "Almost clear" (1) at that visit and had a grade change of at least 2 from Baseline. Success rate of PGA at each scheduled time point (trunk): subjects were considered a success at a particular visit if they had a PGA score of "Clear" (0) or "Almost clear" (1) at that visit and had a grade change of at least 2 from Baseline.	
For the summary statistics, the categorical variables were summarized by frequency and percentage. No inferential statistical analyses were performed.	
End point type	Secondary
End point timeframe:	
Baseline to Week 52	



## **Statistical analyses**

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No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Baseline to Week 52

Adverse event reporting additional description:

Overall Summary of Treatment Emergent Adverse Events

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	CD5789 50 microgram/g cream
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Reporting group description:

Intent-to-Treat Subjects

Serious adverse events	CD5789 50 microgram/g cream		
Total subjects affected by serious adverse events			
subjects affected / exposed	10 / 453 (2.21%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Investigations			
Liver Functional test abnormal			
subjects affected / exposed	1 / 453 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Post procedural hemorrhage			
subjects affected / exposed	1 / 453 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Complex partial seizures			
subjects affected / exposed	1 / 453 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Complex regional pain syndrome			

subjects affected / exposed	1 / 453 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			
subjects affected / exposed	1 / 453 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Immune system disorders			
Pyelonephritis acute			
subjects affected / exposed	1 / 453 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Crohn's disease			
subjects affected / exposed	1 / 453 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Umbilical hernia repair			
subjects affected / exposed	1 / 453 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Nasal septum deviation			
subjects affected / exposed	1 / 453 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Tonsillar hypertrophy			
subjects affected / exposed	1 / 453 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Appendicitis			

subjects affected / exposed	1 / 453 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

<b>Non-serious adverse events</b>	CD5789 50 microgram/g cream		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	170 / 453 (37.53%)		
Injury, poisoning and procedural complications			
Sunburn			
subjects affected / exposed	27 / 453 (5.96%)		
occurrences (all)	27		
Ligament sprain			
subjects affected / exposed	6 / 453 (1.32%)		
occurrences (all)	6		
Nervous system disorders			
Headache			
subjects affected / exposed	6 / 453 (1.32%)		
occurrences (all)	6		
General disorders and administration site conditions			
Application site pruritus			
subjects affected / exposed	23 / 453 (5.08%)		
occurrences (all)	23		
Application site irritation			
subjects affected / exposed	22 / 453 (4.86%)		
occurrences (all)	22		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	5 / 453 (1.10%)		
occurrences (all)	5		
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	9 / 453 (1.99%)		
occurrences (all)	9		

Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	5 / 453 (1.10%)		
occurrences (all)	5		
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	48 / 453 (10.60%)		
occurrences (all)	48		
Upper respiratory tract infection			
subjects affected / exposed	13 / 453 (2.87%)		
occurrences (all)	13		
Influenza			
subjects affected / exposed	9 / 453 (1.99%)		
occurrences (all)	9		
Infectious mononucleosis			
subjects affected / exposed	5 / 453 (1.10%)		
occurrences (all)	5		
Tonsillitis			
subjects affected / exposed	5 / 453 (1.10%)		
occurrences (all)	5		

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
07 December 2015	<p>Definitions of treated areas: The application of CD5789 50 microgram/g cream on the middle and/or lower back was allowed for safety assessment only, and the definition of SAFT population was redefined to account for this change (i.e., any subjects in the SAF population who also applied the study drug on the upper truncal region and/or on the middle and/or lower back at least once).</p> <p>Safety: PK assessments: In order to comply with specific recommendations regarding PK analysis obtained from FDA during the review of the clinical efficacy protocol via a special protocol assessment procedure (November 03, 2014; IND number 111091):</p> <p>1. It was specified the minimum number of children (aged 9-11 years) to be enrolled for the 4-week PK assessment period (i.e., 16 evaluable subjects, with a minimum of 3 subjects/age).</p> <p>2. To ensure to collect systemic exposure under maximal use conditions, it was specified that during the 4-week PK assessment period, subjects were to apply CD5789 50 microgram/g cream on the face and trunk, even if acne was not visibly present. At Week 4 visit, the study drug was to be applied by study staff at the study center on the same conditions. After the 4-week PK assessment period, subjects were to resume the treatment as indicated in the protocol on areas affected with acne vulgaris only.</p> <p>3. Due to difficulties encountered in the recruitment of 9-11 year-old subjects for the PK assessment (systemic exposure under maximal use conditions), it was decided to perform a POE assessment at Week 52/ET visit. Only subjects who were not originally enrolled for the PK assessment were to be involved in this additional assessment. The procedure and rationale for the POE were detailed.</p> <p>Other changes:</p> <p>1. Japan was removed from the region(s)/countries involved in the study</p>

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.

None

Notes: