



Clinical trial results: Efficacy and safety of CD5024 1% in acne vulgaris Summary

EudraCT number	2016-000063-16
Trial protocol	DE
Global end of trial date	02 November 2016

Results information

Result version number	v1 (current)
This version publication date	21 October 2020
First version publication date	21 October 2020

Trial information

Trial identification

Sponsor protocol code	RD.03.SPR.109807
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03034460
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, +33 493-95-70-85, cta.coordinator@galderma.com
Scientific contact	CTA Coordinator, Galderma R&D SNC, +33 493-95-70-85, 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	02 November 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	02 November 2016
Global end of trial reached?	Yes
Global end of trial date	02 November 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study was to evaluate the efficacy of CD5024 1 percent (%) cream applied once daily over a 6-week treatment period compared to its vehicle in adult subjects suffering from acne vulgaris.

Protection of trial subjects:

This clinical trial was conducted in accordance with the protocol, the Helsinki declaration (1964) and subsequent amendments, and the International Conference on Harmonisation (ICH) Good Clinical Practice (GCP), and in compliance with applicable regulatory requirements.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	25 April 2016
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	France: 35
Country: Number of subjects enrolled	Germany: 20
Country: Number of subjects enrolled	Canada: 15
Worldwide total number of subjects	70
EEA total number of subjects	55

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)	70
From 65 to 84 years	0

85 years and over	0
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Subject disposition

Recruitment

Recruitment details:

This study was conducted at six centers in three countries (Germany, France, Canada) between 25 April 2016 (first subject screened) to 02 November 2016 (last subject completed).

Pre-assignment

Screening details:

A total of 70 subjects were randomized in the study.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Group I: CD5024 Cream Versus its Vehicle

Arm description:

Subjects applied 500 microliter (mCL) of CD5024 1% cream on one side of the face and matching placebo cream on the other side of the face once daily for 5 days a week from Week 1 to Week 5 and 4 days during Week 6 for a total of 29 applications.

Arm type	Experimental
Investigational medicinal product name	CD5024 1% cream
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cream
Routes of administration	Topical use

Dosage and administration details:

CD5024 1% cream was applied once daily for 5 days a week from Week 1 to Week 5 and for 4 days during Week 6 of treatment period.

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cream
Routes of administration	Topical use

Dosage and administration details:

CD5024 1% cream matched placebo was applied once daily for 5 days a week from Week 1 to Week 5 and for 4 days during Week 6 of treatment period.

Arm title	Group II: Epiduo Gel Versus its Vehicle
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Arm description:

Subjects applied 500 mCL of Adapalene benzoyl peroxyde (Epiduo) gel on one side of the face and matching placebo cream on the other side of the face once daily for 5 days a week from Week 1 to Week 5 and 4 days during Week 6 for a total of 29 applications.

Arm type	Active comparator
Investigational medicinal product name	Adapalene Benzoyl Peroxyde
Investigational medicinal product code	
Other name	Epiduo
Pharmaceutical forms	Gel
Routes of administration	Topical use

Dosage and administration details:

Adapalene benzoyl peroxyde gel was applied once daily for 5 days a week from Week 1 to Week 5 and for 4 days during Week 6 of treatment period.

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cream
Routes of administration	Topical use

Dosage and administration details:

Epiduo Gel matched placebo was applied once daily for 5 days a week from Week 1 to Week 5 and for 4 days during Week 6, for a total of 29 applications.

Notes:

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

Justification: The study was considered to be an investigator-blinded study design.

Number of subjects in period 1	Group I: CD5024 Cream Versus its Vehicle	Group II: Epiduo Gel Versus its Vehicle
Started	48	22
Completed	45	19
Not completed	3	3
Consent withdrawn by subject	2	2
Subject discontinued due to "personal reasons"	1	-
Adverse event, non-fatal	-	1

Baseline characteristics

Reporting groups

Reporting group title	Group I: CD5024 Cream Versus its Vehicle
Reporting group description: Subjects applied 500 microliter (mL) of CD5024 1% cream on one side of the face and matching placebo cream on the other side of the face once daily for 5 days a week from Week 1 to Week 5 and 4 days during Week 6 for a total of 29 applications.	
Reporting group title	Group II: Epiduo Gel Versus its Vehicle
Reporting group description: Subjects applied 500 mL of Adapalene benzoyl peroxyde (Epiduo) gel on one side of the face and matching placebo cream on the other side of the face once daily for 5 days a week from Week 1 to Week 5 and 4 days during Week 6 for a total of 29 applications.	

Reporting group values	Group I: CD5024 Cream Versus its Vehicle	Group II: Epiduo Gel Versus its Vehicle	Total
Number of subjects	48	22	70
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)			0
Adolescents (12-17 years)			0
Adults (18-64 years)			0
From 65-84 years			0
85 years and over			0
Age continuous Units: years			
arithmetic mean	23.3	23.4	
standard deviation	± 4.7	± 4.4	-
Gender categorical Units: Subjects			
Female	34	14	48
Male	14	8	22
Race (NIH/OMB) Units: Subjects			
White	46	14	60
Black or African American	2	4	6
Unknown or not reported	0	2	2
Asian	0	2	2
Number of inflammatory lesions			
Inflammatory lesion counts corresponded to the sum of papules and pustules.			
Units: Lesion Count			
arithmetic mean	34.0	34.2	
standard deviation	± 11.6	± 15.1	-

End points

End points reporting groups

Reporting group title	Group I: CD5024 Cream Versus its Vehicle
Reporting group description: Subjects applied 500 microliter (mL) of CD5024 1% cream on one side of the face and matching placebo cream on the other side of the face once daily for 5 days a week from Week 1 to Week 5 and 4 days during Week 6 for a total of 29 applications.	
Reporting group title	Group II: Epiduo Gel Versus its Vehicle
Reporting group description: Subjects applied 500 mL of Adapalene benzoyl peroxyde (Epiduo) gel on one side of the face and matching placebo cream on the other side of the face once daily for 5 days a week from Week 1 to Week 5 and 4 days during Week 6 for a total of 29 applications.	
Subject analysis set title	CD5024 1% Cream
Subject analysis set type	Intention-to-treat
Subject analysis set description: Subjects applied CD5024 1% cream once daily for 5 days a week from Week 1 to Week 5 and for 4 days during Week 6.	
Subject analysis set title	CD5024 1% Cream Matched Placebo
Subject analysis set type	Intention-to-treat
Subject analysis set description: Subjects applied CD5024 1% cream matched placebo once daily for 5 days a week from Week 1 to Week 5 and for 4 days during Week 6.	
Subject analysis set title	Adapalene Benzoyl Peroxyde
Subject analysis set type	Intention-to-treat
Subject analysis set description: Subjects applied Adapalene Benzoyl Peroxyde once daily for 5 days a week from Week 1 to Week 5 and for 4 days during Week 6.	
Subject analysis set title	Adapalene Benzoyl Peroxyde Matched Placebo
Subject analysis set type	Intention-to-treat
Subject analysis set description: Subjects applied Adapalene Benzoyl Peroxyde matched placebo once daily for 5 days a week from Week 1 to Week 5 and for 4 days during Week 6.	

Primary: Inflammatory Lesion Count (Papules and Pustules) at Day 40

End point title	Inflammatory Lesion Count (Papules and Pustules) at Day 40
End point description: Inflammatory lesion count corresponded to the sum of papules and pustules. This analysis was performed on ITT- last observation carried forward (LOCF) population. ITT-population included all subjects who were randomized. Endpoint data was summarized using the LOCF at Day 40.	
End point type	Primary
End point timeframe: Day 40	

End point values	CD5024 1% Cream	CD5024 1% Cream Matched Placebo	Adapalene Benzoyl Peroxyde	Adapalene Benzoyl Peroxyde Matched Placebo
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	48	48	22	22
Units: lesion count				

arithmetic mean (standard deviation)	10.1 (\pm 5.8)	8.9 (\pm 5.0)	6.1 (\pm 4.9)	9.4 (\pm 5.7)
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Statistical analyses

Statistical analysis title	CD5024 Cream Versus its Vehicle
Statistical analysis description: This analysis was performed for paired difference between Active - Vehicle (CD5024 1% Cream Matched Placebo [subjects (n)=48] versus CD5024 1% Cream [n=48]).	
Comparison groups	CD5024 1% Cream Matched Placebo v CD5024 1% Cream
Number of subjects included in analysis	96
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.158
Method	Wilcoxon rank signed test

Statistical analysis title	Epiduo Gel Versus its Vehicle
Statistical analysis description: This analysis was performed for paired difference between Active - Vehicle (Adapalene Benzoyl Peroxyde [n=22] versus Adapalene Benzoyl Peroxyde Matched Placebo [22]).	
Comparison groups	Adapalene Benzoyl Peroxyde v Adapalene Benzoyl Peroxyde Matched Placebo
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.002
Method	Wilcoxon rank signed test

Secondary: Inflammatory Lesion Count (Papules and Pustules) at Baseline (Day 1)

End point title	Inflammatory Lesion Count (Papules and Pustules) at Baseline (Day 1)
End point description: Inflammatory lesion count corresponded to the sum of papules and pustules. This analysis was performed on ITT population. ITT population included all subjects who were randomized.	
End point type	Secondary
End point timeframe: Baseline (Day 1), and Day 40	

End point values	CD5024 1% Cream	CD5024 1% Cream Matched Placebo	Adapalene Benzoyl Peroxyde	Adapalene Benzoyl Peroxyde Matched Placebo
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	48	48	22	22
Units: lesion count				
arithmetic mean (standard deviation)				
Baseline (Day 1)	16.5 (± 4.9)	17.5 (± 7.4)	17.6 (± 8.6)	16.6 (± 7.2)

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Reduction from Baseline (Day 1) in Inflammatory Lesion Count at Day 40

End point title	Percent Reduction from Baseline (Day 1) in Inflammatory Lesion Count at Day 40
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End point description:

Inflammatory lesion count corresponded to the sum of papules and pustules. This analysis was performed on ITT population. ITT population included all subjects who were randomized.

End point type	Secondary
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End point timeframe:

Baseline (Day 1), and Day 40

End point values	CD5024 1% Cream	CD5024 1% Cream Matched Placebo	Adapalene Benzoyl Peroxyde	Adapalene Benzoyl Peroxyde Matched Placebo
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	48	48	22	22
Units: percent reduction of lesion count				
arithmetic mean (standard deviation)	35.7 (± 43.4)	44.4 (± 32.3)	65.5 (± 24.0)	42.5 (± 30.1)

Statistical analyses

No statistical analyses for this end point

Secondary: Total Lesion Count at Baseline (Day 1) and Day 40

End point title	Total Lesion Count at Baseline (Day 1) and Day 40
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End point description:

Total lesion counts corresponded to the sum of inflammatory and non-inflammatory lesions, and papules. This analysis was performed on ITT- last observation carried forward (LOCF) population. ITT population included all subjects who were randomized. Endpoint data was summarized using the LOCF

at Day 40.

End point type	Secondary
End point timeframe:	
Baseline (Day 1), and Day 40	

End point values	CD5024 1% Cream	CD5024 1% Cream Matched Placebo	Adapalene Benzoyl Peroxyde	Adapalene Benzoyl Peroxyde Matched Placebo
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	48	48	22	22
Units: lesion count				
arithmetic mean (standard deviation)				
Baseline (Day 1)	37.7 (± 11.2)	39.4 (± 13.7)	37.3 (± 20.2)	36.4 (± 18.0)
Day 40	26.4 (± 16.8)	25.9 (± 14.3)	19.3 (± 15.0)	25.5 (± 17.2)

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Reduction from Baseline (Day 1) in Total Lesions at Day 40

End point title	Percent Reduction from Baseline (Day 1) in Total Lesions at Day 40
End point description:	
Total lesion counts corresponded to the sum of inflammatory and non-inflammatory lesions, and papules. This analysis was performed on ITT population. ITT population included all subjects who were randomized.	
End point type	Secondary
End point timeframe:	
Baseline (Day 1), and Day 40	

End point values	CD5024 1% Cream	CD5024 1% Cream Matched Placebo	Adapalene Benzoyl Peroxyde	Adapalene Benzoyl Peroxyde Matched Placebo
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	48	48	22	22
Units: percent reduction in total lesion count				
arithmetic mean (standard deviation)				
Day 40	32.5 (± 32.2)	34.0 (± 27.1)	50.2 (± 27.2)	27.8 (± 31.8)

Statistical analyses

No statistical analyses for this end point

Secondary: Non-Inflammatory Lesion Count at Baseline (Day 1) and Day 40

End point title	Non-Inflammatory Lesion Count at Baseline (Day 1) and Day 40
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End point description:

Non-inflammatory lesion counts corresponded to the sum of open and closed comedones. This analysis was performed on ITT population. ITT population included all subjects who were randomized.

End point type	Secondary
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End point timeframe:

Baseline (Day 1), and Day 40

End point values	CD5024 1% Cream	CD5024 1% Cream Matched Placebo	Adapalene Benzoyl Peroxyde	Adapalene Benzoyl Peroxyde Matched Placebo
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	48	48	22	22
Units: lesion count				
arithmetic mean (standard deviation)				
Baseline (Day 1)	21.1 (± 9.5)	21.8 (± 10.7)	19.6 (± 14.1)	19.6 (± 13.6)
Day 40	16.2 (± 13.1)	16.9 (± 12.7)	13.0 (± 12.0)	16.0 (± 14.1)

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Reduction from Baseline in Non-Inflammatory Lesion at Day 40

End point title	Percent Reduction from Baseline in Non-Inflammatory Lesion at Day 40
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End point description:

Non-inflammatory lesion counts corresponded to the sum of open and closed comedones. This analysis was performed on ITT population. ITT population included all subjects who were randomized.

End point type	Secondary
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End point timeframe:

Baseline (Day 1), and Day 40

End point values	CD5024 1% Cream	CD5024 1% Cream Matched Placebo	Adapalene Benzoyl Peroxyde	Adapalene Benzoyl Peroxyde Matched Placebo
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	48	48	22	22
Units: percent reduction of lesion count				
arithmetic mean (standard deviation)				
Day 40	27.8 (± 39.4)	21.3 (± 42.0)	36.9 (± 36.1)	11.7 (± 48.6)

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects Reported for Investigator's Preference on a 5-Point Scale at Day 40

End point title	Number of Subjects Reported for Investigator's Preference on a 5-Point Scale at Day 40
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End point description:

The Investigator gave opinion on their preference after comparison of the left and right sides of the face using the 5-point scale ranging from -2 to 2. The score and description indicated as follows: -2= left side of the face much better than right side, -1= left side of the face better than right side, 0= no clinical difference between the right and left sides of the face, 1= right side of the face better than the left side, 2= right side of the face much better than the left side. This analysis was performed on ITT population. ITT population included all subjects who were randomized. Here 'N' (number of subjects analyzed) signifies subjects who were evaluable for this endpoint.

End point type	Secondary
End point timeframe:	
Day 40	

End point values	Group I: CD5024 Cream Versus its Vehicle	Group II: Epiduo Gel Versus its Vehicle		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	47	21		
Units: number of subjects				
Day 40 (Active much better than Vehicle)	0	4		
Day 40 (Active better than Vehicle)	16	7		
Day 40 (No clinical difference between A and V)	16	6		
Day 40 (Vehicle better than Active)	14	4		
Day 40 (Vehicle much better than Active)	1	0		

Statistical analyses

Secondary: Number of Subjects Reported for Subject's Preference on 5-Point Scale at Day 40

End point title	Number of Subjects Reported for Subject's Preference on 5-Point Scale at Day 40
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End point description:

The subjects gave opinion on their preference after comparison of the left and right sides of the face using the 5-point scale ranging from -2 to 2. The score and description indicated as follows: -2= left side of the face much better than right side, -1= left side of the face better than right side, 0= no clinical difference between the right and left sides of the face, 1= right side of the face better than the left side, 2= right side of the face much better than the left side. This analysis was performed on ITT population. ITT population included all subjects who were randomized. Here 'N' (number of subjects analyzed) signifies subjects who were evaluable for this endpoint.

End point type	Secondary
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End point timeframe:

Day 40

End point values	Group I: CD5024 Cream Versus its Vehicle	Group II: Epiduo Gel Versus its Vehicle		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	47	21		
Units: number of subjects				
Day 40 (Active much better than Vehicle)	2	2		
Day 40 (Active better than Vehicle)	11	11		
Day 40 (No clinical difference between A and V)	15	4		
Day 40 (Vehicle better than Active)	16	3		
Day 40 (Vehicle much better than Active)	3	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Adverse Events (AEs)

End point title	Number of Subjects With Adverse Events (AEs)
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End point description:

AE was any untoward medical occurrence in a subject or clinical investigation subject administered a pharmaceutical product and which does not necessarily had a causal relationship with this treatment. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory value), symptom, or disease temporally associated with the use of a medicinal (investigational) product, whether or not related to the medicinal (investigational) product. This analysis was performed on safety population. Safety population included subjects in the ITT population who received at least 1 application of the investigational product. Number of subjects with AE's were reported.

End point type	Secondary
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End point timeframe:

From start of study up to follow up (Week 7)

End point values	Group I: CD5024 Cream Versus its Vehicle	Group II: Epiduo Gel Versus its Vehicle		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	48	22		
Units: number of subjects	32	14		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects Reported Worst Local Tolerability Score on Treated Areas (Face and Ear) From Day 1 to Follow up (Week 7)

End point title	Number of Subjects Reported Worst Local Tolerability Score on Treated Areas (Face and Ear) From Day 1 to Follow up (Week 7)
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End point description:

Signs and symptoms of local cutaneous irritation(local tolerability [erythema, scaling, dryness, stinging/burning, pruritus]) were evaluated on all treated areas (face and behind ears if applicable) every day from Day 1 up to follow-up (Week 7) using a 4-point scale of None (0), Mild (1), Moderate (2), or Severe (3). Safety population included subjects in the ITT population who received at least 1 application of the investigational product. Number of subjects reported worst local tolerability score on treated areas from Day 1 to follow up (Week 7) was reported. Here 'n' (number analyzed) signifies number of subjects who were evaluable for each specified category.

End point type	Secondary
End point timeframe:	
From Day 1 up Follow up (Week 7)	

End point values	CD5024 1% Cream	CD5024 1% Cream Matched Placebo	Adapalene Benzoyl Peroxyde	Adapalene Benzoyl Peroxyde Matched Placebo
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	48	48	22	22
Units: number of subjects				
Face: Erythema: 0-None (n=48,48,22,22)	37	38	8	15
Face: Erythema: 1-Mild (n=48,48,22,22)	9	9	11	6
Face: Erythema: 2-Moderate (n=48,48,22,22)	2	1	3	1
Face: Scaling/Desquamation: 0-None (n=48,48,22,22)	38	38	5	16
Face: Scaling/Desquamation: 1-Mild (n=48,48,22,22)	10	10	13	5

Face: Scaling/Desquamation: 2-Moderate (n=48,48,22)	0	0	4	1
Face: Dryness: 0-None (n=48,48,22,22)	38	37	4	10
Face: Dryness: 1-Mild (n=48,48,22,22)	10	11	13	12
Face: Dryness: 2-Moderate (n=48,48,22,22)	0	0	5	0
Face: Stinging/Burning: 0-None (n=48,48,22,22)	44	43	8	17
Face: Stinging/Burning: 1-Mild (n=48,48,22,22)	3	4	8	5
Face: Stinging/Burning: 2-Moderate (n=48,48,22,22)	1	1	6	0
Ear: Erythema: 0-None (n=22,22,11,11)	20	20	8	11
Ear: Erythema: 1-Mild (n=22,22,11,11)	2	2	2	0
Ear: Erythema: 2-Moderate (n=22,22,11,11)	0	0	1	0
Ear: Scaling/Desquamation: 0-None (n=22,22,11,11)	22	22	7	11
Ear: Scaling/Desquamation: 1-Mild (n=22,22,11,11)	0	0	3	0
Ear: Scaling/Desquamation: 2-Moderate (n=22,22,11,11)	0	0	1	0
Ear: Dryness: 0-None (n=22,22,11,11)	22	22	7	10
Ear: Dryness: 1-Mild (n=22,22,11,11)	0	0	3	1
Ear: Dryness: 2-Moderate (n=22,22,11,11)	0	0	1	0
Ear: Stinging/Burning: 0-None (n=22,22,11,11)	22	22	8	11
Ear: Stinging/Burning: 1-Mild (n=22,22,11,11)	0	0	2	0
Ear: Stinging/Burning: 2-Moderate (n=22,22,11,11)	0	0	1	0

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From start of study up to follow up (Week 7)

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	Group I
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Reporting group description:

Subjects applied 500 mcL of CD5024 1% cream on one side of the face and matching placebo cream on the other side of the face once daily for 5 days a week from Week 1 to Week 5 and 4 days during Week 6 for a total of 29 applications.

Reporting group title	Group II
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Reporting group description:

Subjects applied 500 mcL of Adapalene Benzoyl Peroxyde (Epiduo) gel on one side of the face and matching placebo cream on the other side of the face once daily for 5 days a week from Week 1 to Week 5 and 4 days during Week 6 for a total of 29 applications.

Serious adverse events	Group I	Group II	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 48 (0.00%)	0 / 22 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Group I	Group II	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	32 / 48 (66.67%)	11 / 22 (50.00%)	
Nervous system disorders			
Headache			
subjects affected / exposed	13 / 48 (27.08%)	5 / 22 (22.73%)	
occurrences (all)	13	5	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	3 / 48 (6.25%)	0 / 22 (0.00%)	
occurrences (all)	3	0	
Respiratory, thoracic and mediastinal			

disorders			
Oropharyngeal pain			
subjects affected / exposed	3 / 48 (6.25%)	0 / 22 (0.00%)	
occurrences (all)	3	0	
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	0 / 48 (0.00%)	2 / 22 (9.09%)	
occurrences (all)	0	2	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	14 / 48 (29.17%)	4 / 22 (18.18%)	
occurrences (all)	14	4	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
22 September 2016	<p>Amendment 1:</p> <ul style="list-style-type: none">- Modified the primary efficacy endpoint to evaluate only inflammatory acne lesion count at Day 40 per half face and not percent reduction- Changed "inflammatory lesion count and percent reduction per half face (at each evaluation visit)" from primary to secondary efficacy criteria- Created a last visit for treatment period (Endpoint), which contained the last observation carried forward (LOCF). The ITT population was to be analyzed for efficacy only at Baseline and at Day 40 (Endpoint/LOCF)- Added that all safety data would be summarized based on the Safety population- Revised the description of inferential statistical analyses to: This is an exploratory Phase 2a study used to inform sponsor for an internal go/no decision. Primary endpoint is inflammatory acne lesion count at Day 40 per half face on ITT-LOCF population. Significance would be declared for 2-sided tests when the p-value did not exceed 0.05- The others endpoints were exploratory. P-values were to be given for indicative purpose so no adjustment was to be made- Changed confidence interval from 90% to 95%- Corrected country code for study numbers of studies used for historical data with respect to sample size determination

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported