



Clinical trial results:

A Phase 2, Multicenter, Randomized, Double-Blind, Vehicle-Controlled, Dose Escalating Study to Evaluate the Safety and Efficacy of Cortexolone 17-Propionate (CB-03-01) Cream Applied Once or Twice-Daily for 12 Weeks in Subjects with Facial Acne Vulgaris

Summary

EudraCT number	2023-000461-13
Trial protocol	Outside EU/EEA
Global end of trial date	19 February 2014

Results information

Result version number	v1 (current)
This version publication date	27 May 2023
First version publication date	27 May 2023

Trial information

Trial identification

Sponsor protocol code	171-7151-201
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01631474
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Intrepid Therapeutics Inc.
Sponsor organisation address	12463 Rancho Bernardo Road, #537, San Diego, United States, CA 92128-2143
Public contact	Cassiopea SpA, Cosmo SpA, +39 02868 91124, dermatology@cosmopharma.com
Scientific contact	Cassiopea SpA, Cosmo SpA, +39 02868 91124, dermatology@cosmopharma.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMA-003330-PIP01-22
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	21 January 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	19 February 2014
Global end of trial reached?	Yes
Global end of trial date	19 February 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study is to compare the safety and efficacy of topical creams containing 0.1% (BID), 0.5% (BID) or 1% (QD and BID) CB-03-01 and the vehicle cream (QD or BID) in subjects with facial acne vulgaris.

Protection of trial subjects:

Approval on the conduct of the trial was obtained by an IRB and by the FDA prior to study initiation. The study protocol, consent/assent form, participant recruitment materials/process, and other relevant documents were submitted for approval in compliance with the requirements set forth in Title 21 of the Code of Federal Regulations (CFR), Parts 56.107 to 56.115. The study was conducted in accordance with principles of the Declaration of Helsinki, with the current Good Clinical Practice (GCP) Guideline and with other applicable regulations.

Background therapy:

No background therapy was planned

Evidence for comparator:

No comparators were used in the study

Actual start date of recruitment	11 June 2012
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	United States: 363
Worldwide total number of subjects	363
EEA total number of subjects	0

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)	165
Adults (18-64 years)	198
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

505 subjects were screened for the study; 363 subjects (72: CB-03-01 0.1% BID; 76: CB-03-01 0.5% BID; 70: CB-03-01 1% QD; 70 CB-03-01 1% BID; and 75: vehicle QD or BID) were enrolled into the study; 142 subjects were screen failures.

Period 1

Period 1 title	Overall Study (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	Low-dose Active, BID

Arm description:

Low dose of CB-03-01, 0.1% topical cream applied twice a day

Arm type	Experimental
Investigational medicinal product name	CB-03-01
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cream
Routes of administration	Topical

Dosage and administration details:

0.1% applied twice a day

Arm title	Medium-dose Active, BID
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Arm description:

Medium dose of CB-03-01, 0.5% topical cream applied twice a day

Arm type	Experimental
Investigational medicinal product name	CB-03-01
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cream
Routes of administration	Topical

Dosage and administration details:

0.5% applied twice a day

Arm title	High-dose Active, QD
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Arm description:

High dose of CB-03-01, 1% topical cream applied once a day

Arm type	Experimental
Investigational medicinal product name	CB-03-01
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cream
Routes of administration	Topical

Dosage and administration details:

1% applied once a day

Arm title	High-dose Active, BID
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Arm description:

High dose of CB-03-01, 1% topical cream applied twice a day

Arm type	Experimental
Investigational medicinal product name	CB-03-01
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cream
Routes of administration	Topical

Dosage and administration details:

1% applied twice a day

Arm title	Vehicle, QD or BID
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Arm description:

Vehicle topical cream, applied once or twice a day

Arm type	Placebo
Investigational medicinal product name	Vehicle
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cream
Routes of administration	Topical

Dosage and administration details:

Topical cream applied once or twice a day

Number of subjects in period 1	Low-dose Active, BID	Medium-dose Active, BID	High-dose Active, QD
Started	72	76	70
Completed	58	64	61
Not completed	14	12	9
Consent withdrawn by subject	4	4	2
Adverse event, non-fatal	-	1	-
Noncompliance with study drug	-	-	-
Lost to follow-up	8	5	7
Lack of efficacy	2	2	-

Number of subjects in period 1	High-dose Active, BID	Vehicle, QD or BID
Started	70	75
Completed	59	62
Not completed	11	13
Consent withdrawn by subject	6	5
Adverse event, non-fatal	-	-

Noncompliance with study drug	-	1
Lost to follow-up	5	5
Lack of efficacy	-	2

Baseline characteristics

Reporting groups

Reporting group title	Low-dose Active, BID
Reporting group description:	
Low dose of CB-03-01, 0.1% topical cream applied twice a day	
Reporting group title	Medium-dose Active, BID
Reporting group description:	
Medium dose of CB-03-01, 0.5% topical cream applied twice a day	
Reporting group title	High-dose Active, QD
Reporting group description:	
High dose of CB-03-01, 1% topical cream applied once a day	
Reporting group title	High-dose Active, BID
Reporting group description:	
High dose of CB-03-01, 1% topical cream applied twice a day	
Reporting group title	Vehicle, QD or BID
Reporting group description:	
Vehicle topical cream, applied once or twice a day	

Reporting group values	Low-dose Active, BID	Medium-dose Active, BID	High-dose Active, QD
Number of subjects	72	76	70
Age categorical			
Units: Subjects			

Age continuous			
Units: years			
arithmetic mean	19.8	20.4	18.3
standard deviation	± 5.77	± 6.31	± 6.14
Gender categorical			
Units: Subjects			
Female	36	42	38
Male	36	34	32
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	22	20	6
Not Hispanic or Latino	50	56	64
Unknown or Not Reported	0	0	0
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	0	1	0
Asian	1	3	4
Native Hawaiian or Other Pacific Islander	0	1	0
Black or African American	12	14	16
White	58	54	50
More than one race	1	2	0
Unknown or Not Reported	0	1	0
Baseline IGA Measure			
Units: Subjects			

0 - Clear	0	0	0
1 - Almost clear	0	0	0
2 - Mild	10	6	15
3 - Moderate	56	62	44
4 - Severe	6	8	11
Baseline lesions counts			
Units: Inflammatory Lesions			
arithmetic mean	29.9	29.0	31.9
full range (min-max)	20 to 74	20 to 74	20 to 72

Reporting group values	High-dose Active, BID	Vehicle, QD or BID	Total
Number of subjects	70	75	363
Age categorical			
Units: Subjects			

Age continuous			
Units: years			
arithmetic mean	21.0	19.2	
standard deviation	± 6.22	± 5.25	-
Gender categorical			
Units: Subjects			
Female	37	43	196
Male	33	32	167
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	15	13	76
Not Hispanic or Latino	55	62	287
Unknown or Not Reported	0	0	0
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	2	0	3
Asian	4	4	16
Native Hawaiian or Other Pacific Islander	0	1	2
Black or African American	20	12	74
White	42	53	257
More than one race	2	4	9
Unknown or Not Reported	0	1	2
Baseline IGA Measure			
Units: Subjects			
0 - Clear	0	0	0
1 - Almost clear	0	0	0
2 - Mild	18	11	60
3 - Moderate	32	53	247
4 - Severe	20	11	56
Baseline lesions counts			
Units: Inflammatory Lesions			
arithmetic mean	28.6	30.5	
full range (min-max)	20 to 63	20 to 75	-

Subject analysis sets

Subject analysis set title	ITT Population
Subject analysis set type	Intention-to-treat

Subject analysis set description:

ITT Population. The ITT population included all subjects enrolled in the study who were randomized and dispensed test article.

Reporting group values	ITT Population		
Number of subjects	363		
Age categorical Units: Subjects			
Age continuous Units: years arithmetic mean standard deviation	19.7 ± 5.99		
Gender categorical Units: Subjects			
Female Male	196 197		
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino Not Hispanic or Latino Unknown or Not Reported	76 287 0		
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native Asian Native Hawaiian or Other Pacific Islander Black or African American White More than one race Unknown or Not Reported	3 16 2 74 257 9 2		
Baseline IGA Measure Units: Subjects			
0 - Clear 1 - Almost clear 2 - Mild 3 - Moderate 4 - Severe	0 0 60 247 56		
Baseline lesions counts Units: Inflammatory Lesions arithmetic mean full range (min-max)	30.0 20 to 75		

End points

End points reporting groups

Reporting group title	Low-dose Active, BID
Reporting group description: Low dose of CB-03-01, 0.1% topical cream applied twice a day	
Reporting group title	Medium-dose Active, BID
Reporting group description: Medium dose of CB-03-01, 0.5% topical cream applied twice a day	
Reporting group title	High-dose Active, QD
Reporting group description: High dose of CB-03-01, 1% topical cream applied once a day	
Reporting group title	High-dose Active, BID
Reporting group description: High dose of CB-03-01, 1% topical cream applied twice a day	
Reporting group title	Vehicle, QD or BID
Reporting group description: Vehicle topical cream, applied once or twice a day	
Subject analysis set title	ITT Population
Subject analysis set type	Intention-to-treat
Subject analysis set description: ITT Population. The ITT population included all subjects enrolled in the study who were randomized and dispensed test article.	

Primary: Investigator's Global Assessment (IGA) "Success" - Week 12

End point title	Investigator's Global Assessment (IGA) "Success" - Week 12
End point description: Count and percentage of subjects achieving success in each treatment group at Week 12 using the dichotomized IGA with success defined as a score of "clear" or "almost clear" (IGA Score of 0 or 1) and a two or more grade improvement from Baseline using a five-point scale (0=clear to 4=severe).	
End point type	Primary
End point timeframe: Baseline and Week 12	

End point values	Low-dose Active, BID	Medium-dose Active, BID	High-dose Active, QD	High-dose Active, BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	72	76	70	70
Units: Participants	6	3	2	6

End point values	Vehicle, QD or BID			
Subject group type	Reporting group			
Number of subjects analysed	75			
Units: Participants	2			

Statistical analyses

Statistical analysis title	Treatment Success Based on IGA at Week 12
Statistical analysis description: The treatment groups were compared with respect to the proportion of subjects with "treatment success" at Week 12/EOS using Fisher's exact test. Treatment success was defined as a score of "clear" or "almost clear" (IGA score of 0 or 1) AND a two or more grade improvement from Baseline.	
Comparison groups	Low-dose Active, BID v Medium-dose Active, BID v High-dose Active, QD v High-dose Active, BID v Vehicle, QD or BID
Number of subjects included in analysis	363
Analysis specification	Pre-specified
Analysis type	other
P-value	≤ 0.05
Method	Fisher exact

Primary: Inflammatory and Non-Inflammatory Lesion Counts - Week 12

End point title	Inflammatory and Non-Inflammatory Lesion Counts - Week 12
End point description: Absolute change from Baseline in inflammatory and non-inflammatory lesion counts in each treatment group at Week 12.	
End point type	Primary
End point timeframe: Baseline and Week 12	

End point values	Low-dose Active, BID	Medium-dose Active, BID	High-dose Active, QD	High-dose Active, BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	72	76	70	70
Units: Lesions				
arithmetic mean (standard deviation)				
Inflammatory Lesions	-7.3 (± 14.20)	-5.6 (± 11.26)	-7.9 (± 12.31)	-11.1 (± 14.07)
Non-inflammatory Lesions	-8.8 (± 17.38)	-6.3 (± 26.68)	-8.1 (± 20.47)	-15.8 (± 20.11)

End point values	Vehicle, QD or BID			
Subject group type	Reporting group			
Number of subjects analysed	75			
Units: Lesions				

arithmetic mean (standard deviation)				
Inflammatory Lesions	-8.3 (± 12.86)			
Non-inflammatory Lesions	-5.9 (± 18.47)			

Statistical analyses

Statistical analysis title	Absolute Change from Baseline in ILC at Week 12
Statistical analysis description:	
The absolute change from Baseline to Week 12/EOS in total inflammatory lesion counts was analyzed by rank analysis of covariance (ANCOVA) with the model including terms for treatment and study site with the Baseline total inflammatory lesion count serving as the covariate. Pairwise comparisons of the treatments were performed by rank ANCOVA.	
Comparison groups	Low-dose Active, BID v Medium-dose Active, BID v High-dose Active, QD v High-dose Active, BID v Vehicle, QD or BID
Number of subjects included in analysis	363
Analysis specification	Pre-specified
Analysis type	other
P-value	≤ 0.05
Method	ANCOVA

Secondary: Inflammatory and Non-Inflammatory Lesion Counts - Week 8

End point title	Inflammatory and Non-Inflammatory Lesion Counts - Week 8
End point description:	
Absolute change from Baseline in inflammatory and non-inflammatory lesion counts in each treatment group at Week 8.	
End point type	Secondary
End point timeframe:	
Baseline and Week 8	

End point values	Low-dose Active, BID	Medium-dose Active, BID	High-dose Active, QD	High-dose Active, BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	59	66	66	59
Units: Lesions				
arithmetic mean (standard deviation)				
Inflammatory Lesions	-11.0 (± 10.49)	-7.1 (± 11.74)	-6.0 (± 16.50)	-11.9 (± 10.83)
Non-inflammatory Lesions	-7.5 (± 14.05)	-6.8 (± 15.85)	-4.3 (± 33.75)	-14.1 (± 18.21)

End point values	Vehicle, QD or BID			
Subject group type	Reporting group			
Number of subjects analysed	63			

Units: Lesions				
arithmetic mean (standard deviation)				
Inflammatory Lesions	-9.8 (± 13.09)			
Non-inflammatory Lesions	-8.0 (± 16.61)			

Statistical analyses

Statistical analysis title	Absolute Change in ILC/NILC at Week 8
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Statistical analysis description:

The absolute change from Baseline to Week 8 in total inflammatory/non-inflammatory lesion counts was analyzed by rank ANCOVA with the model including terms for treatment and study site with the Baseline total inflammatory/non-inflammatory lesion counts serving as the covariate. Pairwise comparisons of the treatments were performed by rank ANCOVA.

Comparison groups	Low-dose Active, BID v Medium-dose Active, BID v High-dose Active, QD v High-dose Active, BID v Vehicle, QD or BID
Number of subjects included in analysis	313
Analysis specification	Pre-specified
Analysis type	other
P-value	≤ 0.05
Method	ANCOVA

Secondary: Percent Change in Lesion Counts - Week 8

End point title	Percent Change in Lesion Counts - Week 8
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End point description:

Percent change from Baseline in lesion counts (inflammatory and noninflammatory) in each treatment group at Week 8

End point type	Secondary
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End point timeframe:

Week 8

End point values	Low-dose Active, BID	Medium-dose Active, BID	High-dose Active, QD	High-dose Active, BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	59	66	66	59
Units: Percentage of Change				
arithmetic mean (standard deviation)				
Inflammatory Lesions	-37.1 (± 34.40)	-26.5 (± 36.54)	-23.4 (± 44.47)	-43.1 (± 36.19)
Non-Inflammatory Lesions	-18.6 (± 34.35)	-20.3 (± 35.72)	-12.5 (± 53.54)	-33.3 (± 38.09)

End point values	Vehicle, QD or BID			
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Subject group type	Reporting group			
Number of subjects analysed	63			
Units: Percentage of Change				
arithmetic mean (standard deviation)				
Inflammatory Lesions	-31.9 (± 36.42)			
Non-Inflammatory Lesions	-23.8 (± 42.11)			

Statistical analyses

Statistical analysis title	Percent Change in ILC/NILC at Week 8
Statistical analysis description: The treatment groups were compared with respect to the percent change in total inflammatory and non-inflammatory lesion counts at Week 8 using the Kruskal-Wallis test considering all treatments and pairwise comparisons of treatments.	
Comparison groups	Low-dose Active, BID v Medium-dose Active, BID v High-dose Active, QD v High-dose Active, BID v Vehicle, QD or BID
Number of subjects included in analysis	313
Analysis specification	Pre-specified
Analysis type	other
P-value	≤ 0.05
Method	Kruskal-wallis

Secondary: Investigator's Global Assessment (IGA) "Success" - Week 8

End point title	Investigator's Global Assessment (IGA) "Success" - Week 8
End point description: Count and percentage of subjects achieving success per the IGA in each treatment group at Week 8 ("success" as defined in the primary endpoints section).	
End point type	Secondary
End point timeframe: Baseline and Week 8	

End point values	Low-dose Active, BID	Medium-dose Active, BID	High-dose Active, QD	High-dose Active, BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	59	66	66	59
Units: Participants	1	3	2	4

End point values	Vehicle, QD or BID			
Subject group type	Reporting group			
Number of subjects analysed	63			

Units: Participants	2			
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Statistical analyses

Statistical analysis title	Treatment Success Based on IGA at Week 8
Statistical analysis description: The treatment groups were compared with respect to the proportion of subjects with "treatment success", as defined for the primary efficacy endpoint, at Week 8 using Fisher's exact test.	
Comparison groups	Low-dose Active, BID v Medium-dose Active, BID v High-dose Active, QD v High-dose Active, BID v Vehicle, QD or BID
Number of subjects included in analysis	313
Analysis specification	Pre-specified
Analysis type	other
P-value	≤ 0.05
Method	Fisher exact

Secondary: Investigator's Global Assessment (IGA) "Clear" or "Almost Clear" - Week 4

End point title	Investigator's Global Assessment (IGA) "Clear" or "Almost Clear" - Week 4
End point description: Count and percentage of subjects who are "clear" or "almost clear" (IGA Grade 0 or 1) in each treatment group at Week 4.	
End point type	Secondary
End point timeframe: Week 4	

End point values	Low-dose Active, BID	Medium-dose Active, BID	High-dose Active, QD	High-dose Active, BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	62	73	66	64
Units: Participants				
Week 4	4	2	5	7

End point values	Vehicle, QD or BID			
Subject group type	Reporting group			
Number of subjects analysed	70			
Units: Participants				
Week 4	2			

Statistical analyses

Statistical analysis title	"Clear" or "Almost Clear" Based on IGA - Week 4
Statistical analysis description: The treatment groups were compared with respect to the proportion of subjects scored as "clear" (IGA=0) or "almost clear" (IGA=1) at Week 4 using Fisher's exact test. The Cochran-Armitage test for trend was used to assess if an increase in dose corresponded to an increase in "clear"/"almost clear" rates.	
Comparison groups	Low-dose Active, BID v Medium-dose Active, BID v High-dose Active, QD v High-dose Active, BID v Vehicle, QD or BID
Number of subjects included in analysis	335
Analysis specification	Pre-specified
Analysis type	other
P-value	≤ 0.05
Method	Fisher exact

Secondary: Investigator's Global Assessment (IGA) "Clear" or "Almost Clear" - Week 8

End point title	Investigator's Global Assessment (IGA) "Clear" or "Almost Clear" - Week 8
End point description: Count and percentage of subjects who are "clear" or "almost clear" (IGA Grade 0 or 1) in each treatment group at Week 8.	
End point type	Secondary
End point timeframe: Week 8	

End point values	Low-dose Active, BID	Medium-dose Active, BID	High-dose Active, QD	High-dose Active, BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	59	66	66	59
Units: Participants				
Week 8	3	4	4	6

End point values	Vehicle, QD or BID			
Subject group type	Reporting group			
Number of subjects analysed	63			
Units: Participants				
Week 8	4			

Statistical analyses

Statistical analysis title	"Clear" or "Almost Clear" Based on IGA - Week 8
Statistical analysis description: The treatment groups were compared with respect to the proportion of subjects scored as "clear" (IGA=0) or "almost clear" (IGA=1) at Week 8 using Fisher's exact test. The Cochran-Armitage test for trend was used to assess if an increase in dose corresponded to an increase in "clear"/"almost clear" rates.	
Comparison groups	Low-dose Active, BID v Medium-dose Active, BID v High-dose Active, QD v High-dose Active, BID v Vehicle, QD or BID
Number of subjects included in analysis	313
Analysis specification	Pre-specified
Analysis type	other
P-value	≤ 0.05
Method	Fisher exact

Secondary: Investigator's Global Assessment (IGA) "Clear" or "Almost Clear" - Week 12

End point title	Investigator's Global Assessment (IGA) "Clear" or "Almost Clear" - Week 12
End point description: Count and percentage of subjects who are "clear" or "almost clear" (IGA Grade 0 or 1) in each treatment group at Week 12.	
End point type	Secondary
End point timeframe: Week 12	

End point values	Low-dose Active, BID	Medium-dose Active, BID	High-dose Active, QD	High-dose Active, BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	72	76	70	70
Units: Participants				
Week 12	8	4	3	9

End point values	Vehicle, QD or BID			
Subject group type	Reporting group			
Number of subjects analysed	75			
Units: Participants				
Week 12	4			

Statistical analyses

Statistical analysis title	"Clear" or "Almost Clear" Based on IGA - Week 12
Statistical analysis description: The treatment groups were compared with respect to the proportion of subjects scored as "clear" (IGA=0) or "almost clear" (IGA=1) at Week 12/EOS using Fisher's exact test. The Cochran-Armitage test for trend was used to assess if an increase in dose corresponded to an increase in "clear"/"almost clear" rates.	
Comparison groups	Low-dose Active, BID v Medium-dose Active, BID v High-dose Active, QD v High-dose Active, BID v Vehicle, QD or BID
Number of subjects included in analysis	363
Analysis specification	Pre-specified
Analysis type	other
P-value	≤ 0.05
Method	Fisher exact

Secondary: Percent Change in Lesion Counts - Week 12

End point title	Percent Change in Lesion Counts - Week 12
End point description: Percent change from Baseline in lesion counts (inflammatory and noninflammatory) in each treatment group at Week 12	
End point type	Secondary
End point timeframe: Week 12	

End point values	Low-dose Active, BID	Medium-dose Active, BID	High-dose Active, QD	High-dose Active, BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	72	76	70	70
Units: Percentage of Change				
arithmetic mean (standard deviation)				
Inflammatory Lesions	-24.8 (± 49.72)	-21.0 (± 42.59)	-25.9 (± 36.68)	-37.2 (± 51.15)
Non-Inflammatory Lesions	-23.5 (± 36.46)	-17.3 (± 51.32)	-18.3 (± 39.36)	-32.9 (± 43.5)

End point values	Vehicle, QD or BID			
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Subject group type	Reporting group			
Number of subjects analysed	75			
Units: Percentage of Change				
arithmetic mean (standard deviation)				
Inflammatory Lesions	-27.0 (± 39.97)			
Non-Inflammatory Lesions	-16.1 (± 45.61)			

Statistical analyses

Statistical analysis title	Percent Change in ILC/NILC at Week 12
Statistical analysis description:	
The treatment groups were compared with respect to the percent change in total inflammatory and non-inflammatory lesion counts at Week 12/EOS using the Kruskal-Wallis test considering all treatments and pairwise comparisons of treatments.	
Comparison groups	Low-dose Active, BID v Medium-dose Active, BID v High-dose Active, QD v High-dose Active, BID v Vehicle, QD or BID
Number of subjects included in analysis	363
Analysis specification	Pre-specified
Analysis type	other
P-value	≤ 0.05
Method	Kruskal-wallis

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events (AEs) were collected from screening visit, Baseline (Day 1) and up to Week 12/early termination

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	16
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Reporting groups

Reporting group title	Low-dose Active, BID
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Reporting group description:

Low dose of CB-03-01, 0.1% topical cream applied twice a day

Reporting group title	Medium-dose Active, BID
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Reporting group description:

Medium dose of CB-03-01, 0.5% topical cream applied twice a day

Reporting group title	High-dose Active, QD
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Reporting group description:

High dose of CB-03-01, 1% topical cream applied once a day

Reporting group title	High-dose Active, BID
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Reporting group description:

High dose of CB-03-01, 1% topical cream applied twice a day

Reporting group title	Vehicle, QD or BID
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Reporting group description:

Vehicle topical cream, applied once or twice a day

Serious adverse events	Low-dose Active, BID	Medium-dose Active, BID	High-dose Active, QD
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 72 (0.00%)	0 / 76 (0.00%)	0 / 70 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			

Serious adverse events	High-dose Active, BID	Vehicle, QD or BID	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 70 (0.00%)	0 / 75 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			

Frequency threshold for reporting non-serious adverse events: 2 %

Non-serious adverse events	Low-dose Active, BID	Medium-dose Active, BID	High-dose Active, QD
Total subjects affected by non-serious adverse events			
subjects affected / exposed	12 / 72 (16.67%)	18 / 76 (23.68%)	9 / 70 (12.86%)
Injury, poisoning and procedural complications			
Laceration			
subjects affected / exposed	2 / 72 (2.78%)	1 / 76 (1.32%)	0 / 70 (0.00%)
occurrences (all)	2	1	0
Nervous system disorders			
Headache			
subjects affected / exposed	2 / 72 (2.78%)	1 / 76 (1.32%)	0 / 70 (0.00%)
occurrences (all)	2	1	0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 72 (0.00%)	2 / 76 (2.63%)	2 / 70 (2.86%)
occurrences (all)	0	2	2
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	1 / 72 (1.39%)	4 / 76 (5.26%)	1 / 70 (1.43%)
occurrences (all)	1	4	1
Nasal congestion			
subjects affected / exposed	0 / 72 (0.00%)	2 / 76 (2.63%)	0 / 70 (0.00%)
occurrences (all)	0	2	0
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	6 / 72 (8.33%)	8 / 76 (10.53%)	2 / 70 (2.86%)
occurrences (all)	6	8	2
Nasopharyngitis			
subjects affected / exposed	1 / 72 (1.39%)	0 / 76 (0.00%)	4 / 70 (5.71%)
occurrences (all)	1	0	4

Non-serious adverse events	High-dose Active, BID	Vehicle, QD or BID	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 70 (7.14%)	5 / 75 (6.67%)	
Injury, poisoning and procedural complications			

Laceration subjects affected / exposed occurrences (all)	0 / 70 (0.00%) 0	0 / 75 (0.00%) 0	
Nervous system disorders Headache subjects affected / exposed occurrences (all)	0 / 70 (0.00%) 0	2 / 75 (2.67%) 2	
General disorders and administration site conditions Pyrexia subjects affected / exposed occurrences (all)	0 / 70 (0.00%) 0	0 / 75 (0.00%) 0	
Respiratory, thoracic and mediastinal disorders Oropharyngeal pain subjects affected / exposed occurrences (all) Nasal congestion subjects affected / exposed occurrences (all)	0 / 70 (0.00%) 0 1 / 70 (1.43%) 0	0 / 75 (0.00%) 0 1 / 75 (1.33%) 1	
Infections and infestations Upper respiratory tract infection subjects affected / exposed occurrences (all) Nasopharyngitis subjects affected / exposed occurrences (all)	3 / 70 (4.29%) 3 1 / 70 (1.43%) 1	2 / 75 (2.67%) 2 0 / 75 (0.00%) 0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
05 April 2012	Protocol Amendment #1
09 May 2012	Protocol Amendment #2
12 June 2012	Protocol Amendment #3
26 December 2012	Protocol Amendment #4

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported