Clinical trial results:
Clinical evaluation of efficacy at 2 weeks of Duac fixed dose combination gel in treatment of facial acne vulgaris in Japanese Subjects.

Summary

EudraCT number	2017-001575-23
Trial protocol	Outside EU/EEA
Global end of trial date	17 February 2016

Results information

Result version number	v1 (current)
This version publication date	01 November 2017
First version publication date	01 November 2017

Trial information

Trial identification

Sponsor protocol code	201884

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	GlaxoSmithKline
Sponsor organisation address	980 Great West Road, Brentford, Middlesex, United Kingdom,
Public contact	GSK Response Center, GlaxoSmithKline, 1 866-435-7343,
Scientific contact	GSK Response Center, GlaxoSmithKline, 1 866-435-7343,

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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	14 April 2016
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	17 February 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To compare the early efficacy of Duac Combination Gel once daily (QD) to the combination therapy of ADA QD and CLDM twice daily (BID) at Week 2.

Protection of trial subjects:

Not appicable

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	07 October 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	Japan: 349
Worldwide total number of subjects	349
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)	130
Adults (18-64 years)	219
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 349 participants were randomized.

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	DUAC

Arm description:

Participants were instructed to use DUAC, a fixed dose combination gel (clindamycin phosphate 1.2% and benzoyl peroxide 3%) with quantity of 2 finger tip unit (FTU) about 0.6 gram (g) which was sufficient to cover entire face (including the forehead, nose, cheeks and chin) once daily in the evening (at bedtime) for 12 weeks.

Arm type	Experimental
Investigational medicinal product name	DUAC
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Gel
Routes of administration	Topical use

Dosage and administration details:

Participants were instructed to use 2 FTU (about 0.6 g) of DUAC which was sufficient to cover entire face (including the forehead, nose, cheeks and chin) once daily in the evening (at bedtime) for 12 weeks.

Arm title	ADA 0.1% +CLDM 1%

Arm description:

Participants were instructed to use combination therapy of Adapalene (ADA) 0.1% gel with quantity of 1 FTU about 0.5 g sufficient to cover entire face (including the forehead, nose, cheeks and chin) once daily in the evening (at bedtime) and clindamycin (CLDM) 1% gel twice daily, once in the morning and once in the evening (at bedtime) for 12 weeks. The CLDM 1% gel was applied subsequent to the application of ADA 0.1% gel in the evening. The CLDM 1% gel was applied to inflammatory lesions (ILs) only.

Arm type	Active comparator
Investigational medicinal product name	ADA 0.1%
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Gel
Routes of administration	Topical use

Dosage and administration details:

Participants were instructed to use ADA 0.1% gel with quantity of 1 FTU (about 0.5 g) sufficient to cover entire face (including the forehead, nose, cheeks and chin) once daily in the evening (at bedtime) for 12 weeks.

Investigational medicinal product name	CLDM 1%
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Gel

Routes of administration	Topical use

Dosage and administration details:

Participants were instructed to use CLDM 1% gel twice daily, once in the morning and once in the evening (at bedtime) for 12 weeks. The CLDM 1% gel was applied subsequent to the application of ADA 0.1% gel in the evening. The CLDM 1% gel was applied to inflammatory lesions only.

Notes:

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

Justification: Investigator was blinded for this study.

Number of subjects in period 1	DUAC	ADA 0.1% +CLDM 1%
Started	172	177
Completed	165	169
Not completed	7	8
Consent withdrawn by subject	1	1
Protocol-defined stopping criteria	-	1
Adverse event, non-fatal	6	5
Protocol deviation	-	1

Baseline characteristics

Reporting groups	
Reporting group title	DUAC
Reporting group description:	
Participants were instructed to use DUAC, a fixed dose combination gel (clindamycin phosphate 1.2% and benzoyl peroxide 3%) with quantity of 2 finger tip unit (FTU) about 0.6 gram (g) which was sufficient to cover entire face (including the forehead, nose, cheeks and chin) once daily in the evening (at bedtime) for 12 weeks.	
Reporting group title	ADA 0.1% +CLDM 1%
Reporting group description:	
Participants were instructed to use combination therapy of Adapalene (ADA) 0.1% gel with quantity of 1 FTU about 0.5 g sufficient to cover entire face (including the forehead, nose, cheeks and chin) once daily in the evening (at bedtime) and clindamycin (CLDM) 1% gel twice daily, once in the morning and once in the evening (at bedtime) for 12 weeks. The CLDM 1% gel was applied subsequent to the application of ADA 0.1% gel in the evening. The CLDM 1% gel was applied to inflammatory lesions (ILs) only.	

Reporting group values	DUAC	ADA 0.1% +CLDM 1%	Total
Number of subjects	172	177	349
Age categorical Units: Subjects			
Age continuous			
Age continuous description			
Units: years			
arithmetic mean	20.3	19.8	
standard deviation	± 5.91	± 4.90	-
Gender categorical			
Gender categorical description			
Units: Subjects			
Female	97	110	207
Male	75	67	142
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	172	177	349
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	0	0	0
More than one race	0	0	0
Unknown or Not Reported	0	0	0

End points

End points reporting groups

Reporting group title	DUAC

Reporting group description:

Participants were instructed to use DUAC, a fixed dose combination gel (clindamycin phosphate 1.2% and benzoyl peroxide 3%) with quantity of 2 finger tip unit (FTU) about 0.6 gram (g) which was sufficient to cover entire face (including the forehead, nose, cheeks and chin) once daily in the evening (at bedtime) for 12 weeks.

Reporting group title	ADA 0.1% +CLDM 1%

Reporting group description:

Participants were instructed to use combination therapy of Adapalene (ADA) 0.1% gel with quantity of 1 FTU about 0.5 g sufficient to cover entire face (including the forehead, nose, cheeks and chin) once daily in the evening (at bedtime) and clindamycin (CLDM) 1% gel twice daily, once in the morning and once in the evening (at bedtime) for 12 weeks. The CLDM 1% gel was applied subsequent to the application of ADA 0.1% gel in the evening. The CLDM 1% gel was applied to inflammatory lesions (ILs) only.

Primary: Percent change in total lesion counts (TLs) from Baseline to Week 2

End point title	Percent change in total lesion counts (TLs) from Baseline to Week 2

End point description:

The assessor performed a count of IL (papules, pustules, nodular lesions), non-ILs (open and closed comedones) and total lesions (the sum of IL and non-IL) at each study visit. Lesion counts were confined to the face. Change from baseline was calculated as the value at endpoint minus the value at baseline. Data for adjusted mean has been reported. Percent change from Baseline is the change from Baseline divided by Baseline value multiplied by 100. The Baseline value was the latest pre-dose assessment value. The non-inflammatory lesions were counted by diagnosis based on palpation of the investigator (or sub-investigator). ITT population: comprise of all randomized participants who received at least one application of study product. Only those participants with data available at the specified time points were analyzed (represented by n=x ,x ,x) in the category titles.

End point type	Primary

End point timeframe:

Baseline (Day 1) and Week 2

End point values	DUAC	ADA 0.1% +CLDM 1%		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	169[1]	176[2]		
Units: Percent change in lesions				
least squares mean (standard error)	-42.16 (± 1.890)	-35.33 (± 1.850)		

Notes:

[1] - ITT population

[2] - ITT population

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Comparison between DUAC and ADA 0.1% +CLDM 1% at Week 2

Comparison groups	DUAC v ADA 0.1% +CLDM 1%

Number of subjects included in analysis	345
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.008 [3]
Method	mixed model repeated measures analysis
Parameter estimate	difference in percent
Point estimate	-6.83
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.88
upper limit	-1.78

Notes:

[3] - The analysis method was MMRM with treatment, center, visit, treatment-by-visit interaction, Baseline TLs counts, Baseline-by-visit interaction as fixed effects. A negative treatment difference indicates a benefit of Duac relative to ADA+CLDM.

Secondary: Percent change from Baseline in TLs to Weeks 1, 4, 8 and 12

End point title	Percent change from Baseline in TLs to Weeks 1, 4, 8 and 12

End point description:

The assessor performed a count of IL (papules, pustules, nodular lesions), non-ILs (open and closed comedones) and total lesions (the sum of IL and non-IL) at each study visit. Lesion counts were confined to the face. Change from Baseline was calculated as the value at endpoint minus the value at Baseline. Data for adjusted mean has been reported. Percent change from Baseline is the change from Baseline divided by Baseline value multiplied by 100. The Baseline value was the latest pre-dose assessment value. The non-ILs were counted by diagnosis based on palpation of the investigator (or sub-investigator). A negative treatment difference indicates a benefit of Duac relative to ADA+CLDM.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Week 1, 4, 8, 12

End point values	DUAC	ADA 0.1% +CLDM 1%		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	172[4]	177[5]		
Units: Percent change in lesions				
least squares mean (standard error)				
Week 1, n= 172, 176	-24.58 (± 1.729)	-24.33 (± 1.697)		
Week 4, n=169, 174	-55.51 (± 1.670)	-49.65 (± 1.637)		
Week 8, n= 167, 172	-65.23 (± 1.544)	-62.88 (± 1.514)		
Week 12, n= 164, 169	-74.60 (± 1.314)	-71.36 (± 1.288)		

Notes:

[4] - ITT population

[5] - ITT population

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:	
Comparison between DUAC and ADA 0.1% +CLDM 1% at Week 1	
Comparison groups	DUAC v ADA 0.1% +CLDM 1%
Number of subjects included in analysis	349
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.916 [6]
Method	mixed model repeated measures analysis
Parameter estimate	difference in percent
Point estimate	-0.25
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.85
upper limit	4.35

Notes:

[6] - The analysis method was mixed-model for repeated measures with treatment, center, visit, treatment-by-visit interaction, Baseline TLs counts, Baseline-by-visit interaction as fixed effects.

Statistical analysis title	Statistical analysis 2
Statistical analysis description:	
Comparison between DUAC and ADA 0.1% +CLDM 1% at Week 4	
Comparison groups	DUAC v ADA 0.1% +CLDM 1%
Number of subjects included in analysis	349
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.01 [7]
Method	mixed model repeated measures analysis
Parameter estimate	difference in percent
Point estimate	-5.85
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.29
upper limit	-1.42

Notes:

[7] - The analysis method was mixed-model for repeated measures with treatment, center, visit, treatment-by-visit interaction, Baseline TLs counts, Baseline-by-visit interaction as fixed effects.

Statistical analysis title	Statistical analysis 3
Statistical analysis description:	
Comparison between DUAC and ADA 0.1% +CLDM 1% at Week 8	
Comparison groups	DUAC v ADA 0.1% +CLDM 1%
Number of subjects included in analysis	349
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.257 [8]
Method	mixed model repeated measures analysis
Parameter estimate	difference in percent
Point estimate	-2.35

Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.42
upper limit	1.72

Notes:

[8] - The analysis method was mixed-model for repeated measures with treatment, center, visit, treatment-by-visit interaction, Baseline TLs counts, Baseline-by-visit interaction as fixed effects.

Statistical analysis title	Statistical analysis 4

Statistical analysis description:

Comparison between DUAC and ADA 0.1% +CLDM 1% at Week 12

Comparison groups	DUAC v ADA 0.1% +CLDM 1%
Number of subjects included in analysis	349
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.062 [9]
Method	mixed model repeated measures analysis
Parameter estimate	difference in percent
Point estimate	-3.24
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.64
upper limit	0.16

Notes:

[9] - The analysis method was mixed-model for repeated measures with treatment, center, visit, treatment-by-visit interaction, Baseline TLs counts, Baseline-by-visit interaction as fixed effects.

Secondary: Percent change form Baseline in lesion counts (ILs and non-ILs) to Weeks 1, 2, 4, 8 and 12

End point title	Percent change form Baseline in lesion counts (ILs and non-ILs) to Weeks 1, 2, 4, 8 and 12

End point description:

The assessor performed a count of IL (papules, pustules, nodular lesions), non-ILs (open and closed comedones). Lesion counts were confined to the face. Change from Baseline was calculated as the value at endpoint minus the value at Baseline. Data for adjusted mean has been reported. Percent change from Baseline is the change from Baseline divided by Baseline value multiplied by 100. The Baseline value was the latest pre-dose assessment value. The non-ILs were counted by diagnosis based on palpation of the investigator (or sub-investigator).

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Week 1, 2, 4, 8, 12

End point values	DUAC	ADA 0.1% +CLDM 1%		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	172[10]	177[11]		
Units: Percent change in lesions				
least squares mean (standard error)				
Week 1 ILs n= 172, 176	-42.97 (± 2.349)	-37.89 (± 2.309)		

Week 2 ILs n= 169, 176	-60.92 (± 2.209)	-52.49 (± 2.162)		
Week 4 ILs n= 169, 174	-70.68 (± 1.898)	-61.30 (± 1.860)		
Week 8 ILs n= 167, 172	-76.33 (± 1.717)	-69.64 (± 1.682)		
Week 12 ILs n= 164, 169	-82.07 (± 1.403)	-77.58 (± 1.374)		
Week 1 non-ILs n= 172, 176	-15.13 (± 2.279)	-17.85 (± 2.239)		
Week 2 non-ILs n= 169, 176	-32.71 (± 2.419)	-27.01 (± 2.367)		
Week 4 non-ILs n= 169, 174	-47.64 (± 2.171)	-43.74 (± 2.129)		
Week 8 non-ILs n= 167, 172	-59.50 (± 1.910)	-58.91 (± 1.872)		
Week 12 non-ILs n= 164, 169	-71.07 (± 1.603)	-67.29 (± 1.571)		

Notes:

[10] - ITT population

[11] - ITT population

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Comparison between DUAC and ADA 0.1% +CLDM 1% at Week 1 for ILs. A negative treatment difference indicates a benefit of Duac relative to ADA+CLDM.

Comparison groups	ADA 0.1% +CLDM 1% v DUAC
Number of subjects included in analysis	349
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.115 [12]
Method	mixed model repeated measures analysis
Parameter estimate	difference in percent
Point estimate	-5.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.41
upper limit	1.25

Notes:

[12] - The analysis method was mixed-model for repeated measures with treatment, center, visit, treatment-by-visit interaction, Baseline ILs counts, Baseline-by-visit interaction as fixed effects.

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

Comparison between DUAC and ADA 0.1% +CLDM 1% at Week 2 for ILs. A negative treatment difference indicates a benefit of Duac relative to ADA+CLDM.

Comparison groups	ADA 0.1% +CLDM 1% v DUAC

Number of subjects included in analysis	349
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.005 [13]
Method	mixed model repeated measures analysis
Parameter estimate	difference in percent
Point estimate	-8.43
Confidence interval	
level	95 %
sides	2-sided
lower limit	-14.35
upper limit	-2.51

Notes:

[13] - The analysis method was mixed-model for repeated measures with treatment, center, visit, treatment-by-visit interaction, Baseline ILs counts, Baseline-by-visit interaction as fixed effects.

Statistical analysis title	Statistical analysis 3

Statistical analysis description:

Comparison between DUAC and ADA 0.1% +CLDM 1% at Week 4 for ILs. A negative treatment difference indicates a benefit of Duac relative to ADA+CLDM.

Comparison groups	ADA 0.1% +CLDM 1% v DUAC
Number of subjects included in analysis	349
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001 [14]
Method	mixed model repeated measures analysis
Parameter estimate	difference in percent
Point estimate	-9.37
Confidence interval	
level	95 %
sides	2-sided
lower limit	-14.42
upper limit	-4.33

Notes:

[14] - The analysis method was mixed-model for repeated measures with treatment, center, visit, treatment-by-visit interaction, Baseline ILs counts, Baseline-by-visit interaction as fixed effects.

Statistical analysis title	Statistical analysis 4

Statistical analysis description:

Comparison between DUAC and ADA 0.1% +CLDM 1% at Week 8 for ILs. A negative treatment difference indicates a benefit of Duac relative to ADA+CLDM.

Comparison groups	ADA 0.1% +CLDM 1% v DUAC
Number of subjects included in analysis	349
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.004 [15]
Method	mixed model repeated measures analysis
Parameter estimate	difference in percent
Point estimate	-6.69

Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.21
upper limit	-2.16

Notes:

[15] - The analysis method was mixed-model for repeated measures with treatment, center, visit, treatment-by-visit interaction, Baseline ILs counts, Baseline-by-visit interaction as fixed effects.

Statistical analysis title	Statistical analysis 5

Statistical analysis description:

Comparison between DUAC and ADA 0.1% +CLDM 1% at Week 12 for ILs

Comparison groups	ADA 0.1% +CLDM 1% v DUAC
Number of subjects included in analysis	349
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.015 [16]
Method	mixed model repeated measures analysis
Parameter estimate	Mean difference (net)
Point estimate	-4.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.1
upper limit	-0.89

Notes:

[16] - The analysis method was mixed-model for repeated measures with treatment, center, visit, treatment-by-visit interaction, Baseline ILs counts, Baseline-by-visit interaction as fixed effects.

Statistical analysis title	Statistical analysis 6

Statistical analysis description:

Comparison between DUAC and ADA 0.1% +CLDM 1% at Week 1 for non-ILs. A negative treatment difference indicates a benefit of Duac relative to ADA+CLDM.

Comparison groups	ADA 0.1% +CLDM 1% v DUAC
Number of subjects included in analysis	349
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.382 [17]
Method	mixed model repeated measures analysis
Parameter estimate	difference in percent
Point estimate	2.71
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.38
upper limit	8.8

Notes:

[17] - The analysis method was mixed-model for repeated measures with treatment, center, visit, treatment-by-visit interaction, Baseline non-ILs counts, Baseline-by-visit interaction as fixed effects.

Statistical analysis title	Statistical analysis 7

Statistical analysis description:

Comparison between DUAC and ADA 0.1% +CLDM 1% at Week 2 for non-ILs. A negative treatment

difference indicates a benefit of Duac relative to ADA+CLDM.

Comparison groups	ADA 0.1% +CLDM 1% v DUAC
Number of subjects included in analysis	349
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.085 [18]
Method	mixed model repeated measures analysis
Parameter estimate	difference in percent
Point estimate	-5.69
Confidence interval	
level	95 %
sides	2-sided
lower limit	-12.17
upper limit	0.78

Notes:

[18] - The analysis method was mixed-model for repeated measures with treatment, center, visit, treatment-by-visit interaction, Baseline non-ILs counts, Baseline-by-visit interaction as fixed effects.

Statistical analysis title	Statistical analysis 8

Statistical analysis description:

Comparison between DUAC and ADA 0.1% +CLDM 1% at Week 4 for non-ILs. A negative treatment difference indicates a benefit of Duac relative to ADA+CLDM.

Comparison groups	ADA 0.1% +CLDM 1% v DUAC
Number of subjects included in analysis	349
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.186 [19]
Method	mixed model repeated measures analysis
Parameter estimate	difference in percent
Point estimate	-3.89
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.67
upper limit	1.88

Notes:

[19] - The analysis method was mixed-model for repeated measures with treatment, center, visit, treatment-by-visit interaction, Baseline non-ILs counts, Baseline-by-visit interaction as fixed effects.

Statistical analysis title	Statistical analysis 9

Statistical analysis description:

Comparison between DUAC and ADA 0.1% +CLDM 1% at Week 8 for non-ILs. A negative treatment difference indicates a benefit of Duac relative to ADA+CLDM.

Comparison groups	ADA 0.1% +CLDM 1% v DUAC
Number of subjects included in analysis	349
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.818 [20]
Method	mixed model repeated measures analysis
Parameter estimate	difference in percent
Point estimate	-0.59

Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.61
upper limit	4.44

Notes:

[20] - The analysis method was mixed-model for repeated measures with treatment, center, visit, treatment-by-visit interaction, Baseline non-ILs counts, Baseline-by-visit interaction as fixed effects.

Statistical analysis title	Statistical analysis 10

Statistical analysis description:

Comparison between DUAC and ADA 0.1% +CLDM 1% at Week 12 for non-ILs. A negative treatment difference indicates a benefit of Duac relative to ADA+CLDM.

Comparison groups	ADA 0.1% +CLDM 1% v DUAC
Number of subjects included in analysis	349
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.073 [21]
Method	mixed model repeated measures analysis
Parameter estimate	difference in percent
Point estimate	-3.78
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.92
upper limit	0.35

Notes:

[21] - The analysis method was mixed-model for repeated measures with treatment, center, visit, treatment-by-visit interaction, Baseline non-ILs counts, Baseline-by-visit interaction as fixed effects.

Secondary: Absolute Change from Baseline in lesion counts (TLs, ILs and non-ILs) to Weeks 1, 2, 4, 8 and 12

End point title	Absolute Change from Baseline in lesion counts (TLs, ILs and non-ILs) to Weeks 1, 2, 4, 8 and 12

End point description:

The assessor performed a count of IL (papules, pustules, nodular lesions), non-ILs (open and closed comedones) and total lesions (the sum of IL and non-IL) at each study visit. Lesion counts were confined to the face. Change from Baseline was calculated as the value at endpoint minus the value at Baseline. Data for adjusted mean has been reported. The non-ILs were counted by diagnosis based on palpation of the investigator (or sub-investigator). A negative treatment difference indicates a benefit of Duac relative to ADA+CLDM.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Week 1, 2, 4, 8, 12

End point values	DUAC	ADA 0.1% +CLDM 1%		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	172[22]	177[23]		
Units: Change in lesion count				
least squares mean (standard error)				
Week 1 =TLs n= 172, 176	-24.4 (± 1.70)	-24.3 (± 1.67)		

Week 2 TLs n= 169, 176	-41.8 (± 1.88)	-35.6 (± 1.84)		
Week 4 TLs n= 169, 174	-56.3 (± 1.71)	-51.6 (± 1.67)		
Week 8 TLs n= 167, 172	-66.4 (± 1.60)	-65.7 (± 1.57)		
Week 12 TLs n= 164, 169	-76.2 (± 1.37)	-74.5 (± 1.34)		
Week 1 ILs n= 172, 176	-13.3 (± 0.74)	-11.5 (± 0.72)		
Week 2 ILs n= 169, 176	-19.3 (± 0.70)	-16.3 (± 0.68)		
Week 4 ILs n= 169, 174	-22.4 (± 0.62)	-19.8 (± 0.60)		
Week 8 ILs n= 167, 172	-24.3 (± 0.56)	-22.4 (± 0.55)		
Week 12 ILs n= 164, 169	-26.0 (± 0.48)	-24.9 (± 0.47)		
Week 1 non-ILs n= 172, 176	-11.1 (± 1.46)	-12.9 (± 1.43)		
Week 2 non-ILs n= 169, 176	-22.5 (± 1.59)	-19.3 (± 1.56)		
Week 4 non-ILs n= 169, 174	-34.0 (± 1.46)	-32.0 (± 1.44)		
Week 8 non-ILs n= 167, 172	-42.2 (± 1.33)	-43.4 (± 1.31)		
Week 12 non-ILs n= 164, 169	-50.2 (± 1.11)	-49.6 (± 1.09)		

Notes:

[22] - ITT population

[23] - ITT population

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Comparison between DUAC and ADA 0.1% +CLDM 1% at Week 1 for TLs. negative treatment difference indicates a benefit of Duac relative to ADA+CLDM.

Comparison groups	ADA 0.1% +CLDM 1% v DUAC
Number of subjects included in analysis	349
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.961 [24]
Method	mixed model repeated measures analysis
Parameter estimate	Mean difference (net)
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.6
upper limit	4.4

Notes:

[24] - The analysis method was mixed-model for repeated measures with treatment, center, visit, treatment-by-visit interaction, Baseline TLs counts, Baseline-by-visit interaction as fixed effects.

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

Comparison between DUAC and ADA 0.1% +CLDM 1% at Week 2 for TLs. A negative treatment difference indicates a benefit of Duac relative to ADA+CLDM.

Comparison groups	ADA 0.1% +CLDM 1% v DUAC
Number of subjects included in analysis	349
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.015 [25]
Method	mixed model repeated measures analysis
Parameter estimate	Mean difference (net)
Point estimate	-6.2

Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.2
upper limit	-1.2

Notes:

[25] - The analysis method was mixed-model for repeated measures with treatment, center, visit, treatment-by-visit interaction, Baseline TLs counts, Baseline-by-visit interaction as fixed effects.

Statistical analysis title	Statistical analysis 3

Statistical analysis description:

Comparison between DUAC and ADA 0.1% +CLDM 1% at Week 4 for TLs. A negative treatment difference indicates a benefit of Duac relative to ADA+CLDM.

Comparison groups	ADA 0.1% +CLDM 1% v DUAC
Number of subjects included in analysis	349
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.044 [26]
Method	mixed model repeated measures analysis
Parameter estimate	Mean difference (net)
Point estimate	-4.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.2
upper limit	-0.1

Notes:

[26] - The analysis method was mixed-model for repeated measures with treatment, center, visit, treatment-by-visit interaction, Baseline TLs counts, Baseline-by-visit interaction as fixed effects.

Statistical analysis title	Statistical analysis 4

Statistical analysis description:

Comparison between DUAC and ADA 0.1% +CLDM 1% at Week 8 for TLs. A negative treatment difference indicates a benefit of Duac relative to ADA+CLDM.

Comparison groups	ADA 0.1% +CLDM 1% v DUAC
Number of subjects included in analysis	349
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.747 [27]
Method	mixed model repeated measures analysis
Parameter estimate	Mean difference (net)
Point estimate	-0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.9
upper limit	3.5

Notes:

[27] - The analysis method was mixed-model for repeated measures with treatment, center, visit, treatment-by-visit interaction, Baseline TLs counts, Baseline-by-visit interaction as fixed effects.

Statistical analysis title	Statistical analysis 5

Statistical analysis description:

Comparison between DUAC and ADA 0.1% +CLDM 1% at Week 12 for TLs. A negative treatment difference indicates a benefit of Duac relative to ADA+CLDM.

Comparison groups	ADA 0.1% +CLDM 1% v DUAC
Number of subjects included in analysis	349
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.338 [28]
Method	mixed model repeated measures analysis
Parameter estimate	Mean difference (net)
Point estimate	-1.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.3
upper limit	1.8

Notes:

[28] - The analysis method was mixed-model for repeated measures with treatment, center, visit, treatment-by-visit interaction, Baseline TLs counts, Baseline-by-visit interaction as fixed effects.

Statistical analysis title	Statistical analysis 6

Statistical analysis description:

Comparison between DUAC and ADA 0.1% +CLDM 1% at Week 1 for ILs. A negative treatment difference indicates a benefit of Duac relative to ADA+CLDM.

Comparison groups	ADA 0.1% +CLDM 1% v DUAC
Number of subjects included in analysis	349
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.068 [29]
Method	mixed model repeated measures analysis
Parameter estimate	Mean difference (net)
Point estimate	-1.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.8
upper limit	0.1

Notes:

[29] - The analysis method was mixed-model for repeated measures with treatment, center, visit, treatment-by-visit interaction, Baseline ILs counts, Baseline-by-visit interaction as fixed effects.

Statistical analysis title	Statistical analysis 7

Statistical analysis description:

Comparison between DUAC and ADA 0.1% +CLDM 1% at Week 2 for ILs. A negative treatment difference indicates a benefit of Duac relative to ADA+CLDM.

Comparison groups	ADA 0.1% +CLDM 1% v DUAC
Number of subjects included in analysis	349
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.002 [30]
Method	mixed model repeated measures analysis
Parameter estimate	Mean difference (net)
Point estimate	-3

Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.8
upper limit	-1.1

Notes:

[30] - The analysis method was mixed-model for repeated measures with treatment, center, visit, treatment-by-visit interaction, Baseline ILs counts, Baseline-by-visit interaction as fixed effects.

Statistical analysis title	Statistical analysis 8

Statistical analysis description:

Comparison between DUAC and ADA 0.1% +CLDM 1% at Week 4 for ILs. A negative treatment difference indicates a benefit of Duac relative to ADA+CLDM.

Comparison groups	ADA 0.1% +CLDM 1% v DUAC
Number of subjects included in analysis	349
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.002 [31]
Method	mixed model repeated measures analysis
Parameter estimate	Mean difference (net)
Point estimate	-2.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.3
upper limit	-1

Notes:

[31] - The analysis method was mixed-model for repeated measures with treatment, center, visit, treatment-by-visit interaction, Baseline ILs counts, Baseline-by-visit interaction as fixed effects.

Statistical analysis title	Statistical analysis 9

Statistical analysis description:

Comparison between DUAC and ADA 0.1% +CLDM 1% at Week 8 for ILs. A negative treatment difference indicates a benefit of Duac relative to ADA+CLDM.

Comparison groups	ADA 0.1% +CLDM 1% v DUAC
Number of subjects included in analysis	349
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.012 [32]
Method	mixed model repeated measures analysis
Parameter estimate	Mean difference (net)
Point estimate	-1.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.4
upper limit	-0.4

Notes:

[32] - The analysis method was mixed-model for repeated measures with treatment, center, visit, treatment-by-visit interaction, Baseline ILs counts, Baseline-by-visit interaction as fixed effects.

Statistical analysis title	Statistical analysis 10

Statistical analysis description:

Comparison between DUAC and ADA 0.1% +CLDM 1% at Week 12 for ILs. A negative treatment difference indicates a benefit of Duac relative to ADA+CLDM.

Comparison groups	ADA 0.1% +CLDM 1% v DUAC
Number of subjects included in analysis	349
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.078 [33]
Method	mixed model repeated measures analysis
Parameter estimate	Mean difference (net)
Point estimate	-1.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.4
upper limit	0.1

Notes:

[33] - The analysis method was mixed-model for repeated measures with treatment, center, visit, treatment-by-visit interaction, Baseline ILs counts, Baseline-by-visit interaction as fixed effects.

Statistical analysis title	Statistical analysis 11

Statistical analysis description:

Comparison between DUAC and ADA 0.1% +CLDM 1% at Week 1 for non-ILs. A negative treatment difference indicates a benefit of Duac relative to ADA+CLDM.

Comparison groups	ADA 0.1% +CLDM 1% v DUAC
Number of subjects included in analysis	349
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.367 [34]
Method	mixed model repeated measures analysis
Parameter estimate	Mean difference (net)
Point estimate	1.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.1
upper limit	5.7

Notes:

[34] - The analysis method was mixed-model for repeated measures with treatment, center, visit, treatment-by-visit interaction, Baseline non-ILs counts, Baseline-by-visit interaction as fixed effects.

Statistical analysis title	Statistical analysis 12

Statistical analysis description:

Comparison between DUAC and ADA 0.1% +CLDM 1% at Week 2 for non-ILs. A negative treatment difference indicates a benefit of Duac relative to ADA+CLDM.

Comparison groups	ADA 0.1% +CLDM 1% v DUAC
Number of subjects included in analysis	349
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.148 [35]
Method	mixed model repeated measures analysis
Parameter estimate	Mean difference (net)
Point estimate	-3.1

Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.4
upper limit	1.1

Notes:

[35] - The analysis method was mixed-model for repeated measures with treatment, center, visit, treatment-by-visit interaction, Baseline non-ILs counts, Baseline-by-visit interaction as fixed effects.

Statistical analysis title	Statistical analysis 13

Statistical analysis description:

Comparison between DUAC and ADA 0.1% +CLDM 1% at Week 4 for non-ILs. A negative treatment difference indicates a benefit of Duac relative to ADA+CLDM.

Comparison groups	ADA 0.1% +CLDM 1% v DUAC
Number of subjects included in analysis	349
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.314 [36]
Method	mixed model repeated measures analysis
Parameter estimate	Mean difference (net)
Point estimate	-2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.9
upper limit	1.9

Notes:

[36] - The analysis method was mixed-model for repeated measures with treatment, center, visit, treatment-by-visit interaction, Baseline non-ILs counts, Baseline-by-visit interaction as fixed effects.

Statistical analysis title	Statistical analysis 14

Statistical analysis description:

Comparison between DUAC and ADA 0.1% +CLDM 1% at Week 8 for non-ILs. A negative treatment difference indicates a benefit of Duac relative to ADA+CLDM.

Comparison groups	ADA 0.1% +CLDM 1% v DUAC
Number of subjects included in analysis	349
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.494 [37]
Method	mixed model repeated measures analysis
Parameter estimate	Mean difference (net)
Point estimate	1.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.3
upper limit	4.7

Notes:

[37] - The analysis method was mixed-model for repeated measures with treatment, center, visit, treatment-by-visit interaction, Baseline non-ILs counts, Baseline-by-visit interaction as fixed effects.

Statistical analysis title	Statistical analysis 15

Statistical analysis description:

Comparison between DUAC and ADA 0.1% +CLDM 1% at Week 12 for non-ILs. A negative treatment difference indicates a benefit of Duac relative to ADA+CLDM.

Comparison groups	ADA 0.1% +CLDM 1% v DUAC
Number of subjects included in analysis	349
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.684 [38]
Method	mixed model repeated measures analysis
Parameter estimate	Mean difference (net)
Point estimate	-0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.5
upper limit	2.3

Notes:

[38] - The analysis method was mixed-model for repeated measures with treatment, center, visit, treatment-by-visit interaction, Baseline non-ILs counts, Baseline-by-visit interaction as fixed effects.

Secondary: Percentage of participants with a minimum of 2-grade improvement in investigator's static global assessment (ISGA) score from Baseline to Weeks 1, 2, 4, 8 and 12

End point title	Percentage of participants with a minimum of 2-grade improvement in investigator's static global assessment (ISGA) score from Baseline to Weeks 1, 2, 4, 8 and 12

End point description:

Responder was defined as participants with a minimum 2-grade improvement in ISGA score from Baseline. ISGA scale was scored from 0-5 (0= Clear skin with no inflammatory or non-ILs, 1= Almost clear: rare non-ILs present, with no more than rare papules, 2= Mild severity: greater than Grade 1, some non-ILs with no more than few inflammatory lesions, 3= Moderate severity: greater than Grade 2, many non-ILS, may have some ILs, but no more than 1 small nodular lesion, 4= Severe: greater than Grade 3, up to many non-ILs and ILs, but no more than a few nodular lesions, 5= Very severe: many non -ILs and ILs and more than a few nodular lesions. May have cystic lesions). Percentage of participants was calculated by dividing number of participants with 2-grade improvement in ISGA score from Baseline by total number of participants value multiplied by 100.

End point type	Secondary

End point timeframe:

Week 1, 2, 4, 8, 12

End point values	DUAC	ADA 0.1% +CLDM 1%		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	172[39]	177[40]		
Units: Percentage of participants				
Week 1	2	0		
Week 2	6	3		
Week 4	12	8		
Week 8	22	12		
Week 12	37	27		

Notes:

[39] - ITT population

[40] - ITT population

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Comparison between DUAC and ADA 0.1% +CLDM 1% at Week 1.The participants with missing data at a visit were included in the denominator (n) at the visit. That is, those participants were treated as non-responder at the visit.

Comparison groups	ADA 0.1% +CLDM 1% v DUAC
Number of subjects included in analysis	349
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.047 [41]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in percentage
Point estimate	2.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.1
upper limit	4.6

Notes:

[41] - The P-value was based on the Cochran-Mantel-Haenszel test stratified by center.

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

Comparison between DUAC and ADA 0.1% +CLDM 1% at Week 2. The participants with missing data at a visit were included in the denominator (n) at the visit. That is, those participants were treated as non-responder at the visit.

Comparison groups	ADA 0.1% +CLDM 1% v DUAC
Number of subjects included in analysis	349
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.185 [42]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in percentage
Point estimate	3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.3
upper limit	7.3

Notes:

[42] - The P-value was based on the Cochran-Mantel-Haenszel test stratified by center.

Statistical analysis title	Statistical analysis 3

Statistical analysis description:

Comparison between DUAC and ADA 0.1% +CLDM 1% at Week 4. The participants with missing data at a visit were included in the denominator (n) at the visit. That is, those participants were treated as non-responder at the visit.

Comparison groups	ADA 0.1% +CLDM 1% v DUAC
Number of subjects included in analysis	349
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.251 [43]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in percentage
Point estimate	3.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.5
upper limit	9.9

Notes:

[43] - The P-value was based on the Cochran-Mantel-Haenszel test stratified by center.

Statistical analysis title	Statistical analysis 4

Statistical analysis description:

Comparison between DUAC and ADA 0.1% +CLDM 1% at Week 8. The participants with missing data at a visit were included in the denominator (n) at the visit. That is, those participants were treated as non-responder at the visit.

Comparison groups	ADA 0.1% +CLDM 1% v DUAC
Number of subjects included in analysis	349
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.006 [44]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in percentage
Point estimate	10.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.4
upper limit	18

Notes:

[44] - The P-value was based on the Cochran-Mantel-Haenszel test stratified by center.

Statistical analysis title	Statistical analysis 5

Statistical analysis description:

Comparison between DUAC and ADA 0.1% +CLDM 1% at Week 12. The participants with missing data at a visit were included in the denominator (n) at the visit. That is, those participants were treated as non-responder at the visit.

Comparison groups	ADA 0.1% +CLDM 1% v DUAC

Number of subjects included in analysis	349
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.022 [45]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in percentage
Point estimate	10.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.9
upper limit	20.4

Notes:

[45] - The P-value was based on the Cochran-Mantel-Haenszel test stratified by center.

Secondary: Percentage of participants with ISGA score of 0 or 1 at Weeks 1, 2, 4, 8 and 12

End point title	Percentage of participants with ISGA score of 0 or 1 at Weeks 1, 2, 4, 8 and 12

End point description:

Responder was defined as participant with ISGA score of 0 or 1. ISGA scale was scored from 0-5 (0= Clear skin with no inflammatory or non-ILs, 1= Almost clear: rare non-ILs present, with no more than rare papules, 2= Mild severity: greater than Grade 1, some non-ILs with no more than few inflammatory lesions, 3= Moderate severity: greater than Grade 2, many non-ILS, may have some ILs, but no more than 1 small nodular lesion, 4= Severe: greater than Grade 3, up to many non-ILs and ILs, but no more than a few nodular lesions, 5= Very severe: many non -ILs and ILs and more than a few nodular lesions. May have cystic lesions). Percentage of participants was calculated by dividing number of participants with 0-1 ISGA score post Baseline by total number of participants value multiplied by 100.

End point type	Secondary

End point timeframe:

Week 1, 2, 4, 8 and 12

End point values	DUAC	ADA 0.1% +CLDM 1%		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	172[46]	177[47]		
Units: Percentage of participants				
Week 1	2	1		
Week 2	6	5		
Week 4	13	6		
Week 8	20	12		
Week 12	41	29		

Notes:

[46] - ITT population

[47] - ITT population

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Comparison between DUAC and ADA 0.1% +CLDM 1% at Week 1. The participants with missing data at a visit were included in the denominator (n) at the visit. That is, those participants were treated as non-

responder at the visit.

Comparison groups	ADA 0.1% +CLDM 1% v DUAC
Number of subjects included in analysis	349
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.129 [48]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in percentage
Point estimate	1.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.7
upper limit	4.3

Notes:

[48] - The P-value was based on the Cochran-Mantel-Haenszel test stratified by center.

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

Comparison between DUAC and ADA 0.1% +CLDM 1% at Week 2. The participants with missing data at a visit were included in the denominator (n) at the visit. That is, those participants were treated as non-responder at the visit.

Comparison groups	ADA 0.1% +CLDM 1% v DUAC
Number of subjects included in analysis	349
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.612 [49]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in percentage
Point estimate	1.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.4
upper limit	5.9

Notes:

[49] - The P-value was based on the Cochran-Mantel-Haenszel test stratified by center.

Statistical analysis title	Statistical analysis 3

Statistical analysis description:

Comparison between DUAC and ADA 0.1% +CLDM 1% at Week 4. The participants with missing data at a visit were included in the denominator (n) at the visit. That is, those participants were treated as non-responder at the visit.

Comparison groups	ADA 0.1% +CLDM 1% v DUAC
Number of subjects included in analysis	349
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.016 [50]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in percentage
Point estimate	7.1

Confidence interval	
level	95 %
sides	2-sided
lower limit	1.1
upper limit	13.2

Notes:

[50] - The P-value was based on the Cochran-Mantel-Haenszel test stratified by center.

Statistical analysis title	Statistical analysis 4

Statistical analysis description:

Comparison between DUAC and ADA 0.1% +CLDM 1% at Week 8. The participants with missing data at a visit were included in the denominator (n) at the visit. That is, those participants were treated as non-responder at the visit.

Comparison groups	ADA 0.1% +CLDM 1% v DUAC
Number of subjects included in analysis	349
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.034 [51]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in percentage
Point estimate	7.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.3
upper limit	15.5

Notes:

[51] - The P-value was based on the Cochran-Mantel-Haenszel test stratified by center.

Statistical analysis title	Statistical analysis 5

Statistical analysis description:

Comparison between DUAC and ADA 0.1% +CLDM 1% at Week 12. The participants with missing data at a visit were included in the denominator (n) at the visit. That is, those participants were treated as non-responder at the visit.

Comparison groups	ADA 0.1% +CLDM 1% v DUAC
Number of subjects included in analysis	349
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.018 [52]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in percentage
Point estimate	11.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.4
upper limit	21.3

Notes:

[52] - The P-value was based on the Cochran-Mantel-Haenszel test stratified by center.

Secondary: Percentage of participants with at least 50% reduction in lesion counts

(TLs, ILs and non-ILs) from Baseline at Weeks 1, 2, 4, 8 and 12	
End point title	Percentage of participants with at least 50% reduction in lesion counts (TLs, ILs and non-ILs) from Baseline at Weeks 1, 2, 4, 8 and 12

End point description:

Responder was defined as participants with at least a 50% reduction in TLs, ILs and non-ILs. Data for number of participants is reported. Percentage of participants was calculated by dividing number of responders by total number of participants value multiplied by 100.

End point type	Secondary

End point timeframe:

Week 1, 2, 4, 8 and 12

End point values	DUAC	ADA 0.1% +CLDM 1%		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	172[53]	177[54]		
Units: Percentage of participants				
Week 1 TLs, n= 172, 176	22	18		
Week 2 TLs, n= 172, 177	47	42		
Week 4 TLs, n= 172, 177	67	60		
Week 8 TLs, n= 172, 177	81	81		
Week 12 TLs, n= 172, 177	88	86		
Week 1 ILs, n= 172, 176	51	42		
Week 2 ILs, n= 172, 177	77	66		
Week 4 ILs, n= 172, 177	85	76		
Week 8 ILs, n= 172, 177	87	84		
Week 12 ILs, n= 172, 177	92	89		
Week 1 non-ILs, n= 172, 176	14	16		
Week 2 non-ILs, n= 172, 177	37	34		
Week 4 non-ILs, n= 172, 177	58	54		
Week 8 non-ILs, n= 172, 177	73	73		
Week 12 non-ILs, n= 172, 177	83	80		

Notes:

[53] - ITT population

[54] - ITT population

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Comparison between DUAC and ADA 0.1% +CLDM 1% at Week 1 for TLs. The participants with missing data at a visit were included in the denominator (n) at the visit. That is, those participants were treated as non-responder at the visit.

Comparison groups	ADA 0.1% +CLDM 1% v DUAC
Number of subjects included in analysis	349
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.379 [55]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in percentage
Point estimate	3.9

Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.5
upper limit	12.3

Notes:

[55] - The P-value was based on the Cochran-Mantel-Haenszel test stratified by center.

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

Comparison between DUAC and ADA 0.1% +CLDM 1% at Week 2 for TLs. The participants with missing data at a visit were included in the denominator (n) at the visit. That is, those participants were treated as non-responder at the visit.

Comparison groups	ADA 0.1% +CLDM 1% v DUAC
Number of subjects included in analysis	349
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.409 [56]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in percentage
Point estimate	4.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.7
upper limit	15.1

Notes:

[56] - The P-value was based on the Cochran-Mantel-Haenszel test stratified by center.

Statistical analysis title	Statistical analysis 3

Statistical analysis description:

Comparison between DUAC and ADA 0.1% +CLDM 1% at Week 4 for TLs. The participants with missing data at a visit were included in the denominator (n) at the visit. That is, those participants were treated as non-responder at the visit.

Comparison groups	ADA 0.1% +CLDM 1% v DUAC
Number of subjects included in analysis	349
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.18 [57]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in percentage
Point estimate	7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.1
upper limit	17

Notes:

[57] - The P-value was based on the Cochran-Mantel-Haenszel test stratified by center.

Statistical analysis title	Statistical analysis 4

Statistical analysis description:

Comparison between DUAC and ADA 0.1% +CLDM 1% at Week 8 for TLs. The participants with missing data at a visit were included in the denominator (n) at the visit. That is, those participants were treated as non-responder at the visit.

Comparison groups	ADA 0.1% +CLDM 1% v DUAC
Number of subjects included in analysis	349
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.81 [58]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in percentage
Point estimate	-0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.8
upper limit	7.7

Notes:

[58] - The P-value was based on the Cochran-Mantel-Haenszel test stratified by center.

Statistical analysis title	Statistical analysis 5

Statistical analysis description:

Comparison between DUAC and ADA 0.1% +CLDM 1% at Week 12 for TLs. The participants with missing data at a visit were included in the denominator (n) at the visit. That is, those participants were treated as non-responder at the visit.

Comparison groups	ADA 0.1% +CLDM 1% v DUAC
Number of subjects included in analysis	349
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.648 [59]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in percentage
Point estimate	1.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.2
upper limit	9

Notes:

[59] - The P-value was based on the Cochran-Mantel-Haenszel test stratified by center.

Statistical analysis title	Statistical analysis 6

Statistical analysis description:

Comparison between DUAC and ADA 0.1% +CLDM 1% at Week 1 for ILs. The participants with missing data at a visit were included in the denominator (n) at the visit. That is, those participants were treated as non-responder at the visit.

Comparison groups	ADA 0.1% +CLDM 1% v DUAC

Number of subjects included in analysis	349
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.048 [60]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in percentage
Point estimate	9.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.3
upper limit	19.6

Notes:

[60] - The P-value was based on the Cochran-Mantel-Haenszel test stratified by center.

Statistical analysis title	Statistical analysis 7

Statistical analysis description:

Comparison between DUAC and ADA 0.1% +CLDM 1% at Week 2 for ILs. The participants with missing data at a visit were included in the denominator (n) at the visit. That is, those participants were treated as non-responder at the visit.

Comparison groups	ADA 0.1% +CLDM 1% v DUAC
Number of subjects included in analysis	349
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.016 [61]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in percentage
Point estimate	11.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.8
upper limit	20.6

Notes:

[61] - The P-value was based on the Cochran-Mantel-Haenszel test stratified by center.

Statistical analysis title	Statistical analysis 8

Statistical analysis description:

Comparison between DUAC and ADA 0.1% +CLDM 1% at Week 4 for ILs. The participants with missing data at a visit were included in the denominator (n) at the visit. That is, those participants were treated as non-responder at the visit.

Comparison groups	ADA 0.1% +CLDM 1% v DUAC
Number of subjects included in analysis	349
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.044 [62]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in percentage
Point estimate	8.6

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.4
upper limit	16.9

Notes:

[62] - The P-value was based on the Cochran-Mantel-Haenszel test stratified by center.

Statistical analysis title	Statistical analysis 9

Statistical analysis description:

Comparison between DUAC and ADA 0.1% +CLDM 1% at Week 8 for ILs. The participants with missing data at a visit were included in the denominator (n) at the visit. That is, those participants were treated as non-responder at the visit.

Comparison groups	ADA 0.1% +CLDM 1% v DUAC
Number of subjects included in analysis	349
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.345 [63]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in percentage
Point estimate	3.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.8
upper limit	11

Notes:

[63] - The P-value was based on the Cochran-Mantel-Haenszel test stratified by center.

Statistical analysis title	Statistical analysis 10

Statistical analysis description:

Comparison between DUAC and ADA 0.1% +CLDM 1% at Week 12 for ILs. The participants with missing data at a visit were included in the denominator (n) at the visit. That is, those participants were treated as non-responder at the visit.

Comparison groups	ADA 0.1% +CLDM 1% v DUAC
Number of subjects included in analysis	349
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.424 [64]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in percentage
Point estimate	2.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.5
upper limit	8.7

Notes:

[64] - The P-value was based on the Cochran-Mantel-Haenszel test stratified by center.

Statistical analysis title	Statistical analysis 11

Statistical analysis description:

Comparison between DUAC and ADA 0.1% +CLDM 1% at Week 1 for non-ILs. The participants with missing data at a visit were included in the denominator (n) at the visit. That is, those participants were treated as non-responder at the visit.

Comparison groups	ADA 0.1% +CLDM 1% v DUAC
Number of subjects included in analysis	349
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.527 [65]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in percentage
Point estimate	-2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.4
upper limit	5.5

Notes:

[65] - The P-value was based on the Cochran-Mantel-Haenszel test stratified by center.

Statistical analysis title	Statistical analysis 12

Statistical analysis description:

Comparison between DUAC and ADA 0.1% +CLDM 1% at Week 2 for non-ILs. The participants with missing data at a visit were included in the denominator (n) at the visit. That is, those participants were treated as non-responder at the visit.

Comparison groups	ADA 0.1% +CLDM 1% v DUAC
Number of subjects included in analysis	349
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.584 [66]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in percentage
Point estimate	3.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.7
upper limit	13.4

Notes:

[66] - The P-value was based on the Cochran-Mantel-Haenszel test stratified by center.

Statistical analysis title	Statistical analysis 13

Statistical analysis description:

Comparison between DUAC and ADA 0.1% +CLDM 1% at Week 4 for non-ILs. The participants with missing data at a visit were included in the denominator (n) at the visit. That is, those participants were treated as non-responder at the visit.

Comparison groups	ADA 0.1% +CLDM 1% v DUAC

Number of subjects included in analysis	349
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.519 [67]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in percentage
Point estimate	3.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.5
upper limit	14.3

Notes:

[67] - The P-value was based on the Cochran-Mantel-Haenszel test stratified by center.

Statistical analysis title	Statistical analysis 14

Statistical analysis description:

Comparison between DUAC and ADA 0.1% +CLDM 1% at Week 8 for non-ILs. The participants with missing data at a visit were included in the denominator (n) at the visit. That is, those participants were treated as non-responder at the visit.

Comparison groups	ADA 0.1% +CLDM 1% v DUAC
Number of subjects included in analysis	349
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.766 [68]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in percentage
Point estimate	-0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.1
upper limit	8.5

Notes:

[68] - The P-values are based on the Cochran-Mantel-Haenszel test stratified by center.

Statistical analysis title	Statistical analysis 15

Statistical analysis description:

Comparison between DUAC and ADA 0.1% +CLDM 1% at Week 12 for non-ILs. The participants with missing data at a visit were included in the denominator (n) at the visit. That is, those participants were treated as non-responder at the visit.

Comparison groups	ADA 0.1% +CLDM 1% v DUAC
Number of subjects included in analysis	349
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.666 [69]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	2.3

Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.8
upper limit	10.5

Notes:

[69] - The P-value was based on the Cochran-Mantel-Haenszel test stratified by center.

Secondary: Number of participants with treatment adherence rate at Weeks 1, 2, 4, 8 and 12

End point title	Number of participants with treatment adherence rate at Weeks 1, 2, 4, 8 and 12

End point description:

The investigator (or sub-investigator), the product storage manager, or the blinded coordinator dispensed a study compliance log to record participant's compliance with investigational product application from Baseline to the end of study treatment. The product storage manager or the blinded coordinator evaluated the participant's compliance with study treatment, using the study compliance log at each visit, and recorded the compliance data in the eCRF. Data for this outcome measure was not analyzed.

End point type	Secondary

End point timeframe:

Week 1, 2, 4, 8 and 12

End point values	DUAC	ADA 0.1% +CLDM 1%		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[70]	0[71]		
Units: Participants				

Notes:

[70] - Subjects were not analysed.

[71] - Subjects were not analysed.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants who continue treatment at Weeks 1, 2, 4, 8 and 12

End point title	Number of participants who continue treatment at Weeks 1, 2, 4, 8 and 12

End point description:

Number of participants who continue treatment till Weeks 12 was measured. Data for this outcome measure was not analyzed.

End point type	Secondary

End point timeframe:

Week 1, 2, 4, 8 and 12

End point values	DUAC	ADA 0.1% +CLDM 1%		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[72]	0[73]		
Units: Participants				

Notes:

[72] - Subjects were not analysed.

[73] - Subjects were not analysed.

Statistical analyses

No statistical analyses for this end point

Secondary: Participant's treatment preference at Weeks 1, 2, 4, 8 and 12

End point title	Participant's treatment preference at Weeks 1, 2, 4, 8 and 12

End point description:

Participants had to rate each question on a 5-point scale of 0 to 4 (4: yes, very easy to use, 3: yes, easy, 2: slightly easy, 1: slightly difficult, 0: No) where larger score indicates more preferable participant's feeling. There were 5 questions in the questionnaire: ease of application, comfort, satisfaction with treatment (ST), comparison with prior therapies (CPT) and willingness to continue using the product (WCP).

End point type	Secondary

End point timeframe:

Week 1, 2, 4, 8 and 12

End point values	DUAC	ADA 0.1% +CLDM 1%		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	172[74]	177[75]		
Units: Participants				
Week 1: Ease of application, Score 4, n= 172, 176	131	95		
Week 1: Ease of application, Score 3, n= 172, 176	38	66		
Week 1: Ease of application, Score 2, n= 172, 176	2	13		
Week 1: Ease of application, Score 1, n= 172, 176	1	2		
Week 2: Ease of application, Score 4, n= 169, 176	128	83		
Week 2: Ease of application, Score 3, n= 169, 176	38	75		
Week 2: Ease of application, Score 2, n= 169, 176	2	17		
Week 2: Ease of application, Score 1, n= 169, 176	1	1		
Week 4: Ease of application, Score 4, n= 169, 174	118	85		
Week 4: Ease of application, Score 3, n= 169, 174	49	70		
Week 4: Ease of application, Score 2, n= 169, 174	2	18		
Week 4: Ease of application, Score 1, n= 169, 174	0	1		

Week 8: Ease of application, Score 4, n= 167, 172	114	90		
Week 8: Ease of application, Score 3, n= 167, 172	50	60		
Week 8: Ease of application, Score 2, n= 167, 172	3	19		
Week 8: Ease of application, Score 1, n= 167, 172	0	3		
Week 12: Ease of application, Score 4, n= 164, 169	116	81		
Week 12: Ease of application, Score 3, n= 164, 169	44	68		
Week 12: Ease of application, Score 2, n= 164, 169	4	18		
Week 12: Ease of application, Score 1, n= 164, 169	0	2		
Week 1: Comfort, Score 4, n= 172, 176	37	24		
Week 1: Comfort, Score 3, n= 172, 176	86	69		
Week 1: Comfort, Score 2, n= 172, 176	37	45		
Week 1: Comfort, Score 1, n= 172, 176	7	32		
Week 1: Comfort, Score 0, n= 172, 176	5	6		
Week 2: Comfort, Score 4, n= 169, 176	56	35		
Week 2: Comfort, Score 3, n= 169, 176	70	81		
Week 2: Comfort, Score 2, n= 169, 176	36	42		
Week 2: Comfort, Score 1, n= 169, 176	6	17		
Week 2: Comfort, Score 0, n= 169, 176	1	1		
Week 4: Comfort, Score 4, n= 169, 174	72	47		
Week 4: Comfort, Score 3, n= 169, 174	75	80		
Week 4: Comfort, Score 2, n= 169, 174	17	31		
Week 4: Comfort, Score 1, n= 169, 174	5	15		
Week 4: Comfort, Score 0, n= 169, 174	0	1		
Week 8: Comfort, Score 4, n= 167, 172	79	53		
Week 8: Comfort, Score 3, n= 167, 172	69	68		
Week 8: Comfort, Score 2, n= 167, 172	18	36		
Week 8: Comfort, Score 1, n= 167, 172	1	13		
Week 8: Comfort, Score 0, n= 167, 172	0	2		
Week 12: Comfort, Score 4, n= 164, 169	84	56		
Week 12: Comfort, Score 3, n= 164, 169	66	73		
Week 12: Comfort, Score 2, n= 164, 169	13	26		
Week 12: Comfort, Score 1, n= 164, 169	1	13		
Week 12: Comfort, Score 0, n= 164, 169	0	1		
Week 1: ST, Score 4, n= 172, 176	36	21		
Week 1: ST, Score 3, n= 172, 176	79	75		
Week 1: ST, Score 2, n= 172, 176	46	49		
Week 1: ST, Score 1, n= 172, 176	11	23		
Week 1: ST, Score 0, n= 172, 176	0	8		
Week 2: ST, Score 4, n= 169, 176	58	38		
Week 2: ST, Score 3, n= 169, 176	70	81		
Week 2: ST, Score 2, n= 169, 176	37	47		
Week 2: ST, Score 1, n= 169, 176	4	7		
Week 2: ST, Score 0, n= 169, 176	0	3		

Week 4: ST, Score 4, n= 169, 174	66	44		
Week 4: ST, Score 3, n= 169, 174	72	81		
Week 4: ST, Score 2, n= 169, 174	27	40		
Week 4: ST, Score 1, n= 169, 174	4	8		
Week 4: ST, Score 0, n= 169, 174	0	1		
Week 8: ST, Score 4, n= 167, 172	78	58		
Week 8: ST, Score 3, n= 167, 172	67	72		
Week 8: ST, Score 2, n= 167, 172	17	33		
Week 8: ST, Score 1, n= 167, 172	5	6		
Week 8: ST, Score 0, n= 167, 172	0	3		
Week 12: ST, Score 4, n= 164, 169	82	63		
Week 12: ST, Score 3, n= 164, 169	61	70		
Week 12: ST, Score 2, n= 164, 169	20	29		
Week 12: ST, Score 1, n= 164, 169	1	6		
Week 12: ST, Score 0, n= 164, 169	0	1		
Week 1: CPT, Score 4, n= 172, 176	77	53		
Week 1: CPT, Score 3, n= 172, 176	50	45		
Week 1: CPT, Score 2, n= 172, 176	38	61		
Week 1: CPT, Score 1, n= 172, 176	7	11		
Week 1: CPT, Score 0, n= 172, 176	0	6		
Week 2: CPT, Score 4, n= 169, 176	90	57		
Week 2: CPT, Score 3, n= 169, 176	51	55		
Week 2: CPT, Score 2, n= 169, 176	25	54		
Week 2: CPT, Score 1, n= 169, 176	2	10		
Week 2: CPT, Score 0, n= 169, 176	1	0		
Week 4: CPT, Score 4, n= 169, 174	100	67		
Week 4: CPT, Score 3, n= 169, 174	47	52		
Week 4: CPT, Score 2, n= 169, 174	18	46		
Week 4: CPT, Score 1, n= 169, 174	4	8		
Week 4: CPT, Score 0, n= 169, 174	0	1		
Week 8: CPT, Score 4, n= 167, 172	109	73		
Week 8: CPT, Score 3, n= 167, 172	38	50		
Week 8: CPT, Score 2, n= 167, 172	19	40		
Week 8: CPT, Score 1, n= 167, 172	1	8		
Week 8: CPT, Score 0, n= 167, 172	0	1		
Week 12: CPT, Score 4, n= 164, 169	112	78		
Week 12: CPT, Score 3, n= 164, 169	42	47		
Week 12: CPT, Score 2, n= 164, 169	8	35		
Week 12: CPT, Score 1, n= 164, 169	2	7		
Week 12: CPT, Score 0, n= 164, 169	0	2		
Week 1: WCP, Score 4, n= 172, 176	64	36		
Week 1: WCP, Score 3, n= 172, 176	79	78		
Week 1: WCP, Score 2, n= 172, 176	25	39		
Week 1: WCP, Score 1, n= 172, 176	4	19		
Week 1: WCP, Score 0, n= 172, 176	0	4		
Week 2: WCP, Score 4, n= 169, 176	75	55		
Week 2: WCP, Score 3, n= 169, 176	72	70		
Week 2: WCP, Score 2, n= 169, 176	19	38		
Week 2: WCP, Score 1, n= 169, 176	3	13		
Week 4: WCP, Score 4, n= 169, 174	88	63		
Week 4: WCP, Score 3, n= 169, 174	63	75		
Week 4: WCP, Score 2, n= 169, 174	15	26		

Week 4: WCP, Score 1, n= 169, 174	3	10		
Week 8: WCP, Score 4, n= 167, 172	90	62		
Week 8: WCP, Score 3, n= 167, 172	59	74		
Week 8: WCP, Score 2, n= 167, 172	15	27		
Week 8: WCP, Score 1, n= 167, 172	3	9		
Week 12: WCP, Score 4, n= 164, 169	94	70		
Week 12: WCP, Score 3, n= 164, 169	56	65		
Week 12: WCP, Score 2, n= 164, 169	12	23		
Week 12: WCP, Score 1, n= 164, 169	1	11		
Week 12: WCP, Score 0, n= 164, 169	1	0		

Notes:

[74] - ITT population

[75] - ITT population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Quality of life (QoL) score at Week 2, 4, 8 and 12

End point title	Change from Baseline in Quality of life (QoL) score at Week 2, 4, 8 and 12

End point description:

QOL questionnaire was assessed using Skindex-16 with 16 questions in 3 multi-item scales: symptoms, emotions and functioning for the past week: skin condition-itching, burning or stinging, hurting, being irritated, persistence/reoccurrence of skin condition, worry about condition, appearance of skin, frustration about skin, embarrassment about skin, being annoyed about your skin, feeling depressed about skin, effects of your skin on your interactions with others, effects of your skin condition on your desire to be with people, skin condition making it hard to show affection, effects of your skin condition on your daily activities and skin condition making it hard to work or do what you enjoy. Data for adjusted mean has been reported. The baseline value was the latest pre-dose assessment value. Change from baseline was calculated as the value at endpoint minus the value at Baseline. Scores range from 0-never bothered to 100-always bothered.

End point type	Secondary

End point timeframe:

Baseline(Day 1) and Week 2, 4, 8 and 12

End point values	DUAC	ADA 0.1% +CLDM 1%		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	172[76]	177		
Units: Score on scale				
least squares mean (standard error)				
Week 2, n= 169, 176	-0.71 (± 0.070)	-0.49 (± 0.068)		
Week 4, n= 169, 174	-1.02 (± 0.069)	-0.80 (± 0.068)		
Week 8, n= 167, 172	-1.14 (± 0.073)	-0.92 (± 0.071)		
Week 12, n= 164, 169	-1.27 (± 0.073)	-1.10 (± 0.072)		

Notes:
[76] - ITT population

Statistical analyses

Statistical analysis title	Statistical analysis 1
Statistical analysis description:	
Comparison between DUAC and ADA 0.1% +CLDM 1% at Week 2. A negative treatment difference indicates a benefit of Duac relative to ADA+CLDM.	
Comparison groups	DUAC v ADA 0.1% +CLDM 1%
Number of subjects included in analysis	349
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.017
Method	MMRM
Parameter estimate	Mean difference (net)
Point estimate	-0.22
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.4
upper limit	-0.04

Statistical analysis title	Statistical analysis 2
Statistical analysis description:	
Comparison between DUAC and ADA 0.1% +CLDM 1% at Week 4. A negative treatment difference indicates a benefit of Duac relative to ADA+CLDM.	
Comparison groups	DUAC v ADA 0.1% +CLDM 1%
Number of subjects included in analysis	349
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.017
Method	MMRM
Parameter estimate	Mean difference (net)
Point estimate	-0.22
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.4
upper limit	-0.04

Statistical analysis title	Statistical analysis 3
Statistical analysis description:	
Comparison between DUAC and ADA 0.1% +CLDM 1% at Week 8. A negative treatment difference	

indicates a benefit of Duac relative to ADA+CLDM.

Comparison groups	DUAC v ADA 0.1% +CLDM 1%
Number of subjects included in analysis	349
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.024
Method	MMRM
Parameter estimate	Mean difference (net)
Point estimate	-0.22
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.41
upper limit	-0.03

Statistical analysis title	Statistical analysis 4

Statistical analysis description:

Comparison between DUAC and ADA 0.1% +CLDM 1% at Week 12. A negative treatment difference indicates a benefit of Duac relative to ADA+CLDM.

Comparison groups	DUAC v ADA 0.1% +CLDM 1%
Number of subjects included in analysis	349
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.08
Method	MMRM
Parameter estimate	Mean difference (net)
Point estimate	-0.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.36
upper limit	0.02

Secondary: Number of participants with any adverse events (AEs) and serious adverse events (SAEs)

End point title	Number of participants with any adverse events (AEs) and serious adverse events (SAEs)

End point description:

An AE was defined as any untoward medical occurrence that occurred during the course of the trial after study treatment had started. An adverse event was therefore any unfavorable and unintended sign, symptom, or disease temporally associated with the use of study drug, whether or not considered related to the study drug. A SAE is any untoward medical occurrence that at any dose results in death, are life threatening, requires hospitalization or prolongation of hospitalization or results in disability/incapacity, and congenital anomaly/birth defect. Medical or scientific judgment was exercised in deciding whether reporting was appropriate. For liver injury and impaired liver function, alanine aminotransferase greater than or equal to (>=)3 times upper limit of normal (ULN) and total bilirubin >=2xULN (less than [>] 35% direct) was defined.

End point type	Secondary

End point timeframe:

Up to Week 12

End point values	DUAC	ADA 0.1% +CLDM 1%		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	172[77]	177		
Units: Participants				
Any AE	53	100		
Any SAE	1	0		

Notes:

[77] - ITT population

Statistical analyses

No statistical analyses for this end point

Secondary: Local tolerability score for erythema, dryness, peeling, itching, and burning or stinging

End point title	Local tolerability score for erythema, dryness, peeling, itching, and burning or stinging

End point description:

Local tolerability score for erythema (no redness, faint red or pink coloration, barely perceptible, light red or pink coloration, medium red coloration, beet red coloration), dryness (none, barely perceptible dryness with no flakes or fissure formation, easily perceptible dryness with no flakes or fissure formation, easily noted dryness and flakes but no fissure formation, easily noted dryness with flakes and fissure formation), peeling (no peeling, mild localized peeling, mild and diffuse peeling, moderate and diffuse peeling, moderate to prominent, dense peeling) and itching and burning/stinging (normal-no discomfort, noticeable discomfort that causes intermittent awareness, continuous awareness, intermittent awareness and interferes occasionally with normal daily activities, a definite continuous discomfort that interferes with normal daily activities) was assessed on a scale of 0 to 4 (0= absent, 1= slight, 2= mild, 3= moderate and 4= severe).

End point type	Secondary

End point timeframe:

Week 1, 2, 4, 8 and 12

End point values	DUAC	ADA 0.1% +CLDM 1%		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	172[78]	177		
Units: Score on scale				
arithmetic mean (standard deviation)				
Erythema Week 1, n= 170, 175	0.0 (± 0.61)	0.3 (± 0.72)		
Erythema Week 2, n= 169, 175	0.0 (± 0.68)	0.0 (± 0.70)		
Erythema Week 4, n= 169, 174	-0.1 (± 0.57)	-0.1 (± 0.64)		
Erythema Week 8, n= 165, 171	-0.2 (± 0.68)	-0.2 (± 0.69)		
Erythema Week 12, n= 165, 168	-0.2 (± 0.78)	-0.3 (± 0.67)		
Dryness Week 1, n= 170, 175	0.1 (± 0.54)	0.6 (± 0.95)		
Dryness Week 2, n= 169, 175	0.0 (± 0.50)	0.1 (± 0.58)		

Dryness Week 4, n= 169, 174	0.0 (± 0.52)	0.1 (± 0.49)		
Dryness Week 8, n= 165, 171	0.0 (± 0.58)	0.1 (± 0.46)		
Dryness Week 12, n= 165, 168	0.0 (± 0.45)	0.0 (± 0.35)		
Peeling Week 1, n= 170, 175	0.1 (± 0.43)	0.5 (± 0.88)		
Peeling Week 2, n= 169, 175	0.1 (± 0.33)	0.2 (± 0.55)		
Peeling Week 4, n= 169, 174	0.0 (± 0.34)	0.1 (± 0.42)		
Peeling Week 8, n= 165, 171	0.1 (± 0.39)	0.1 (± 0.46)		
Peeling Week 12, n= 165, 168	0.0 (± 0.31)	0.0 (± 0.32)		
Itching Week 1, n= 170, 175	0.0 (± 0.64)	0.1 (± 0.81)		
Itching Week 2, n= 169, 175	0.0 (± 0.60)	0.1 (± 0.77)		
Itching Week 4, n= 169, 174	-0.1 (± 0.68)	-0.1 (± 0.62)		
Itching Week 8, n= 165, 171	-0.2 (± 0.63)	-0.1 (± 0.58)		
Itching Week 12, n= 165, 168	-0.2 (± 0.66)	-0.2 (± 0.56)		
Burning/Stinging Week 1, n= 170, 175	0.0 (± 0.48)	0.5 (± 0.85)		
Burning/Stinging Week 2, n= 169, 175	0.0 (± 0.44)	0.2 (± 0.66)		
Burning/Stinging Week 4, n= 169, 174	0.0 (± 0.44)	0.0 (± 0.47)		
Burning/Stinging Week 8, n= 165, 171	0.0 (± 0.34)	0.1 (± 0.53)		
Burning/Stinging Week 12, n= 165, 168	0.0 (± 0.39)	0.0 (± 0.40)		

Notes:

[78] - ITT population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with Severity of AEs

End point title	Number of participants with Severity of AEs

End point description:

The severity of AEs was assessed by the investigator; events were assigned to one of the following categories: mild, an event that was easily tolerated by the participant, causing minimal discomfort and not interfering with everyday activities; moderate, an event that was sufficiently discomforting to interfere with normal everyday activities; and severe, an event that prevented normal everyday activities.

End point type	Secondary

End point timeframe:

Up to Week 12

End point values	DUAC	ADA 0.1% +CLDM 1%		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	172[79]	177		
Units: Participants				
Mild	46	91		
Modertae	6	7		
Severe	1	2		

Notes:

[79] - ITT population

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
AE and SAE were collected up to Week 12.	
Adverse event reporting additional description:	
For AE and SAE, ITT population was analyzed.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	18.1

Reporting groups	
Reporting group title	ADA 0.1% +CLDM 1%

Reporting group description:

Participants were instructed to use combination therapy of Adapalene (ADA) 0.1% gel with quantity of 1 FTU about 0.5 g sufficient to cover entire face (including the forehead, nose, cheeks and chin) once daily in the evening (at bedtime) and clindamycin (CLDM) 1% gel twice daily, once in the morning and once in the evening (at bedtime) for 12 weeks. The CLDM 1% gel was applied subsequent to the application of ADA 0.1% gel in the evening. The CLDM 1% gel was applied to inflammatory lesions (ILs) only.

Reporting group title	Duac

Reporting group description:

Participants were instructed to use DUAC, a fixed dose combination gel (clindamycin phosphate 1.2% and benzoyl peroxide 3%) with quantity of 2 FTU about 0.6 gram (g) which was sufficient to cover entire face (including the forehead, nose, cheeks and chin) once daily in the evening (at bedtime) for 12 weeks.

Serious adverse events	ADA 0.1% +CLDM 1%	Duac	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 177 (0.00%)	1 / 172 (0.58%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Gastrointestinal disorders			
Duodenal ulcer			
subjects affected / exposed	0 / 177 (0.00%)	1 / 172 (0.58%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	ADA 0.1% +CLDM 1%	Duac	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	78 / 177 (44.07%)	34 / 172 (19.77%)	

General disorders and administration site conditions			
Application site dryness			
subjects affected / exposed	44 / 177 (24.86%)	16 / 172 (9.30%)	
occurrences (all)	46	16	
Application site pain			
subjects affected / exposed	20 / 177 (11.30%)	3 / 172 (1.74%)	
occurrences (all)	21	3	
Application site erythema			
subjects affected / exposed	11 / 177 (6.21%)	4 / 172 (2.33%)	
occurrences (all)	12	4	
Skin and subcutaneous tissue disorders			
Eczema			
subjects affected / exposed	10 / 177 (5.65%)	2 / 172 (1.16%)	
occurrences (all)	11	2	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	15 / 177 (8.47%)	12 / 172 (6.98%)	
occurrences (all)	16	13	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported