



Clinical trial results:

A Phase 3, 4-Week, Parallel Group, Double Blind, Vehicle-Controlled Study of the Safety and Efficacy of ARQ-151 Cream 0.15% Administered QD in Subjects with Atopic Dermatitis

Summary

EudraCT number	2021-006884-67
Trial protocol	PL
Global end of trial date	29 September 2022

Results information

Result version number	v1 (current)
This version publication date	24 January 2025
First version publication date	24 January 2025

Trial information

Trial identification

Sponsor protocol code	ARQ-151-312
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04773600
WHO universal trial number (UTN)	-
Other trial identifiers	IND: 135681

Notes:

Sponsors

Sponsor organisation name	Arcutis Biotherapeutics, Inc.
Sponsor organisation address	3027 Townsgate Rd #300, Westlake Village, CA, United States, 91361
Public contact	Arcutis Medical Information, Arcutis Biotherapeutics, Inc., +1 8446926729, information@arcutis.com
Scientific contact	Arcutis Medical Information, Arcutis Biotherapeutics, Inc., +1 8446926729, information@arcutis.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	29 September 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	29 September 2022
Global end of trial reached?	Yes
Global end of trial date	29 September 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This study will assess the safety and efficacy of ARQ-151 cream vs vehicle applied once a day for 4 weeks by subjects with atopic dermatitis (eczema). This is a parallel group, double blind, vehicle-controlled study in which ARQ-151 0.15% cream or vehicle is applied once daily (qd) for 4 weeks by participants with atopic dermatitis.

Protection of trial subjects:

This study was conducted in accordance with the Declaration of Helsinki, ICH Good Clinical Practice, and all applicable local laws/regulations.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	24 February 2021
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Poland: 74
Country: Number of subjects enrolled	Canada: 160
Country: Number of subjects enrolled	United States: 449
Worldwide total number of subjects	683
EEA total number of subjects	74

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)	187
Adolescents (12-17 years)	132
Adults (18-64 years)	333
From 65 to 84 years	31

85 years and over	0
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Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Participants were enrolled at sites in the US, Canada, and Poland.

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, Assessor

Arms

Are arms mutually exclusive?	Yes
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Arm title	Roflumilast Cream 0.15%
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Arm description:

Participants applied roflumilast cream 0.15% qd for 4 weeks.

Arm type	Experimental
Investigational medicinal product name	Roflumilast cream 0.15%
Investigational medicinal product code	
Other name	ARQ-151
Pharmaceutical forms	Cream
Routes of administration	Topical

Dosage and administration details:

Roflumilast cream 0.15% for topical application

Arm title	Vehicle Cream
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Arm description:

Participants apply vehicle cream qd for 4 weeks.

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

Dosage and administration details:

Vehicle cream for topical application

Number of subjects in period 1	Roflumilast Cream 0.15%	Vehicle Cream
Started	451	232
Completed	410	211
Not completed	41	21
Consent withdrawn by subject	15	9
Physician decision	-	1

Adverse event, non-fatal	8	2
Caregiver elected other therapy	1	-
Lost to follow-up	10	6
Emergency travel out of country	1	-
Lack of efficacy	2	3
Protocol deviation	2	-
Noncompliance	2	-

Baseline characteristics

Reporting groups

Reporting group title	Roflumilast Cream 0.15%
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Reporting group description:

Participants applied roflumilast cream 0.15% qd for 4 weeks.

Reporting group title	Vehicle Cream
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Reporting group description:

Participants apply vehicle cream qd for 4 weeks.

Reporting group values	Roflumilast Cream 0.15%	Vehicle Cream	Total
Number of subjects	451	232	683
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	126	61	187
Adolescents (12-17 years)	80	52	132
Adults (18-64 years)	225	108	333
From 65-84 years	20	11	31
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	27.7	26.2	-
standard deviation	± 19.60	± 18.94	-
Gender categorical Units: Subjects			
Female	252	143	395
Male	199	89	288
Ethnicity Units: Subjects			
Hispanic or Latino	51	16	67
Not Hispanic or Latino	397	213	610
Unknown or Not Reported	3	3	6
Race Units: Subjects			
White	268	138	406
Black or African- American	96	50	146
Asian	51	30	81
American-Indian or Alaska Native	5	1	6
Native Hawaiian or Other Pacific Islander	0	0	0
Multiple	12	8	20
other	19	5	24
Verified viGA Analyzed Baseline Score			

viGA-AD is a 5-point scale assessing the severity of AD, with scores ranging from 0 ('clear') to 4 ('severe'), and higher scores indicate greater symptom severity. This is the baseline viGA data that have undergone data verification by the investigator.			
Units: Subjects			
Mild	108	53	161
Moderate	343	179	522
Baseline EASI Score			
EASI is an instrument to measure the severity and extent of AD. The body is first divided into 4 areas: head {10% of skin), arms (20%), trunk (30%), and legs (40%). Then, the area affected is scored from 0 (0% involvement) to 6 (90-100% involvement), and severity is scored from 0 ('none') to 3 ('severe'). EASI combines the area affected and severity ratings to get a final composite score ranging from 0 (no disease) to 72 (maximal disease). Note that palms and soles were treated as appropriate but were not counted towards any measurements of EASI.			
Units: Units on a scale			
median	8.50	8.4	
inter-quartile range (Q1-Q3)	6.2 to 12.3	6.45 to 12.00	-

End points

End points reporting groups

Reporting group title	Roflumilast Cream 0.15%
Reporting group description:	
Participants applied roflumilast cream 0.15% qd for 4 weeks.	
Reporting group title	Vehicle Cream
Reporting group description:	
Participants apply vehicle cream qd for 4 weeks.	

Primary: Achievement of Validated Investigator Global Assessment for Atopic Dermatitis (vIGA-AD) Success at Week 4

End point title	Achievement of Validated Investigator Global Assessment for Atopic Dermatitis (vIGA-AD) Success at Week 4
End point description:	
The percentage of participants achieving vIGA-AD "success" is presented with multiple imputation of missing observations. vIGA-AD "success" is defined as a vIGA-AD score of 'clear' or 'almost clear' PLUS a 2-grade improvement from Baseline. The vIGA-AD is a static evaluation of qualitative overall AD severity. This global assessment scale is an ordinal scale with five severity grades (reported as 0 = "clear"; 1 = "almost clear"; 2 = "mild"; 3 = "moderate"; and 4 = "severe"), with higher scores indicative of greater symptom severity. All randomized participants are included.	
End point type	Primary
End point timeframe:	
Week 4	

End point values	Roflumilast Cream 0.15%	Vehicle Cream		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	451	232		
Units: Percentage of participants				
number (confidence interval 95%)	28.9 (24.83 to 33.40)	12.0 (8.35 to 16.91)		

Statistical analyses

Statistical analysis title	viGA Success at Week 4
Comparison groups	Roflumilast Cream 0.15% v Vehicle Cream
Number of subjects included in analysis	683
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 ^[1]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	3.19

Confidence interval	
level	95 %
sides	2-sided
lower limit	1.962
upper limit	5.183

Notes:

[1] - Stratified by pooled study site and vIGA-AD randomization strata

Secondary: Achievement of vIGA-AD Success at Week 4 in Participants With "Moderate" Baseline Scores

End point title	Achievement of vIGA-AD Success at Week 4 in Participants With "Moderate" Baseline Scores
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End point description:

The percentage of participants with moderate baseline scores achieving vIGA-AD "success" is presented with multiple imputation of missing observations. vIGA-AD "success" is defined as a vIGA-AD score of 'clear' or 'almost clear' PLUS a 2-grade improvement from baseline in participants with a 'moderate' baseline vIGA-AD score. The vIGA-AD is a static evaluation of qualitative overall AD severity. This global assessment scale is an ordinal scale with five severity grades (reported as 0 = "clear"; 1 = "almost clear"; 2 = "mild"; 3 = "moderate"; and 4 = "severe"), with higher scores indicative of greater symptom severity. All randomized participants are included.

End point type	Secondary
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End point timeframe:

Week 4

End point values	Roflumilast Cream 0.15%	Vehicle Cream		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	342	179		
Units: Percentage of participants				
number (not applicable)	32.9	13.1		

Statistical analyses

Statistical analysis title	viGA Success at Week 4 (Moderate Baseline)
Comparison groups	Roflumilast Cream 0.15% v Vehicle Cream
Number of subjects included in analysis	521
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 ^[2]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	3.37
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.996
upper limit	5.687

Notes:

[2] - Stratified by pooled study site

Secondary: Achievement of a 4-point Reduction at Week 4 in the Average, Weekly Worst Itch Numeric Rating Scale (WI-NRS) in Participants with Baseline WI-NRS Score ≥ 4

End point title	Achievement of a 4-point Reduction at Week 4 in the Average, Weekly Worst Itch Numeric Rating Scale (WI-NRS) in Participants with Baseline WI-NRS Score ≥ 4
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End point description:

The percentage of participants with a baseline WI-NRS ≥ 4 achieving WI-NRS success is presented with multiple imputation of missing observations. The WI-NRS is a simple, single item scale to assess the subject-reported severity of this symptom, on a scale ranging from 0 ("no itch") to 10 ("worst imaginable itch") the participant experienced in the previous 24 hours (higher scores indicate higher itch severity). All randomized participants who were ≥ 12 years of age, had an average weekly WI-NRS pruritus score ≥ 4 at baseline, and completed at least 4 of 7 evaluable daily WI-NRS questionnaires during the last 7 days of the Screening period are included.

End point type	Secondary
End point timeframe:	
Week 4	

End point values	Roflumilast Cream 0.15%	Vehicle Cream		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	264	136		
Units: Percentage of participants				
number (confidence interval 95%)	30.2 (24.77 to 36.31)	12.4 (7.77 to 19.26)		

Statistical analyses

Statistical analysis title	≥ 4 -Point Reduction in WI-NRS at Week 4
Comparison groups	Roflumilast Cream 0.15% v Vehicle Cream
Number of subjects included in analysis	400
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0014 ^[3]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	2.71
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.448
upper limit	5.066

Notes:

[3] - Stratified by pooled study site and vIGA-AD randomization strata

Secondary: Achievement of a 4-point Reduction at Week 2 in the Average, Weekly WI-NRS in Participants with Baseline WI-NRS Score ≥ 4

End point title	Achievement of a 4-point Reduction at Week 2 in the Average, Weekly WI-NRS in Participants with Baseline WI-NRS Score ≥ 4
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End point description:

The percentage of participants with a baseline WI-NRS ≥ 4 achieving WI-NRS success is presented with multiple imputation of missing observations. The WI-NRS is a simple, single item scale to assess the subject-reported severity of this symptom, on a scale ranging from 0 ("no itch") to 10 ("worst imaginable itch") the participant experienced in the previous 24 hours (higher scores indicate higher itch severity). All randomized participants who were ≥ 12 years of age, had an average weekly WI-NRS pruritus score ≥ 4 at baseline, and completed at least 4 of 7 evaluable daily WI-NRS questionnaires during the last 7 days of the Screening period are included.

End point type	Secondary
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End point timeframe:

Week 2

End point values	Roflumilast Cream 0.15%	Vehicle Cream		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	264	136		
Units: Percentage of participants				
number (confidence interval 95%)	22.3 (17.66 to 27.82)	6.9 (3.66 to 12.56)		

Statistical analyses

Statistical analysis title	≥ 4 -Point Reduction in WI-NRS at Week 2
Comparison groups	Roflumilast Cream 0.15% v Vehicle Cream
Number of subjects included in analysis	400
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0015 ^[4]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	3.55
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.591
upper limit	7.927

Notes:

[4] - Stratified by pooled study site and vIGA-AD randomization strata

Secondary: Achievement of a 4-Point Reduction at Week 1 in the WI-NRS in Participants with Baseline WI-NRS ≥ 4

End point title	Achievement of a 4-Point Reduction at Week 1 in the WI-NRS in Participants with Baseline WI-NRS ≥ 4
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End point description:

The percentage of participants with a baseline WI-NRS ≥ 4 achieving WI-NRS success is presented with

multiple imputation of missing observations. The WI-NRS is a simple, single item scale to assess the subject-reported severity of this symptom, on a scale ranging from 0 ("no itch") to 10 ("worst imaginable itch") the participant experienced in the previous 24 hours (higher scores indicate higher itch severity). All randomized participants who were ≥ 12 years of age, had an average weekly WI-NRS pruritus score ≥ 4 at baseline, and completed at least 4 of 7 evaluable daily WI-NRS questionnaires during the last 7 days of the Screening period are included.

End point type	Secondary
End point timeframe:	
Week 1	

End point values	Roflumilast Cream 0.15%	Vehicle Cream		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	264	136		
Units: Percentage of participants				
number (confidence interval 95%)	11.2 (7.89 to 15.57)	1.6 (0.44 to 5.58)		

Statistical analyses

Statistical analysis title	≥ 4 -Point Reduction in WI-NRS at Week 1
Comparison groups	Roflumilast Cream 0.15% v Vehicle Cream
Number of subjects included in analysis	400
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.002 ^[5]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	7.84
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.717
upper limit	35.764

Notes:

[5] - Stratified by pooled study site and vIGA-AD randomization strata

Secondary: Achievement of $\geq 75\%$ Decrease from Baseline at Week 4 in the Eczema Area and Severity Index (EASI-75)

End point title	Achievement of $\geq 75\%$ Decrease from Baseline at Week 4 in the Eczema Area and Severity Index (EASI-75)
End point description:	
The percentage of participants achieving EASI-75 is presented with multiple imputation of missing observations. EASI-75 is a $\sim 75\%$ reduction from the baseline EASI score. EASI combines the assessment of the severity of lesions and the area affected into a single total score in the range 0 (no disease) to 72 (maximal disease). To calculate the EASI, the sum =of the severity rating (0 to 3 with 3 being the most severe) for four clinical signs are multiplied with the numerical value of the area affected and with the percentage of the four body areas. All randomized participants are included.	
End point type	Secondary

End point timeframe:

Week 4

End point values	Roflumilast Cream 0.15%	Vehicle Cream		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	451	232		
Units: Percentage of participants				
number (confidence interval 95%)	42.0 (37.45 to 46.72)	19.7 (15.04 to 25.44)		

Statistical analyses

Statistical analysis title	EASI-75 at Week 4
Comparison groups	Roflumilast Cream 0.15% v Vehicle Cream
Number of subjects included in analysis	683
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 ^[6]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	3.23
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.108
upper limit	4.964

Notes:

[6] - Stratified by pooled study site and vIGA-AD randomization strata

Secondary: Achievement of vIGA-AD Score of 'Clear' or 'Almost Clear' at Week 4

End point title	Achievement of vIGA-AD Score of 'Clear' or 'Almost Clear' at Week 4
End point description:	The percentage of participants scoring 'clear' or 'almost clear' on vIGA-AD is presented with multiple imputation of missing observations. The vIGA-AD is a static evaluation of qualitative overall AD severity. This global assessment scale is an ordinal scale with five severity grades (reported as 0 = "clear"; 1 = "almost clear"; 2 = "mild"; 3 = "moderate"; and 4 = "severe"), with higher scores indicative of greater symptom severity. All randomized participants are included.
End point type	Secondary
End point timeframe:	
Week 4	

End point values	Roflumilast Cream 0.15%	Vehicle Cream		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	451	232		
Units: Percentage of participants				
number (not applicable)	39.0	16.9		

Statistical analyses

Statistical analysis title	vIGA-AD 'Clear' or 'Almost Clear' at Week 4
Comparison groups	Roflumilast Cream 0.15% v Vehicle Cream
Number of subjects included in analysis	683
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 ^[7]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	3.39
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.191
upper limit	5.24

Notes:

[7] - Stratified by pooled study site and vIGA-AD randomization strata

Secondary: Achievement of vIGA-AD Score of 'Clear' or 'Almost Clear' at Week 2

End point title	Achievement of vIGA-AD Score of 'Clear' or 'Almost Clear' at Week 2
End point description:	
The percentage of participants scoring 'clear' or 'almost clear' on vIGA-AD is presented with multiple imputation of missing observations. The vIGA-AD is a static evaluation of qualitative overall AD severity. This global assessment scale is an ordinal scale with five severity grades (reported as 0 = "clear"; 1 = "almost clear"; 2 = "mild"; 3 = "moderate"; and 4 = "severe"), with higher scores indicative of greater symptom severity. All randomized participants are included.	
End point type	Secondary
End point timeframe:	
Week 2	

End point values	Roflumilast Cream 0.15%	Vehicle Cream		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	451	232		
Units: Percentage of participants				
number (not applicable)	27.6	10.7		

Statistical analyses

Statistical analysis title	vIGA-AD 'Clear' or 'Almost Clear' at Week 2
Comparison groups	Roflumilast Cream 0.15% v Vehicle Cream
Number of subjects included in analysis	683
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 ^[8]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	3.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.097
upper limit	5.854

Notes:

[8] - Stratified by pooled study site and vIGA-AD randomization strata

Secondary: Achievement of vIGA-AD Score of 'Clear' or 'Almost Clear' at Week 1

End point title	Achievement of vIGA-AD Score of 'Clear' or 'Almost Clear' at Week 1
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End point description:

The percentage of participants scoring 'clear' or 'almost clear' on vIGA-AD is presented with multiple imputation of missing observations. The vIGA-AD is a static evaluation of qualitative overall AD severity. This global assessment scale is an ordinal scale with five severity grades (reported as 0 = "clear"; 1 = "almost clear"; 2 = "mild"; 3 = "moderate"; and 4 = "severe"), with higher scores indicative of greater symptom severity. All randomized participants are included.

End point type	Secondary
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End point timeframe:

Week 1

End point values	Roflumilast Cream 0.15%	Vehicle Cream		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	451	232		
Units: Percentage of participants				
number (not applicable)	14.2	6.2		

Statistical analyses

Statistical analysis title	vIGA-AD 'Clear' or 'Almost Clear' at Week 1
Comparison groups	Roflumilast Cream 0.15% v Vehicle Cream
Number of subjects included in analysis	683
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.005 ^[9]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	2.56
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.312
upper limit	4.993

Notes:

[9] - Stratified by pooled study site and vIGA-AD randomization strata

Secondary: vIGA Success at Week 2

End point title	vIGA Success at Week 2
End point description:	
The percentage of participants achieving vIGA-AD "success" is presented with multiple imputation of missing observations. vIGA-AD "success" is defined as a vIGA-AD score of 'clear' or 'almost clear' PLUS a 2-grade improvement from Baseline. The vIGA-AD is a static evaluation of qualitative overall AD severity. This global assessment scale is an ordinal scale with five severity grades (reported as 0 = "clear"; 1 = "almost clear"; 2 = "mild"; 3 = "moderate"; and 4 = "severe"), with higher scores indicative of greater symptom severity. All randomized participants are included.	
End point type	Secondary
End point timeframe:	
Week 2	

End point values	Roflumilast Cream 0.15%	Vehicle Cream		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	451	232		
Units: Percentage of participants				
number (confidence interval 95%)	17.7 (14.40 to 21.55)	5.3 (3.06 to 9.01)		

Statistical analyses

Statistical analysis title	vIGA Success at Week 2
Comparison groups	Roflumilast Cream 0.15% v Vehicle Cream

Number of subjects included in analysis	683
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 ^[10]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	4.42
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.281
upper limit	8.568

Notes:

[10] - Stratified by pooled study site and vIGA-AD randomization strata

Secondary: vIGA Success at Week 1

End point title	vIGA Success at Week 1
End point description:	
The percentage of participants achieving vIGA-AD "success" is presented with multiple imputation of missing observations. vIGA-AD "success" is defined as a vIGA-AD score of 'clear' or 'almost clear' PLUS a 2-grade improvement from Baseline. The vIGA-AD is a static evaluation of qualitative overall AD severity. This global assessment scale is an ordinal scale with five severity grades (reported as 0 = "clear"; 1 = "almost clear"; 2 = "mild"; 3 = "moderate"; and 4 = "severe"), with higher scores indicative of greater symptom severity. All randomized participants are included.	
End point type	Secondary
End point timeframe:	
Week 1	

End point values	Roflumilast Cream 0.15%	Vehicle Cream		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	451	232		
Units: Percentage of Participants				
number (confidence interval 95%)	5.9 (4.04 to 8.46)	3.1 (1.52 to 6.29)		

Statistical analyses

Statistical analysis title	vIGA Success at Week 1
Comparison groups	Roflumilast Cream 0.15% v Vehicle Cream
Number of subjects included in analysis	683
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1156 ^[11]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	1.99

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.832
upper limit	4.782

Notes:

[11] - Stratified by pooled study site and vIGA-AD randomization strata

Adverse events

Adverse events information^[1]

Timeframe for reporting adverse events:

Up to ~29 days

Adverse event reporting additional description:

All randomized participants who received ≥ 1 dose of study intervention are included, according to actual treatment received. Note that 1 participant was randomized to vehicle but did not receive ≥ 1 dose of study treatment; one additional participant was randomized to vehicle but instead received active roflumilast.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	25.0
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Reporting groups

Reporting group title	Roflumilast Cream 0.15%
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Reporting group description:

Participants applied roflumilast cream 0.15% qd for 4 weeks.

Reporting group title	Vehicle Cream
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Reporting group description:

Participants apply vehicle cream qd for 4 weeks.

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.

Justification: There were no non-serious events occurring in greater than 5% of participants in any arm.

Serious adverse events	Roflumilast Cream 0.15%	Vehicle Cream	
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 452 (0.88%)	0 / 230 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Nerve compression			
subjects affected / exposed	1 / 452 (0.22%)	0 / 230 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
General physical health deterioration			
subjects affected / exposed	1 / 452 (0.22%)	0 / 230 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Dermatitis atopic			

subjects affected / exposed	1 / 452 (0.22%)	0 / 230 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Staphylococcal scalded skin syndrome			
subjects affected / exposed	1 / 452 (0.22%)	0 / 230 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Roflumilast Cream 0.15%	Vehicle Cream	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 452 (0.00%)	0 / 230 (0.00%)	

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