# 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 |

### 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 |

## 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 |
| **Arm title** | Roflumilast Cream 0.15% |

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 |

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 |
| Noncompliance | 2 | - |
| Protocol deviation | 2 | - |

## Baseline characteristics

| 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. | |

| Reporting group values | Roflumilast Cream 0.15% | Vehicle Cream | Total |
|---|---|---|---|
| Number of subjects | 451 | 232 | 683 |
| Age categorical<br>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<br>Units: years | | | |
| arithmetic mean | 27.7 | 26.2 | |
| standard deviation | ± 19.60 | ± 18.94 | - |
| Gender categorical<br>Units: Subjects | | | |
| Female | 252 | 143 | 395 |
| Male | 199 | 89 | 288 |
| Ethnicity<br>Units: Subjects | | | |
| Hispanic or Latino | 51 | 16 | 67 |
| Not Hispanic or Latino | 397 | 213 | 610 |
| Unknown or Not Reported | 3 | 3 | 6 |
| Race<br>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<br>(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 |

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 |

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 |
|---|---|

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 |
|---|---|

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 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 |
|---|---|

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 ≥75% Decrease from Baseline at Week 4 in the Eczema Area and Severity Index (EASI-75)

| End point title | Achievement of ≥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 ~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 |
|---|---|

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 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 |

### Dictionary used

| | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 25.0 |

### 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.

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