# Clinical trial results:
# A multi-centre, single-blind, parallel group, clinical evaluation of the efficacy and safety of clindamycin 1% / benzoyl peroxide 3% and azelaic acid 20% in the topical treatment of mild to moderate acne vulgaris

## Summary

| | |
|---|---|
| EudraCT number | 2013-004158-81 |
| Trial protocol | Outside EU/EEA |
| Global end of trial date | 08 September 2014 |

**Results information**

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 15 March 2016 |
| First version publication date | 14 March 2015 |

## Trial information

**Trial identification**

| | |
|---|---|
| Sponsor protocol code | 200398 |

**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? | No |

Notes:

## Results analysis stage

| | |
|---|---|
| Analysis stage | Final |
| Date of interim/final analysis | 17 November 2014 |
| Is this the analysis of the primary completion data? | No |

| | |
|---|---|
| Global end of trial reached? | Yes |
| Global end of trial date | 08 September 2014 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

The primary objective is to compare the efficacy and safety of a gel formulation containing a combination of clindamycin 10mg/g + benzoyl peroxide 30mg/g with a cream containing azelaic acid 20%.

Main Hypothesis to test:
- clindamycin 1% /benezoyl peroxide 3% is more effective than azelaic acid 20% in treating inflammatory acne lesions;
- clindamycin 1% /benezoyl peroxide 3% has faster speed of onset;
- clindamycin 1% /benezoyl peroxide 3% results in higher patient satisfaction
- Both treatment have an equal tolerability

Protection of trial subjects:

Duac and Skinoren administered according to SPC. Hence, no specific measures that were put in place to protect trial participants.

Background therapy: -

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 21 February 2014 |
| 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 | Germany: 222 |
| Worldwide total number of subjects | 222 |
| EEA total number of subjects | 222 |

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) | 106 |

| | |
|---|---|
| Adults (18-64 years) | 116 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

Overall 222 participants (par.) with facial acne (vulgaris) were enrolled; of these, 111 par. were randomized in the combination treatment of 1.2% clindamycin phosphate (10mg/g) + 3% benzoyl peroxide [30mg/g]) (Duac) Arm and 110 par. in the 20% azelaic acid cream (Skinoren) Arm. A total of 217 randomized par. used study medication at least once.

### 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 | Assessor[1] |

### Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | Duac |

Arm description:

Participants topically applied a thin film of Duac gel once daily in the evening for 12 weeks, over the entire face, avoiding the mouth and eyes. Prior to the application, participants were advised to wash their face with the soap free cleanser, rinse thoroughly with warm water, and pat the skin thoroughly dry with a soft towel. After application, the participants had to avoid washing face for 4 hours (preferably 8 hours). Oil free facial moisturizer was used, if required.

| | |
|---|---|
| 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:

Once daily in the evening. Duac 10mg/g + 30mg/g Gel contains 1% clindamycin and 3% BPO in a gel vehicle consisting of carbomer, dimethicone, disodium lauryl sulfosuccinate, edetate disodium, glycerol, colloidal hydrated silica, poloxamer, purified water, and sodium hydroxide

| | |
|---|---|
| **Arm title** | Skinoren |

Arm description:

Participants topically applied a thin film of Skinoren cream twice daily (once in the morning and once in the evening) for 12 weeks, over the entire face, avoiding the mouth and eyes. Prior to the application, participants were advised to wash their face with the soap free cleanser, rinse thoroughly with warm water, and pat the skin thoroughly dry with a soft towel. After application, the participants had to avoid washing face for 4 hours (preferably 8 hours). Oil free facial moisturizer was used, if required.

| | |
|---|---|
| Arm type | Active comparator |
| Investigational medicinal product name | Skinoren |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Cream |
| Routes of administration | Topical use |

Dosage and administration details:

Twice daily in the morning and evening. Skinoren Creme contains 20% azelaic acid in a cream vehicle consisting of Arlatone 983S (polyoxyethylene fatty acid ester), cutina CBS (mixture of mono-diglycerides, fatty alcohols, triglycerides and wax esters), cetearyl octanoate, propylene glycol, glycerol 85% (E422), benzoic acid (E210), purified water.

Notes:

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

Justification: This is an evaluator-blinded study; therefore, participants, study center staff responsible for drug accountability and distribution, and other individuals involved with the conduct, analysis, and reporting of clinical study data were not blinded to study product allocations. The acne lesion assessor was unaware of which study product was being used (blinded).

| **Number of subjects in period 1[2]** | Duac | Skinoren |
|---|---|---|
| Started | 108 | 109 |
| Completed | 104 | 102 |
| Not completed | 4 | 7 |
| Not in Time Schedule | - | 1 |
| Consent withdrawn by subject | 2 | 2 |
| Non Compliance | 1 | - |
| The Visit Date was not in Timeline | - | 1 |
| Adverse event, non-fatal | 1 | - |
| Lost to follow-up | - | 3 |

Notes:

[2] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: Overall 222 participants (par.) with facial acne (vulgaris) were enrolled; of these, 111 par. were randomized in the combination treatment of 1.2% clindamycin phosphate (10mg/g) + 3% benzoyl peroxide [30mg/g]) (Duac) Arm and 110 par. in the 20% azelaic acid cream (Skinoren) Arm.

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | Duac |
| Reporting group description: | |
| Participants topically applied a thin film of Duac gel once daily in the evening for 12 weeks, over the entire face, avoiding the mouth and eyes. Prior to the application, participants were advised to wash their face with the soap free cleanser, rinse thoroughly with warm water, and pat the skin thoroughly dry with a soft towel. After application, the participants had to avoid washing face for 4 hours (preferably 8 hours). Oil free facial moisturizer was used, if required. | |
| Reporting group title | Skinoren |
| Reporting group description: | |
| Participants topically applied a thin film of Skinoren cream twice daily (once in the morning and once in the evening) for 12 weeks, over the entire face, avoiding the mouth and eyes. Prior to the application, participants were advised to wash their face with the soap free cleanser, rinse thoroughly with warm water, and pat the skin thoroughly dry with a soft towel. After application, the participants had to avoid washing face for 4 hours (preferably 8 hours). Oil free facial moisturizer was used, if required. | |

| Reporting group values | Duac | Skinoren | Total |
|---|---|---|---|
| Number of subjects | 108 | 109 | 217 |
| Age categorical<br>Units: Subjects | | | |
| Age continuous | | | |
| Participants presented include the Intent-to-Treat (ITT) Analysis Set, consisting of all randomized participants who used study medication at least once. | | | |
| Units: years | | | |
| arithmetic mean | 20.1 | 20 | |
| standard deviation | ± 7.1 | ± 6.9 | - |
| Gender categorical | | | |
| Participants presented include the Intent-to-Treat (ITT) Analysis Set, consisting of all randomized participants who used study medication at least once. | | | |
| Units: Subjects | | | |
| Female | 47 | 51 | 98 |
| Male | 61 | 58 | 119 |
| Race | | | |
| Participants presented include the Intent-to-Treat (ITT) Analysis Set, consisting of all randomized participants who used study medication at least once. | | | |
| Units: Subjects | | | |
| Asian | 5 | 0 | 5 |
| Caucasian | 94 | 102 | 196 |
| African | 1 | 1 | 2 |
| Other | 8 | 6 | 14 |

## End points

### End points reporting groups

| Reporting group title | Duac |
|---|---|

Reporting group description:

Participants topically applied a thin film of Duac gel once daily in the evening for 12 weeks, over the entire face, avoiding the mouth and eyes. Prior to the application, participants were advised to wash their face with the soap free cleanser, rinse thoroughly with warm water, and pat the skin thoroughly dry with a soft towel. After application, the participants had to avoid washing face for 4 hours (preferably 8 hours). Oil free facial moisturizer was used, if required.

| Reporting group title | Skinoren |
|---|---|

Reporting group description:

Participants topically applied a thin film of Skinoren cream twice daily (once in the morning and once in the evening) for 12 weeks, over the entire face, avoiding the mouth and eyes. Prior to the application, participants were advised to wash their face with the soap free cleanser, rinse thoroughly with warm water, and pat the skin thoroughly dry with a soft towel. After application, the participants had to avoid washing face for 4 hours (preferably 8 hours). Oil free facial moisturizer was used, if required.

### Primary: Percent change from Baseline in inflammatory lesion counts at Week 4

| End point title | Percent change from Baseline in inflammatory lesion counts at Week 4 |
|---|---|

End point description:

Lesions were counted confined to the face; inflammatory lesions (ILs) (considering nasal lesions) included papules and pustules. A papule is a small, raised, red, dome-shaped palpable lesion while a pustule is a raised, dome-shaped palpable lesion containing yellow fluid (pus). Percent change from Baseline was calculated as the value at Week 4 minus the value at Baseline (Day 1) divided by the Baseline value*100. The Modified Intent-to-Treat (mITT) Analysis Set included all participants in the ITT Analysis Set who had a Baseline measurement of the number of ILs and who had at least one post-Baseline measurement of the number of ILs.

| End point type | Primary |
|---|---|

End point timeframe:

Baseline and Week 4

| End point values | Duac | Skinoren | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 107[1] | 108[2] | | |
| Units: Percent change in lesions | | | | |
| arithmetic mean (standard deviation) | -51.9 (± 27.6) | -38.1 (± 30.9) | | |

Notes:

[1] - mITT Analysis Set

[2] - mITT Analysis Set

### Statistical analyses

| Statistical analysis title | Analysis 1 |
|---|---|
| Comparison groups | Skinoren v Duac |

| | |
|---|---|
| Number of subjects included in analysis | 215 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0004 [3] |
| Method | Wilcoxon (Mann-Whitney) |

Notes:

[3] - Two-sided Mann-Whitney U-test for independent samples - normal approximation

## Secondary: Absolute change from Baseline in ILs, NILs and total lesion count at Weeks 2, 4, 8 and 12

| | |
|---|---|
| End point title | Absolute change from Baseline in ILs, NILs and total lesion count at Weeks 2, 4, 8 and 12 |

End point description:

Lesions were counted confined to the face; ILs (considering nasal lesions) included papules and pustules. NILs included open comedones and closed comedones. An open comedo is an open, widely dilated follicle with black-coloured sebum, due to melanin and oxidation, and keratinous material that forms a plug, thereby obstructing the pilosebaceous duct. A closed comedo is a closed follicle filled with impacted sebum covered by keratin that has a whitish color. A papule is a small, raised, red, dome-shaped palpable lesion while a pustule is a raised, dome-shaped palpable lesion containing yellow fluid (pus). The total lesion (TLs) count was calculated as the sum of ILs and NILs. Change from Baseline was calculated as the values at Weeks 2,4,8 and 12 minus the value at Baseline (Day 1).

| | |
|---|---|
| End point type | Secondary |

End point timeframe:

Baseline and Weeks 2, 4, 8 and 12

| End point values | Duac | Skinoren | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 107[4] | 108[5] | | |
| Units: Absolute change in lesions | | | | |
| arithmetic mean (standard deviation) | | | | |
| IL, Week 2, n=105,108 | -10.3 (± 8.3) | -6.3 (± 7.8) | | |
| IL, Week 4, n=105,107 | -14.2 (± 9.1) | -9.7 (± 8.6) | | |
| IL, Week 8, n=104,102 | -17.7 (± 9.7) | -12.7 (± 8.6) | | |
| IL, Week 12 or early withdrawal, n=107,104 | -19.6 (± 10.1) | -14.2 (± 8.9) | | |
| NIL, Week 2, n=105,108 | -13.7 (± 19) | -8.5 (± 13.3) | | |
| NIL, Week 4, n=105,107 | -21.2 (± 21.5) | -16 (± 19.1) | | |
| NIL, Week 8, n=104,102 | -26.8 (± 27.1) | -20.9 (± 23.6) | | |
| NIL, Week 12 or early withdrawal, n=107,104 | -32 (± 27.2) | -23.3 (± 24.9) | | |
| TL, Week 2, n=105,108 | -23.9 (± 22.3) | -14.8 (± 16.7) | | |
| TL, Week 4, n=105,107 | -35.4 (± 25) | -25.7 (± 22.3) | | |
| TL, Week 8, n=104,102 | -44.4 (± 31.3) | -33.6 (± 27.5) | | |
| TL, Week 12 or early withdrawal, n=107,104 | -51.6 (± 30.9) | -37.5 (± 29) | | |

Notes:

[4] - mITT Analysis Set

[5] - mITT Analysis Set

### Statistical analyses

No statistical analyses for this end point

## Secondary: Percent change from Baseline in ILs, NILs and total lesion count at Weeks 2, 4, 8 and 12

| End point title | Percent change from Baseline in ILs, NILs and total lesion count at Weeks 2, 4, 8 and 12 |
|---|---|

End point description:

Lesions were counted confined to the face; ILs (considering nasal lesions) included papules and pustules. NILs included open comedones and closed comedones. An open comedo is an open, widely dilated follicle with black-coloured sebum, due to melanin and oxidation, and keratinous material that forms a plug, thereby obstructing the pilosebaceous duct. A closed comedo is a closed follicle filled with impacted sebum covered by keratin that has a whitish color. A papule is a small, raised, red, dome-shaped palpable lesion while a pustule is a raised, dome-shaped palpable lesion containing yellow fluid (pus). The total lesion count was calculated as the sum of ILs and NILs. Percent change from Baseline was calculated as the values at Weeks 2,4,8 and 12 minus the value at Baseline (Day 1) divided by Baseline value*100.

| End point type | Secondary |
|---|---|

End point timeframe:

Baseline and Weeks 2, 4, 8 and 12

| **End point values** | Duac | Skinoren | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 107[6] | 108[7] | | |
| Units: Percent change in lesions | | | | |
| arithmetic mean (standard deviation) | | | | |
| IL, Week 2, n=105,108 | -37.3 (± 27.7) | -24.2 (± 30.3) | | |
| IL, Week 8, n=104,102 | -65 (± 26.3) | -49.1 (± 30.9) | | |
| IL, Week 12 or early withdrawal, n=107,104 | -72.3 (± 25) | -55 (± 29.8) | | |
| NIL, Week 2, n=105,108 | -23.5 (± 25.3) | -14.9 (± 23.4) | | |
| NIL, Week 4, n=105,107 | -38.1 (± 27.8) | -27 (± 28.2) | | |
| NIL, Week 8, n=104,102 | -48.5 (± 39.8) | -35.5 (± 31.2) | | |
| NIL, Week 12 or early withdrawal, n=107,104 | -60.6 (± 35.3) | -42.1 (± 37.5) | | |
| TL, Week 2, n=105,108 | -28.7 (± 22.3) | -18.4 (± 20.3) | | |
| TL, Week 4, n=105,107 | -43.8 (± 23.3) | -30.8 (± 23) | | |
| TL, Week 8, n=104,102 | -55.2 (± 30.5) | -40.1 (± 27.4) | | |
| TL, Week 12 or early withdrawal, n=107,104 | -64.6 (± 26.9) | -46.1 (± 31.8) | | |

Notes:

[6] - mITT Analysis Set

[7] - mITT Analysis Set

### Statistical analyses

No statistical analyses for this end point

## Secondary: Shift change from Baseline in total lesions count by the Investigator's Static Global Assessment (ISGA) at Weeks 2, 4, 8 and 12

| End point title | Shift change from Baseline in total lesions count by the Investigator's Static Global Assessment (ISGA) at Weeks 2, 4, 8 and 12 |
|---|---|

End point description:

Investigator evaluated the acne severity (S) of the participant's face using the ISGA scale, ranging from 0 to 5: 0=clear skin with no ILs or NILs; 1=almost clear: rare NIL with no more than one small ILs; 2=mild S: >G 1, some NILs with no more than a few ILs (papules/ pustules only, no nodular lesions [NLs]); 3=moderate S: >G 2, up to many NILs and may have some ILs, but no more than one small NL; 4=severe: greater than G 3, up to many NILs and ILs, but no more than a few NLs; 5=very severe: many NILs and ILs and more than a few NLs, may have cystic lesions. A shift table was provided to deduce how the number of participants were varying from the Baseline visit to the post-Baseline visits. Week 12 represents Week 12 or early withdrawal.

| End point type | Secondary |
|---|---|

End point timeframe:

Baseline, Weeks 2, 4, 8 and 12

| **End point values** | Duac | Skinoren | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 107[8] | 108[9] | | |
| Units: Participants | | | | |
| Mild (Baseline) to Almost clear (Week 2) | 4 | 1 | | |
| Mild (Baseline) to Mild (Week 2) | 27 | 28 | | |
| Mild (Baseline) to Moderate (Week 2) | 3 | 8 | | |
| Moderate (Baseline) to Almost Clear (Week 2) | 1 | 1 | | |
| Moderate (Baseline) to Mild (Week 2) | 26 | 14 | | |
| Moderate (Baseline) to Moderate (Week 2) | 44 | 56 | | |
| Moderate (Baseline) to Missing (Week 2) | 2 | 0 | | |
| Mild (Baseline) to Almost clear (Week 4) | 8 | 8 | | |
| Mild (Baseline) to Mild (Week 4) | 25 | 24 | | |
| Mild (Baseline) to Moderate (Week 4) | 1 | 4 | | |
| Mild (Baseline) to Missing (Week 4) | 0 | 1 | | |
| Moderate (Baseline) to Almost Clear (Week 4) | 11 | 3 | | |
| Moderate (Baseline) to Mild (Week 4) | 29 | 24 | | |
| Moderate (Baseline) to Moderate (Week 4) | 31 | 43 | | |
| Moderate (Baseline) to Severe (Week 4) | 0 | 1 | | |
| Moderate (Baseline) to Missing (Week 4) | 2 | 1 | | |
| Mild (Baseline) to Clear (Week 8) | 2 | 0 | | |
| Mild (Baseline) to Almost Clear (Week 8) | 10 | 10 | | |
| Mild (Baseline) to Mild (Week 8) | 19 | 15 | | |
| Mild (Baseline) to Moderate (Week 8) | 3 | 8 | | |
| Mild (Baseline) to Missing (Week 8) | 0 | 4 | | |
| Moderate (Baseline) to Clear (Week 8) | 1 | 0 | | |
| Moderate (Baseline) to Almost Clear (Week 8) | 15 | 5 | | |
| Moderate (Baseline) to Mild (Week 8) | 32 | 27 | | |
| Moderate (Baseline) to Moderate (Week 8) | 22 | 37 | | |
| Moderate (Baseline) to Missing (Week 8) | 3 | 2 | | |
| Mild (Baseline) to Clear (Week 12) | 3 | 1 | | |
| Mild (Baseline) to Almost Clear (Week 12) | 12 | 9 | | |

| | | | | |
|---|---|---|---|---|
| Mild (Baseline) to Mild (Week 12) | 17 | 17 | | |
| Mild (Baseline) to Moderate (Week 12) | 2 | 8 | | |
| Mild (Baseline) to Missing (Week 12) | 0 | 2 | | |
| Moderate (Baseline) to Clear (Week 12) | 2 | 0 | | |
| Moderate (Baseline) to Almost Clear (Week 12) | 19 | 9 | | |
| Moderate (Baseline) to Mild (Week 12) | 33 | 26 | | |
| Moderate (Baseline) to Moderate (Week 12) | 19 | 32 | | |
| Moderate (Baseline) to Severe (Week 12) | 0 | 2 | | |
| Moderate (Baseline) to Missing (Week 12) | 0 | 2 | | |

Notes:

[8] - mITT Analysis Set

[9] - mITT Analysis Set

### Statistical analyses

No statistical analyses for this end point

## Secondary: Time from Baseline to a 50% reduction in TL count

| End point title | Time from Baseline to a 50% reduction in TL count |
|---|---|

End point description:

Time to a 50% reduction in TL count (sum of ILs and NILs) was the time difference between Baseline and the time to a 50% reduction in LC.

| End point type | Secondary |
|---|---|

End point timeframe:

From Baseline up to Week 12

| **End point values** | Duac | Skinoren | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 91[10] | 60[11] | | |
| Units: Days | | | | |
| median (full range (min-max)) | 52 (11 to 104) | 55 (12 to 97) | | |

Notes:

[10] - mITT Analysis Set. Only those participants with a 50% reduction were included in this analysis.

[11] - mITT Analysis Set. Only those participants with a 50% reduction were included in this analysis.

### Statistical analyses

No statistical analyses for this end point

## Secondary: Number of participants reported for the indicated Subject's Global Change Assessment (SGCA) category at Weeks 2, 4, 8 and 12

| End point title | Number of participants reported for the indicated Subject's Global Change Assessment (SGCA) category at Weeks 2, 4, 8 and 12 |
|---|---|

End point description:

Participant reported change in the following categories: "very much improved, much improved, minimally improved, no change, minimally worse, much worse and very much worse". Week 12 represents Week 12 or early withdrawal.

| End point type | Secondary |
|---|---|

End point timeframe:

Weeks 2, 4, 8 and 12

| **End point values** | Duac | Skinoren | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 107[12] | 108[13] | | |
| Units: Participants | | | | |
| Week 2, Very Much Improved | 4 | 2 | | |
| Week 4, Very Much Improved | 5 | 0 | | |
| Week 8, Very Much Improved | 9 | 1 | | |
| Week 12, Very Much Improved | 14 | 8 | | |
| Week 2, Much Improved | 51 | 30 | | |
| Week 4, Much Improved | 48 | 39 | | |
| Week 8, Much Improved | 54 | 44 | | |
| Week 12, Much Improved | 48 | 38 | | |
| Week 2, Minimally Improved | 44 | 56 | | |
| Week 4, Minimally Improved | 44 | 49 | | |
| Week 8, Minimally Improved | 30 | 32 | | |
| Week 12, Minimally Improved | 29 | 33 | | |
| Week 2, No change | 6 | 14 | | |
| Week 4, No change | 2 | 12 | | |
| Week 8, No change | 7 | 15 | | |
| Week 12, No change | 10 | 17 | | |
| Week 2, Minimally Worse | 0 | 6 | | |
| Week 4, Minimally Worse | 6 | 7 | | |
| Week 8, Minimally Worse | 3 | 8 | | |
| Week 12, Minimally Worse | 4 | 5 | | |
| Week 2, Much Worse | 0 | 0 | | |
| Week 4, Much Worse | 0 | 0 | | |
| Week 8, Much Worse | 1 | 1 | | |
| Week 12, Much Worse | 0 | 2 | | |
| Week 2, Very Much Worse | 0 | 0 | | |
| Week 4, Very Much Worse | 0 | 0 | | |
| Week 8, Very Much Worse | 0 | 1 | | |
| Week 12, Very Much Worse | 2 | 1 | | |
| Week 2, Missing | 2 | 0 | | |
| Week 4, Missing | 2 | 1 | | |
| Week 8, Missing | 3 | 6 | | |
| Week 12, Missing | 0 | 4 | | |

Notes:

[12] - mITT Analysis Set

[13] - mITT Analysis Set

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of participants with a shift change from Baseline for erythema,

## peeling and dryness at Weeks 2, 4, 8 and 12, as assessed by the Investigator

| End point title | Number of participants with a shift change from Baseline for erythema, peeling and dryness at Weeks 2, 4, 8 and 12, as assessed by the Investigator |
|---|---|

End point description:

Erythema (Er) is a skin condition characterized by redness or rash; peeling (Pl) skin is damage to and loss of the upper layer of skin; and dry skin (dry) is an uncomfortable condition marked by scaling, itching, and cracking. Local tolerability assessments were performed by the Investigator at each study visit and were graded based on severity as 0 to 3: 0=none; 1=slight; 2=some (erythema and dry skin)/moderate(peeling); 3=very red (erythema)/very dry (dry skin)/strong (peeling). Week 12 represents Week 12 or early withdrawal.

| End point type | Secondary |
|---|---|

End point timeframe:

Weeks 2, 4 ,8 and 12

| **End point values** | Duac | Skinoren | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 107[14] | 108[15] | | |
| Units: Participants | | | | |
| Er, None (Baseline) to None (Week 2) | 39 | 33 | | |
| Er, None (Baseline) to Slight (Week 2) | 11 | 18 | | |
| Er, None (Baseline) to Some (Week 2) | 0 | 1 | | |
| Er, None (Baseline) to Missing (Week 2) | 1 | 0 | | |
| Er, None (Baseline) to None (Week 4) | 40 | 36 | | |
| Er, None (Baseline) to Slight (Week 4) | 9 | 13 | | |
| Er, None (Baseline) to Some (Week 4) | 1 | 3 | | |
| Er, None (Baseline) to Missing (Week 4) | 1 | 0 | | |
| Er, None (Baseline) to None (Week 8) | 40 | 29 | | |
| Er, None (Baseline) to Slight (Week 8) | 10 | 19 | | |
| Er, None (Baseline) to Some (Week 8) | 0 | 2 | | |
| Er, None (Baseline) to Missing (Week 8) | 1 | 2 | | |
| Er, None (Baseline) to None (Week 12) | 45 | 32 | | |
| Er, None (Baseline) to Slight (Week 12) | 6 | 18 | | |
| Er, None (Baseline) to Missing (Week 12) | 0 | 2 | | |
| Er, Slight (Baseline) to None (Week 2) | 12 | 12 | | |
| Er, Slight (Baseline) to Slight (Week 2) | 19 | 18 | | |
| Er, Slight (Baseline) to Some (Week 2) | 1 | 8 | | |
| Er, Slight (Baseline) to Missing (Week 2) | 1 | 0 | | |
| Er, Slight (Baseline)to None (Week 4) | 18 | 19 | | |
| Er, Slight (Baseline) to Slight (Week 4) | 11 | 17 | | |
| Er, Slight (Baseline) to Some (Week 4) | 3 | 1 | | |
| Er, Slight (Baseline) to Missing (Week 4) | 1 | 1 | | |
| Er, Slight (Baseline) to None (Week 8) | 15 | 17 | | |
| Er, Slight (Baseline) to Slight (Week 8) | 11 | 17 | | |
| Er, Slight (Baseline) to Some (Week 8) | 5 | 1 | | |
| Er, Slight (Baseline) to Missing (Week 8) | 2 | 3 | | |
| Er, Slight (Baseline) to None (Week 12) | 21 | 22 | | |
| Er, Slight (Baseline) to Slight (Week 12) | 11 | 13 | | |
| Er, Slight (Baseline) to Some (Week 12) | 0 | 2 | | |

| | | | | |
|---|---|---|---|---|
| Er, Slight (Baseline) to Very red (Week 12) | 1 | 0 | | |
| Er, Slight (Baseline) to Missing (Week 12) | 0 | 1 | | |
| Er, Some (Baseline) to None (Week 2) | 3 | 1 | | |
| Er, Some (Baseline) to Slight (Week 2) | 10 | 11 | | |
| Er, Some (Baseline) to Some (Week 2) | 6 | 3 | | |
| Er, Some (Baseline)to None (Week 4) | 5 | 3 | | |
| Er, Some (Baseline) to Slight (Week 4) | 11 | 9 | | |
| Er, Some (Baseline) to Some (Week 4) | 3 | 2 | | |
| Er, Some (Baseline) to Missing (Week 4) | 0 | 1 | | |
| Er, Some (Baseline) to None (Week 8) | 8 | 1 | | |
| Er, Some (Baseline) to Slight (Week 8) | 9 | 12 | | |
| Er, Some (Baseline) to Some (Week 8) | 1 | 1 | | |
| Er, Some (Baseline) to Very red (Week 8) | 1 | 0 | | |
| Er, Some (Baseline) to Missing (Week 8) | 0 | 1 | | |
| Er, Some (Baseline) to None (Week 12) | 9 | 4 | | |
| Er, Some (Baseline) to Slight (Week 12) | 8 | 9 | | |
| Er, Some (Baseline) to Some (Week 12) | 2 | 1 | | |
| Er, Some (Baseline) to Missing (Week 12) | 0 | 1 | | |
| Er, Very red (Baseline) to Slight (Week 2) | 1 | 1 | | |
| Er, Very red (Baseline) to Some (Week 2) | 2 | 2 | | |
| Er, Very red (Baseline) to Slight (Week 4) | 2 | 2 | | |
| Er, Very red (Baseline) to Some (Week 4) | 1 | 1 | | |
| Er, Very red (Baseline) to None (Week 8) | 2 | 0 | | |
| Er, Very red (Baseline) to Slight (Week 8) | 1 | 3 | | |
| Er, Very red (Baseline) to None (Week 12) | 0 | 2 | | |
| Er, Very red (Baseline) to Slight (Week 12) | 1 | 1 | | |
| Er, Very red (Baseline) to Some (Week 12) | 2 | 0 | | |
| Pl, None (Baseline) to None (Week 2) | 65 | 73 | | |
| Pl, None (Baseline) to Slight (Week 2) | 13 | 11 | | |
| Pl, None (Baseline) to Moderate (Week 2) | 1 | 0 | | |
| Pl, None (Baseline) to Missing (Week 2) | 2 | 0 | | |
| Pl, None (Baseline) to None (Week 4) | 70 | 72 | | |
| Pl, None (Baseline) to Slight (Week 4) | 9 | 11 | | |
| Pl, None (Baseline) to Missing (Week 4) | 2 | 1 | | |
| Pl, None (Baseline) to None (Week 8) | 69 | 69 | | |
| Pl, None (Baseline) to Slight (Week 8) | 9 | 10 | | |
| Pl, None (Baseline) to Missing (Week 8) | 3 | 5 | | |
| Pl, None (Baseline) to None (Week 12) | 74 | 70 | | |
| Pl, None (Baseline) to Slight (Week 12) | 7 | 11 | | |
| Pl, None (Baseline) to Missing (Week 12) | 0 | 3 | | |
| Pl, Slight (Baseline) to None (Week 2) | 8 | 8 | | |
| Pl, Slight (Baseline) to Slight (Week 2) | 10 | 13 | | |

| | | | | |
|---|---|---|---|---|
| Pl, Slight (Baseline) to Moderate (Week 2) | 3 | 2 | | |
| Pl, Slight (Baseline)to None (Week 4) | 15 | 13 | | |
| Pl, Slight (Baseline) to Slight (Week 4) | 5 | 9 | | |
| Pl, Slight (Baseline) to Moderate (Week 4) | 1 | 1 | | |
| Pl, Slight (Baseline) to None (Week 8) | 18 | 12 | | |
| Pl, Slight (Baseline) to Slight (Week 8) | 3 | 10 | | |
| Pl, Slight (Baseline) to Missing (Week 8) | 0 | 1 | | |
| Pl, Slight (Baseline) to None (Week 12) | 14 | 15 | | |
| Pl, Slight (Baseline) to Slight (Week 12) | 7 | 7 | | |
| Pl, Slight (Baseline) to Missing (Week 12) | 0 | 1 | | |
| Pl, Moderate (Baseline) to None (Week 2) | 2 | 0 | | |
| Pl, Moderate (Baseline) to Slight (Week 2) | 2 | 1 | | |
| Pl, Moderate (Baseline)to None (Week 4) | 2 | 1 | | |
| Pl, Moderate (Baseline) to Slight (Week 4) | 1 | 0 | | |
| Pl, Moderate (Baseline) to Moderate (Week 4) | 1 | 0 | | |
| Pl, Moderate (Baseline) to None (Week 8) | 3 | 1 | | |
| Pl, Moderate (Baseline) to Slight (Week 8) | 1 | 0 | | |
| Pl, Moderate (Baseline) to None (Week 12) | 2 | 0 | | |
| Pl, Moderate (Baseline) to Slight (Week 12) | 2 | 1 | | |
| Dry, None (Baseline) to None (Week 2) | 55 | 65 | | |
| Dry, None (Baseline) to Slight (Week 2) | 14 | 9 | | |
| Dry, None (Baseline) to Some (Week 2) | 1 | 3 | | |
| Dry, None (Baseline) to Missing (Week 2) | 2 | 0 | | |
| Dry, None (Baseline)to None (Week 4) | 61 | 64 | | |
| Dry, None (Baseline) to Slight (Week 4) | 9 | 12 | | |
| Dry, None (Baseline) to Missing (Week 4) | 2 | 1 | | |
| Dry, None (Baseline) to None (Week 8) | 61 | 61 | | |
| Dry, None (Baseline) to Slight (Week 8) | 8 | 11 | | |
| Dry, None (Baseline) to Missing (Week 8) | 3 | 5 | | |
| Dry, None (Baseline) to None (Week 12) | 69 | 66 | | |
| Dry, None (Baseline) to Slight (Week 12) | 2 | 8 | | |
| Dry, None (Baseline) to Some (Week 12) | 1 | 0 | | |
| Dry, None (Baseline) to Missing (Week 12) | 0 | 3 | | |
| Dry, Slight (Baseline) to None (Week 2) | 11 | 7 | | |
| Dry, Slight (Baseline) to Slight (Week 2) | 11 | 12 | | |
| Dry, Slight (Baseline) to Some (Week 2) | 3 | 6 | | |
| Dry, Slight (Baseline)to None (Week 4) | 14 | 10 | | |
| Dry, Slight (Baseline) to Slight (Week 4) | 9 | 12 | | |
| Dry, Slight (Baseline) to Some (Week 4) | 2 | 3 | | |
| Dry, Slight (Baseline) to None (Week 8) | 19 | 12 | | |

| | | | | |
|---|---|---|---|---|
| Dry, Slight (Baseline) to Slight (Week 8) | 6 | 11 | | |
| Dry, Slight (Baseline) to Some (Week 8) | 0 | 1 | | |
| Dry, Slight (Baseline) to Missing (Week 8) | 0 | 1 | | |
| Dry, Slight (Baseline) to None (Week 12) | 14 | 15 | | |
| Dry, Slight (Baseline) to Slight (Week 12) | 11 | 8 | | |
| Dry, Slight (Baseline) to Some (Week 12) | 0 | 1 | | |
| Dry, Slight (Baseline) to Missing (Week 12) | 0 | 1 | | |
| Dry, Some (Baseline) to None (Week 2) | 4 | 2 | | |
| Dry, Some (Baseline) to Slight (Week 2) | 1 | 2 | | |
| Dry, Some (Baseline) to Some (Week 2) | 4 | 2 | | |
| Dry, Some (Baseline)to None (Week 4) | 4 | 1 | | |
| Dry, Some (Baseline) to Slight (Week 4) | 3 | 5 | | |
| Dry, Some (Baseline) to Some (Week 4) | 2 | 0 | | |
| Dry, Some (Baseline) to None (Week 8) | 5 | 1 | | |
| Dry, Some (Baseline) to Slight (Week 8) | 4 | 5 | | |
| Dry, Some (Baseline) to None (Week 12) | 6 | 3 | | |
| Dry, Some (Baseline) to Slight (Week 12) | 3 | 3 | | |

Notes:

[14] - mITT Analysis Set

[15] - mITT Analysis Set

### Statistical analyses

No statistical analyses for this end point

## Secondary: Number of participants with a shift change from Baseline for pruritis and burning/stinging at Weeks 2, 4, 8 and 12

| End point title | Number of participants with a shift change from Baseline for pruritis and burning/stinging at Weeks 2, 4, 8 and 12 |
|---|---|

End point description:

Itching or pruritis (Pr) is a sensation that causes the desire or reflex to scratch; burning/stinging (St/Bn) is a pain and burning sensation. Local tolerability assessments for burning/stinging and itching were performed by the participant and were graded based on severity as 0 to 3. 0=none; 1=slight; 2=moderate; 3=strong. Week 12 represents Week 12 or early withdrawal.

| End point type | Secondary |
|---|---|

End point timeframe:

Weeks 2, 4 ,8 and 12

| **End point values** | Duac | Skinoren | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 107[16] | 108[17] | | |
| Units: Participants | | | | |
| St/Bn, None (Baseline) to None (Week 2) | 63 | 42 | | |

| | | | | |
|---|---|---|---|---|
| St/Bn, None (Baseline) to Slight (Week 2) | 14 | 23 | | |
| St/Bn, None (Baseline) to Moderate (Week 2) | 4 | 8 | | |
| St/Bn, None (Baseline) to Strong (Week 2) | 1 | 4 | | |
| St/Bn, None (Baseline) to Missing (Week 2) | 2 | 0 | | |
| St/Bn, None (Baseline) to None (Week 4) | 70 | 41 | | |
| St/Bn, None (Baseline) to Slight (Week 4) | 11 | 29 | | |
| St/Bn, None (Baseline) to Moderate (Week 4) | 1 | 6 | | |
| St/Bn, None (Baseline) to Missing (Week 4) | 2 | 1 | | |
| St/Bn, None (Baseline) to None (Week 8) | 75 | 46 | | |
| St/Bn, None (Baseline) to Slight (Week 8) | 5 | 21 | | |
| St/Bn, None (Baseline) to Moderate (Week 8) | 1 | 4 | | |
| St/Bn, None (Baseline) to Strong (Week 8) | 0 | 1 | | |
| St/Bn, None (Baseline) to Missing (Week 8) | 3 | 5 | | |
| St/Bn, None (Baseline) to None (Week 12) | 75 | 47 | | |
| St/Bn, None (Baseline) to Slight (Week 12) | 6 | 19 | | |
| St/Bn, None (Baseline) to Moderate (Week 12) | 1 | 5 | | |
| St/Bn, None (Baseline) to Strong (Week 12) | 1 | 2 | | |
| St/Bn, None (Baseline) to Missing (Week 12) | 1 | 4 | | |
| St/Bn, Slight (Baseline) to None (Week 2) | 14 | 10 | | |
| St/Bn, Slight (Baseline) to Slight (Week 2) | 4 | 10 | | |
| St/Bn, Slight (Baseline) to Moderate (Week 2) | 3 | 2 | | |
| St/Bn, Slight (Baseline) to Strong (Week 2) | 0 | 2 | | |
| St/Bn, Slight (Baseline)to None (Week 4) | 12 | 9 | | |
| St/Bn, Slight (Baseline) to Slight (Week 4) | 8 | 13 | | |
| St/Bn, Slight (Baseline) to Moderate (Week 4) | 1 | 1 | | |
| St/Bn, Slight (Baseline) to Strong (Week 4) | 0 | 1 | | |
| St/Bn, Slight (Baseline) to None (Week 8) | 18 | 10 | | |
| St/Bn, Slight (Baseline) to Slight (Week 8) | 2 | 12 | | |
| St/Bn, Slight (Baseline) to Moderate (Week 8) | 1 | 1 | | |
| St/Bn, Slight (Baseline) to Strong (Week 8) | 0 | 1 | | |
| St/Bn, Slight (Baseline) to None (Week 12) | 18 | 9 | | |

| | | | | |
|---|---|---|---|---|
| St/Bn, Slight (Baseline) to Slight (Week 12) | 3 | 11 | | |
| St/Bn, Slight (Baseline) to Moderate (Week 12) | 0 | 3 | | |
| St/Bn, Slight (Baseline) to Strong (Week 12) | 0 | 1 | | |
| St/Bn, Moderate (Baseline) to None (Week 2) | 0 | 1 | | |
| St/Bn, Moderate (Baseline) to Slight (Week 2) | 1 | 3 | | |
| St/Bn, Moderate (Baseline)to Moderate (Week 2) | 0 | 2 | | |
| St/Bn, Moderate (Baseline) to None (Week 4) | 0 | 2 | | |
| St/Bn, Moderate (Baseline) to Slight (Week 4) | 1 | 3 | | |
| St/Bn, Moderate (Baseline) to Strong (Week 4) | 0 | 1 | | |
| St/Bn, Moderate (Baseline) to None (Week 8) | 0 | 1 | | |
| St/Bn, Moderate (Baseline) to Slight (Week 8) | 1 | 2 | | |
| St/Bn, Moderate (Baseline) to Moderate (Week 8) | 0 | 2 | | |
| St/Bn, Moderate (Baseline) to Missing (Week 8) | 0 | 1 | | |
| St/Bn, Moderate (Baseline) to None (Week 12) | 1 | 2 | | |
| St/Bn, Moderate (Baseline) to Slight (Week 12) | 0 | 3 | | |
| St/Bn, Moderate (Baseline) to Moderate (Week 12) | 0 | 1 | | |
| St/Bn, Strong (Baseline) to None (Week 2) | 0 | 1 | | |
| St/Bn, Strong (Baseline) to None (Week 4) | 0 | 1 | | |
| St/Bn, Strong (Baseline) to None (Week 8) | 0 | 1 | | |
| St/Bn, Strong (Baseline) to Slight (Week 12) | 0 | 1 | | |
| Pr, None (Baseline) to None (Week 2) | 43 | 28 | | |
| Pr, None (Baseline) to Slight (Week 2) | 14 | 27 | | |
| Pr, None (Baseline) to Moderate (Week 2) | 4 | 7 | | |
| Pr, None (Baseline) to Strong (Week 2) | 0 | 1 | | |
| Pr, None (Baseline) to Missing (Week 2) | 2 | 0 | | |
| Pr, None (Baseline) to None (Week 4) | 45 | 27 | | |
| Pr, None (Baseline) to Slight (Week 4) | 14 | 30 | | |
| Pr, None (Baseline) to Moderate (Week 4) | 2 | 5 | | |
| Pr, None (Baseline) to Missing (Week 4) | 2 | 1 | | |
| Pr, None (Baseline) to None (Week 8) | 47 | 33 | | |
| Pr, None (Baseline) to Slight (Week 8) | 13 | 26 | | |
| Pr, None (Baseline) to Strong (Week 8) | 0 | 1 | | |
| Pr, None (Baseline) to Missing (Week 8) | 3 | 3 | | |
| Pr, None (Baseline) to None (Week 12) | 51 | 33 | | |
| Pr, None (Baseline) to Slight (Week 12) | 11 | 22 | | |
| Pr, None (Baseline) to Moderate (Week 12) | 1 | 3 | | |

| | | | | |
|---|---|---|---|---|
| Pr, None (Baseline) to Strong (Week 12) | 0 | 1 | | |
| Pr, None (Baseline) to Missing (Week 12) | 0 | 4 | | |
| Pr, Slight (Baseline) to None (Week 2) | 13 | 10 | | |
| Pr, Slight (Baseline) to Slight (Week 2) | 20 | 15 | | |
| Pr, Slight (Baseline) to Moderate (Week 2) | 5 | 9 | | |
| Pr, Slight (Baseline) to Strong (Week 2) | 1 | 4 | | |
| Pr, Slight (Baseline)to None (Week 4) | 17 | 12 | | |
| Pr, Slight (Baseline) to Slight (Week 4) | 20 | 19 | | |
| Pr, Slight (Baseline) to Moderate (Week 4) | 2 | 6 | | |
| Pr, Slight (Baseline) to Strong (Week 4) | 0 | 1 | | |
| Pr, Slight (Baseline) to None (Week 8) | 21 | 11 | | |
| Pr, Slight (Baseline) to Slight (Week 8) | 14 | 18 | | |
| Pr, Slight (Baseline) to Moderate (Week 8) | 4 | 4 | | |
| Pr, Slight (Baseline) to Strong (Week 8) | 0 | 2 | | |
| Pr, Slight (Baseline) to Missing (Week 8) | 0 | 3 | | |
| Pr, Slight (Baseline) to None (Week 12) | 22 | 11 | | |
| Pr, Slight (Baseline) to Slight (Week 12) | 15 | 19 | | |
| Pr, Slight (Baseline) to Moderate (Week 12) | 2 | 6 | | |
| Slight (Baseline) to Strong (Week 12) | 0 | 2 | | |
| Pr, Moderate (Baseline) to None (Week 2) | 2 | 4 | | |
| Pr, Moderate (Baseline) to Slight (Week 2) | 1 | 1 | | |
| Pr, Moderate (Baseline)to Moderate (Week 2) | 1 | 0 | | |
| Pr, Moderate (Baseline) to None (Week 4) | 2 | 2 | | |
| Pr, Moderate (Baseline) to Slight (Week 4) | 2 | 2 | | |
| Pr, Moderate (Baseline) to Moderate (Week 4) | 0 | 1 | | |
| Pr, Moderate (Baseline) to None (Week 8) | 3 | 2 | | |
| Pr, Moderate (Baseline) to Slight (Week 8) | 1 | 3 | | |
| Pr, Moderate (Baseline) to None (Week 12) | 3 | 1 | | |
| Pr, Moderate (Baseline) to Slight (Week 12) | 1 | 4 | | |
| Pr, Strong (Baseline) to Strong (Week 2) | 0 | 2 | | |
| Pr, Strong (Baseline) to Strong (Week 4) | 0 | 2 | | |
| Pr, Strong (Baseline) to Moderate (Week 8) | 0 | 1 | | |
| Pr, Strong (Baseline) to Strong (Week 8) | 0 | 1 | | |
| Pr, Strong (Baseline) to Slight (Week 12) | 0 | 1 | | |
| Pr, Strong (Baseline) to Strong (Week 12) | 0 | 1 | | |

Notes:

[16] - mITT Analysis Set

[17] - mITT Analysis Set

## Statistical analyses

No statistical analyses for this end point

## Secondary: Absolute change in the Children's Dermatology Life Quality Index (CDLQI) score from Baseline at Weeks 2, 4, 8 and 12 in participants 12 to 16 years of age

| End point title | Absolute change in the Children's Dermatology Life Quality Index (CDLQI) score from Baseline at Weeks 2, 4, 8 and 12 in participants 12 to 16 years of age |
|---|---|

End point description:

The CDLQI was used in children 12 to 16 years of age. The CDLQI was used to measure how much the participant's skin problem had affected their life over the last week. The CDLQI total score ranges from 0 to 30 where 0-1=no effect at all on the participant's life; 2-6=small effect on the participant's life; 7-12=moderate effect on the participant's life; 13-18=very large effect on the participant's life; 19-30=extremely large effect on the participant's life. The higher the score, the more quality of life was impaired. Absolute change from Baseline was calculated as the values at Weeks 2, 4, 8 and 12 minus the value at Baseline (Day 1).

| End point type | Secondary |
|---|---|

End point timeframe:

Baseline, Weeks 2, 4, 8 and 12

| **End point values** | Duac | Skinoren | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 45[18] | 47[19] | | |
| Units: Absolute change of total score | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 2, n=38,42 | -2.61 (± 2.89) | -1.31 (± 2.29) | | |
| Week 4; n=38,42 | -2.55 (± 2.41) | -1.55 (± 2.01) | | |
| Week 8, n=38,42 | -2.68 (± 2.76) | -1.67 (± 2.34) | | |
| Week 12 or early withdrawal, n=38,42 | -2.87 (± 2.75) | -1.55 (± 2.56) | | |

Notes:

[18] - mITT Analysis Set. Only those participants 12 to 16 years of age were included in the analysis.

[19] - mITT Analysis Set. Only those participants 12 to 16 years of age were included in the analysis.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Absolute change in the Dermatology Life Quality Index (DLQI) score from Baseline at Weeks 2, 4, 8 and 12 in participants 17 years of age or older

| End point title | Absolute change in the Dermatology Life Quality Index (DLQI) score from Baseline at Weeks 2, 4, 8 and 12 in participants 17 years of age or older |
|---|---|

End point description:

The DLQI was used in participants 17 years of age or older. The DLQI was used to measure how much the participant's skin problem had affected their life over the last week. The DLQI total score ranges from 0 to 30 where 0-1=no effect at all on the participant's life; 2-5=small effect on the participant's life; 6-10=moderate effect on the participant's life; 11-20=very large effect on the participant's life; 21-30=extremely large effect on the participant's life. The higher the score, the more quality of life was impaired. Absolute change from Baseline was calculated as the values at Weeks 2, 4, 8 and 12 minus the value at Baseline (Day 1).

| End point type | Secondary |
|---|---|

End point timeframe:

Baseline, Weeks 2, 4, 8 and 12

| **End point values** | Duac | Skinoren | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 62[20] | 61[21] | | |
| Units: Absolute change of total score | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 2, n=54,53 | -2.28 (± 2.81) | -2.17 (± 3.72) | | |
| Week 4, n=56,52 | -3.39 (± 3.33) | -3.15 (± 3.52) | | |
| Week 8, n=55,50 | -4.04 (± 3.7) | -3.38 (± 4.6) | | |
| Week 12 or early withdrawal, n=57,51 | -4.46 (± 3.8) | -3.12 (± 4.94) | | |

Notes:

[20] - mITT Analysis Set. Only those participants 17 years or older were included in the analysis.

[21] - mITT Analysis Set. Only those participants 17 years or older were included in the analysis.

### Statistical analyses

No statistical analyses for this end point

## Secondary: Number of participants with the overall satisfaction score at Week 12, rated using the Product Acceptability and Preference Questionnaire

| End point title | Number of participants with the overall satisfaction score at Week 12, rated using the Product Acceptability and Preference Questionnaire |
|---|---|

End point description:

The Product Acceptability and Preference Questionnaire was completed by the participant at Week 12. The participant rated their overall satisfaction using the following scale: 1-very satisfied; 2- satisfied; 3-neutral; 4-unsatisfied; 5-very unsatisfied.

| End point type | Secondary |
|---|---|

End point timeframe:

Week 12

| **End point values** | Duac | Skinoren | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 107[22] | 108[23] | | |
| Units: Participants | | | | |
| Very satisfied | 41 | 26 | | |
| Satisfied | 61 | 43 | | |
| Neutral | 4 | 21 | | |

| | | | | |
|---|---|---|---|---|
| Unsatisfied | 1 | 11 | | |
| Very unsatisfied | 0 | 3 | | |

Notes:

[22] - mITT Analysis Set

[23] - mITT Analysis Set

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of participants with the number of missed applications of treatment medication from Baseline to Week 12

| End point title | Number of participants with the number of missed applications of treatment medication from Baseline to Week 12 |
|---|---|

End point description:

Number of participants with the number of missed applications of treatment medication from Baseline to Week 12 was analyzed.

| End point type | Secondary |
|---|---|

End point timeframe:

Week 12

| **End point values** | Duac | Skinoren | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 107[24] | 108[25] | | |
| Units: Participants | | | | |
| 0 missed application | 51 | 38 | | |
| 1 missed application | 21 | 8 | | |
| 2 missed application | 12 | 4 | | |
| 3 missed application | 4 | 4 | | |
| 4 missed application | 4 | 5 | | |
| 5 missed application | 1 | 5 | | |
| 6 missed application | 3 | 7 | | |
| 7 missed application | 2 | 6 | | |
| 8 missed application | 1 | 3 | | |
| 9 missed application | 1 | 5 | | |
| 10 missed application | 1 | 2 | | |
| 11 missed application | 1 | 3 | | |
| 12 missed application | 0 | 1 | | |
| 13 missed application | 1 | 2 | | |
| 14 missed application | 1 | 5 | | |
| 16 missed application | 1 | 0 | | |
| 17 missed application | 1 | 1 | | |
| 18 missed application | 1 | 1 | | |
| 19 missed application | 0 | 1 | | |
| 21 missed application | 0 | 2 | | |
| 22 missed application | 0 | 1 | | |
| 23 missed application | 0 | 1 | | |
| 31 missed application | 0 | 1 | | |
| 39 missed application | 0 | 1 | | |

| | | | | |
|---|---|---|---|---|
| Missing | 0 | 1 | | |

Notes:

[24] - mITT Analysis Set

[25] - mITT Analysis Set

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of participants with any adverse event (AE) or serious adverse event (SAE)

| End point title | Number of participants with any adverse event (AE) or serious adverse event (SAE) |
|---|---|

End point description:

AE is defined as any untoward medical occurrence in a participant, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. A SAE is defined as any untoward medical occurrence that, at any dose: results in death, is life threatening, requires hospitalization or prolongation of existing hospitalization, results in disability or incapacity, or is a congenital anomaly or birth defect. Medical or scientific judgment should be exercised in other situations. Refer to the general Adverse AE/SAE module for a complete list of AEs and SAEs.

| End point type | Secondary |
|---|---|

End point timeframe:

From Treatment Day1 until Week 12

| **End point values** | Duac | Skinoren | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 108[26] | 109[27] | | |
| Units: Participants | | | | |
| Any AE | 62 | 76 | | |
| Any SAE | 2 | 3 | | |

Notes:

[26] - ITT Analysis Set

[27] - ITT Analysis Set

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

On-treatment SAEs and non-serious AEs were collected from the start of study medication until the follow-up visit (up to 12 weeks).

Adverse event reporting additional description:

On-treatment SAEs and non-serious AEs are reported for members of the ITT Population, comprised of all participants who were randomized to treatment and received at least one dose of study medication.

| | |
|---|---|
| Assessment type | Systematic |

### Dictionary used

| | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 17.0 |

### Reporting groups

| | |
|---|---|
| Reporting group title | Duac |

Reporting group description:

Participants topically applied a thin film of Duac gel once daily in the evening for 12 weeks, over the entire face, avoiding the mouth and eyes. Prior to the application, participants were advised to wash their face with the soap free cleanser, rinse thoroughly with warm water, and pat the skin thoroughly dry with a soft towel. After application, the participants had to avoid washing face for 4 hours (preferably 8 hours). Oil free facial moisturizer was used, if required.

| | |
|---|---|
| Reporting group title | Skinoren |

Reporting group description:

Participants topically applied a thin film of Skinoren cream twice daily (once in the morning and once in the evening) for 12 weeks, over the entire face, avoiding the mouth and eyes. Prior to the application, participants were advised to wash their face with the soap free cleanser, rinse thoroughly with warm water, and pat the skin thoroughly dry with a soft towel. After application, the participants had to avoid washing face for 4 hours (preferably 8 hours). Oil free facial moisturizer was used, if required.

| Serious adverse events | Duac | Skinoren | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 2 / 108 (1.85%) | 3 / 109 (2.75%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | | | |
| Reproductive system and breast disorders | | | |
| Vulval haematoma | | | |
| subjects affected / exposed | 1 / 108 (0.93%) | 0 / 109 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Psychiatric disorders | | | |
| Stress | | | |
| subjects affected / exposed | 1 / 108 (0.93%) | 0 / 109 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|---|---|---|
| Renal and urinary disorders | | | |
| Urinary retention | | | |
| subjects affected / exposed | 0 / 108 (0.00%) | 1 / 109 (0.92%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Brucellosis | | | |
| subjects affected / exposed | 1 / 108 (0.93%) | 0 / 109 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastroenteritis | | | |
| subjects affected / exposed | 0 / 108 (0.00%) | 1 / 109 (0.92%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metabolism and nutrition disorders | | | |
| Type 1 diabetes mellitus | | | |
| subjects affected / exposed | 0 / 108 (0.00%) | 1 / 109 (0.92%) | |
| 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** | Duac | Skinoren | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 32 / 108 (29.63%) | 55 / 109 (50.46%) | |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 16 / 108 (14.81%) | 18 / 109 (16.51%) | |
| occurrences (all) | 26 | 26 | |
| General disorders and administration site conditions | | | |
| Application site pain | | | |
| subjects affected / exposed | 7 / 108 (6.48%) | 22 / 109 (20.18%) | |
| occurrences (all) | 7 | 24 | |
| Application site pruritus | | | |
| subjects affected / exposed | 8 / 108 (7.41%) | 25 / 109 (22.94%) | |
| occurrences (all) | 8 | 27 | |

| | | | |
|---|---|---|---|
| Infections and infestations<br>Nasopharyngitis<br>subjects affected / exposed<br>occurrences (all) | 10 / 108 (9.26%)<br>12 | 20 / 109 (18.35%)<br>21 | |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---|---|
| 15 January 2014 | 4.3: Exclusion criteria 6, deletion of contraceptives; addition of exclusion criteria 9 -> to ensure consistency between exclusion criteria and section 5.7.1 permitted medications and non-drug therapies.<br>6.2.1.3, 6.2.2.2: Add assessment at week 0 -> to ensure consistency between time and<br>events table and section 6.2.1.3, 6.2.2.2<br>6.3.8.2: Add respiratory rate -> to ensure consistency between time and events table and section 6.3.8.2 |

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported