# Clinical trial results:
# A double blinded, prospective, randomized, vehicle controlled, multi-center study of photodynamic therapy with Visonac cream in patients with acne vulgaris

## Summary

| | |
|---|---|
| EudraCT number | 2012-001296-36 |
| Trial protocol | Outside EU/EEA |
| Global end of trial date | 06 April 2012 |

**Results information**

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 07 November 2020 |
| First version publication date | 07 November 2020 |

## Trial information

**Trial identification**

| | |
|---|---|
| Sponsor protocol code | PCTA206/11 |

**Additional study identifiers**

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01347879 |
| WHO universal trial number (UTN) | - |

Notes:

**Sponsors**

| | |
|---|---|
| Sponsor organisation name | Photocure ASA |
| Sponsor organisation address | Hoffsveien 4, Oslo, Norway, NO-0275 |
| Public contact | Clinical Trials information, Photocure, 47 22062210, info@photocure.no |
| Scientific contact | Clinical Trials information, Photocure, 47 22062210, info@photocure.no |

Notes:

**Paediatric regulatory details**

| | |
|---|---|
| Is trial part of an agreed paediatric investigation plan (PIP) | Yes |
| EMA paediatric investigation plan number(s) | EMEA-000698-PIP02-10 |
| 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 | 09 November 2012 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 06 April 2012 |
| Global end of trial reached? | Yes |
| Global end of trial date | 06 April 2012 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

Evaluate the efficacy and safety of Visonac PDT in patients with severe acne, score 4 on the IGA scale

Protection of trial subjects:

The light source has a built-in fan which cools the treatment area during illumination. If the patient requests a pause in light treatment, the illumination may be paused and started again. After illumination the patients may take "over-the-counter NSAIDS" at the dose recommended on label.

Background therapy: -

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 07 July 2011 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

## Population of trial subjects

### Subjects enrolled per country

| | |
|---|---|
| Country: Number of subjects enrolled | United States: 153 |
| Worldwide total number of subjects | 153 |
| EEA total number of subjects | 0 |

Notes:

### Subjects enrolled per age group

| | |
|---|---|
| In utero | 0 |
| Preterm newborn - gestational age < 37 wk | 0 |
| Newborns (0-27 days) | 0 |
| Infants and toddlers (28 days-23 months) | 0 |
| Children (2-11 years) | 0 |
| Adolescents (12-17 years) | 94 |
| Adults (18-64 years) | 59 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details:

Start of recruitment 7 July 2011
End of recruitment 11 January 2012
Study center(s): 15 centers in the US

### Pre-assignment

Screening details:

Discontinue before first study treatment: topical acne treatments  at least 14 days, oral antibiotics: 1 month, oral isotretinoin at least 6 months, medicated cleansers. Any systemic hormonal treatment for reasons other than acne unchanged during 3 months before first study treatment.

### Period 1

| | |
|---|---|
| Period 1 title | Overall trial (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator, Monitor, Assessor |

Blinding implementation details:

This was a randomized, double-blind study.  The vehicle cream was similar in appearance and consistency to the active (Visonac) cream.  To avoid the risk of unblinding as a consequence of local AEs, the entire treatment procedure and recording of AEs was conducted by an investigator or designee who was not involved in efficacy evaluations.

### Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | Visonac cream with PDT |

Arm description:

Test product and red light illumination

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Visonac |
| Investigational medicinal product code | not applicable |
| Other name | |
| Pharmaceutical forms | Cream |
| Routes of administration | Topical use |

Dosage and administration details:

Visonac (MAL cream 80 mg/g), applied 1.5 hours under occlusion, before illumination with red light

| | |
|---|---|
| **Arm title** | Vehicle cream and PDT |

Arm description:

Vehicle cream and red light illumination

| | |
|---|---|
| Arm type | Placebo |
| Investigational medicinal product name | Vehicle |
| Investigational medicinal product code | Not applicable |
| Other name | |
| Pharmaceutical forms | Cream |
| Routes of administration | Topical use |

Dosage and administration details:

Vehicle cream, applied 1.5 hours under occlusion, before illumination with red light

| **Number of subjects in period 1** | Visonac cream with PDT | Vehicle cream and PDT |
|---|---|---|
| Started | 100 | 53 |
| Completed | 83 | 46 |
| Not completed | 17 | 7 |
| Consent withdrawn by subject | 2 | 3 |
| Adverse event, non-fatal | 12 | - |
| Other | 3 | 1 |
| Non-compliance | - | 1 |
| Lost to follow-up | - | 2 |

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | Visonac cream with PDT |
| Reporting group description:<br>Test product and red light illumination | |
| Reporting group title | Vehicle cream and PDT |
| Reporting group description:<br>Vehicle cream and red light illumination | |

| Reporting group values | Visonac cream with PDT | Vehicle cream and PDT | Total |
|---|---|---|---|
| Number of subjects | 100 | 53 | 153 |
| 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) | 0 | 0 | 0 |
| Adolescents (12-17 years) | 59 | 35 | 94 |
| Adults (18-64 years) | 41 | 18 | 59 |
| From 65-84 years | 0 | 0 | 0 |
| 85 years and over | 0 | 0 | 0 |
| Gender categorical<br>Units: Subjects | | | |
| Female | 44 | 22 | 66 |
| Male | 56 | 31 | 87 |

## End points

| End points reporting groups | |
|---|---|
| Reporting group title | Visonac cream with PDT |
| Reporting group description:<br>Test product and red light illumination | |
| Reporting group title | Vehicle cream and PDT |
| Reporting group description:<br>Vehicle cream and red light illumination | |

### Primary: Absolute Change From Baseline in Facial Inflammatory Lesion Count (Nodules, Papules, and Pustules).

| | |
|---|---|
| End point title | Absolute Change From Baseline in Facial Inflammatory Lesion Count (Nodules, Papules, and Pustules). |
| End point description: | |
| End point type | Primary |
| End point timeframe:<br>From baseline to 12 weeks after first treatment | |

| End point values | Visonac cream with PDT | Vehicle cream and PDT | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 100 | 53 | | |
| Units: Lesion counts | | | | |
| arithmetic mean (standard deviation) | -15.6 (± 16.4) | -7.8 (± 21.4) | | |

### Statistical analyses

| Statistical analysis title | Absolute change in facial inflam. lesion counts |
|---|---|
| Statistical analysis description:<br>The primary efficacy analysis was based on the ITT Analysis Set, comprising all randomized patients who had any aspect of study treatment initiated with imputation for missing data (last observation carried forward [LOCF]). | |
| Comparison groups | Visonac cream with PDT v Vehicle cream and PDT |
| Number of subjects included in analysis | 153 |
| Analysis specification | Pre-specified |
| Analysis type | superiority[1] |
| P-value | = 0.006 |
| Method | ANCOVA |
| Parameter estimate | Least square mean |
| Point estimate | -7.4 |

| | |
|---|---|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -12.5 |
| upper limit | -2.2 |

Notes:

[1] - Fixed terms for treatment and center and the baseline lesion count as covariate

## Secondary: Percent change from baseline in facial inflammatory lesion counts

| | |
|---|---|
| End point title | Percent change from baseline in facial inflammatory lesion counts |

End point description:

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

End point timeframe:

From baseline to 12 weeks after the first treatment

| End point values | Visonac cream with PDT | Vehicle cream and PDT | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 100 | 53 | | |
| Units: percent | | | | |
| median (full range (min-max)) | -43.8 (-100 to 84) | -26.6 (-100 to 176) | | |

### Statistical analyses

| Statistical analysis title | Percent Change in Facial Inflammatory Lesion Count |
|---|---|

Statistical analysis description:

Analysis of secondary endpoints was based on the ITT Analysis Set using LOCF.

| | |
|---|---|
| Comparison groups | Visonac cream with PDT v Vehicle cream and PDT |
| Number of subjects included in analysis | 153 |
| Analysis specification | Pre-specified |
| Analysis type | superiority[2] |
| P-value | = 0.003 |
| Method | ANCOVA |
| Parameter estimate | Least square mean |
| Point estimate | -20 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -33.2 |
| upper limit | -6.8 |

Notes:

[2] - Fixed terms for treatment and center and the baseline lesion count as covariate.

## Secondary: Percent change from baseline in facial non-inflammatory lesion counts

| End point title | Percent change from baseline in facial non-inflammatory lesion counts |
|---|---|

End point description:

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

End point timeframe:

From baseline to 12 weeks after the first treatment

| End point values | Visonac cream with PDT | Vehicle cream and PDT | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 100 | 53 | | |
| Units: percent | | | | |
| median (full range (min-max)) | -31.0 (-100 to 100) | -37.0 (-100 to 196) | | |

### Statistical analyses

| Statistical analysis title | Percent change in facial non-inflam. lesion counts |
|---|---|

Statistical analysis description:

Analysis of secondary endpoints was based on the ITT Analysis Set using LOCF.

| Comparison groups | Visonac cream with PDT v Vehicle cream and PDT |
|---|---|
| Number of subjects included in analysis | 153 |
| Analysis specification | Pre-specified |
| Analysis type | superiority[3] |
| P-value | = 0.72 |
| Method | ANCOVA |
| Parameter estimate | Least square mean |
| Point estimate | -2.6 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -16.5 |
| upper limit | 11.3 |

Notes:

[3] - Fixed terms for treatment and center and the baseline lesion count as covariate.

## Secondary: Number of Patients With Success According to IGA Scale Based on the Facial Assessment.

| End point title | Number of Patients With Success According to IGA Scale Based on the Facial Assessment. |
|---|---|

End point description:

The severity of acne was assessed at each visit using the 5-point IGA scale (0-4)
0 Clear; residual hyperpigmentation and erythema may be present
1 Almost clear; few scattered comedones and a few small papules
2 Mild; easily recognizable, less than half the face is involved. Some comedones and some papules and pustules

3 Moderate; more than half the face is involved. Many comedones, papules, and pustules. One nodule may be present
4 Severe; Most of face is involved, with comedones, numerous papules and pustules, and/or few nodules

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

End point timeframe:

From baseline to 12 weeks after first treatment

| **End point values** | Visonac cream with PDT | Vehicle cream and PDT | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 100 | 53 | | |
| Units: Subjects | 44 | 14 | | |

### Statistical analyses

| **Statistical analysis title** | Treatment success on the IGA scale |
|---|---|

Statistical analysis description:

For categorical variables analyzed with logistic regression, treatment and center were included in the model.

| Comparison groups | Visonac cream with PDT v Vehicle cream and PDT |
|---|---|
| Number of subjects included in analysis | 153 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.013 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 3.24 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.3 |
| upper limit | 8.1 |

## Secondary: IGA Clear or Almost Clear Scores based on the Facial Assessment:

| End point title | IGA Clear or Almost Clear Scores based on the Facial Assessment: |
|---|---|

End point description:

The severity of acne was assessed at each visit using the 5-point IGA scale (0-4)
0 Clear; residual hyperpigmentation and erythema may be present
1 Almost clear; few scattered comedones and a few small papules
2 Mild; easily recognizable, less than half the face is involved. Some comedones and some papules and pustules
3 Moderate; more than half the face is involved. Many comedones, papules, and pustules. One nodule may be present
4 Severe; Most of face is involved, with comedones, numerous papules and pustules, and/or few nodules

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

End point timeframe:

From baseline to 12 weeks after first treatment

| End point values | Visonac cream with PDT | Vehicle cream and PDT | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 100 | 53 | | |
| Units: Subjects | 13 | 2 | | |

### Statistical analyses

| Statistical analysis title | IGA scale clear or almost clear |
|---|---|

Statistical analysis description:

Categorical efficacy endpoints were analyzed using logistic regression including terms for treatment and center.

| | |
|---|---|
| Comparison groups | Visonac cream with PDT v Vehicle cream and PDT |
| Number of subjects included in analysis | 153 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.094 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 3.96 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.8 |
| upper limit | 19.9 |

## Secondary: Absolute change from baseline in facial non-inflammatory lesion count

| End point title | Absolute change from baseline in facial non-inflammatory lesion count |
|---|---|

End point description:

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

End point timeframe:

From baseline to 12 weeks after the first treatment

| End point values | Visonac cream with PDT | Vehicle cream and PDT | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 100 | 53 | | |
| Units: Lesions | | | | |
| arithmetic mean (standard deviation) | -11.8 (± 19.0) | -10.7 (± 22.1) | | |

**Statistical analyses**

| Statistical analysis title | Absolute Change From Baseline in Facial Non-inflam |
|---|---|
| Comparison groups | Visonac cream with PDT v Vehicle cream and PDT |
| Number of subjects included in analysis | 153 |
| Analysis specification | Pre-specified |
| Analysis type | superiority[4] |
| P-value | = 0.85 |
| Method | ANCOVA |
| Parameter estimate | Least square means |
| Point estimate | -0.6 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -6.6 |
| upper limit | 5.5 |

Notes:

[4] - Fixed terms for treatment and center and the baseline lesion count as covariate.

**Secondary: Absolute change in non-facial inflammatory lesion count**

| End point title | Absolute change in non-facial inflammatory lesion count |
|---|---|

End point description:

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

End point timeframe:

From baseline to 12 weeks after the first treatment

| End point values | Visonac cream with PDT | Vehicle cream and PDT | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 24 | 15 | | |
| Units: Lesions | | | | |
| arithmetic mean (standard deviation) | -9.0 (± 9.8) | -4.1 (± 14.5) | | |

**Statistical analyses**

No statistical analyses for this end point

## Secondary: Absolute change from baseline in facial inflammatory lesion counts at week 2, 4 and 6

| End point title | Absolute change from baseline in facial inflammatory lesion counts at week 2, 4 and 6 |
|---|---|

End point description:

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

End point timeframe:

Change from baseline at 2, 4 and 6 weeks after first treatment

| End point values | Visonac cream with PDT | Vehicle cream and PDT | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 100 | 53 | | |
| Units: Lesion count | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 2 | -9.0 (± 14.9) | -4.4 (± 14.0) | | |
| Week 4 | -11.7 (± 18.3) | -6.5 (± 15.7) | | |
| Week 6 | -13.0 (± 19.0) | -6.2 (± 19.1) | | |

### Statistical analyses

No statistical analyses for this end point

## Other pre-specified: Pain during illumination

| End point title | Pain during illumination |
|---|---|

End point description:

Pain during illumination was assessed by the patient using a visual analogue scale (VAS) form 0 to 10, where 0 indicates no pain and 10 the worst pain imaginable.

| End point type | Other pre-specified |
|---|---|

End point timeframe:

Facial pain immediately after first treatment

| End point values | Visonac cream with PDT | Vehicle cream and PDT | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 100 | 53 | | |
| Units: VAS score in cm | | | | |
| median (full range (min-max)) | 3.0 (0 to 8.8) | 0.1 (0 to 3.6) | | |

## Statistical analyses

No statistical analyses for this end point

## Other pre-specified: Erythema score of mild and moderate

| End point title | Erythema score of mild and moderate |
|---|---|

End point description:

Clinical assessment of facial erythema using a 4-point rating scale (ranging from 0= none to 3=severe) before and after each illumination.

| End point type | Other pre-specified |
|---|---|

End point timeframe:

Immediately after first treatment

| End point values | Visonac cream with PDT | Vehicle cream and PDT | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 100 | 53 | | |
| Units: Subjects | 86 | 37 | | |

## Statistical analyses

No statistical analyses for this end point

## Other pre-specified: Erythema score of mild and moderate

| End point title | Erythema score of mild and moderate |
|---|---|

End point description:

Clinical assessment of facial erythema using a 4-point rating scale (ranging from 0= none to 3=severe) before and after each illumination.

| End point type | Other pre-specified |
|---|---|

End point timeframe:

2 days after first treatment

| End point values | Visonac cream with PDT | Vehicle cream and PDT | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 100 | 53 | | |
| Units: Subjects | 65 | 26 | | |

## Statistical analyses

No statistical analyses for this end point

## Other pre-specified: Erythema score of severe

| End point title | Erythema score of severe |
|---|---|

End point description:

Clinical assessment of facial erythema using a 4-point rating scale (ranging from 0= none to 3=severe) before and after each illumination.

| End point type | Other pre-specified |
|---|---|

End point timeframe:

Immediately after first treatment

| End point values | Visonac cream with PDT | Vehicle cream and PDT | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 100 | 53 | | |
| Units: Subjects | 3 | 0 | | |

### Statistical analyses

No statistical analyses for this end point

## Other pre-specified: Erythema score of severe

| End point title | Erythema score of severe |
|---|---|

End point description:

Clinical assessment of facial erythema using a 4-point rating scale (ranging from 0= none to 3=severe) before and after each illumination.

| End point type | Other pre-specified |
|---|---|

End point timeframe:

2 days after first treatment

| End point values | Visonac cream with PDT | Vehicle cream and PDT | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 100 | 53 | | |
| Units: Subjects | 0 | 0 | | |

### Statistical analyses

No statistical analyses for this end point

## Other pre-specified: Change in facial scarring

| End point title | Change in facial scarring |
|---|---|

End point description:

Clinical assessment using a 6 point scale; clear, almost clear, mild, moderate, severe, very severe.

Patients who experienced a worsening of facial scarring score between Baseline and Week 12 with Visonac PDT compared with Vehicle PDT.

| End point type | Other pre-specified |
|---|---|

End point timeframe:

Change from baseline to week 12 after first treatment

| **End point values** | Visonac cream with PDT | Vehicle cream and PDT | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 91 | 46 | | |
| Units: Subjects | 19 | 5 | | |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

| Adverse events information | |
|---|---|
| Timeframe for reporting adverse events: | |
| From administration of investigational medicinal product (IMP) until 12 weeks after first IMP administration. | |
| Assessment type | Systematic |

| Dictionary used | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 12.1 |

| Reporting groups | |
|---|---|
| Reporting group title | Visonac cream with PDT |
| Reporting group description: | |
| Visonac (MAL cream 80 mg/g), applied 1.5 hours under occlusion, before illumination with red ligth | |
| Reporting group title | Vehicle cream with PDT |
| Reporting group description: | |
| Vehicle cream, applied 1.5 hours under occlusion, before illumination with red light | |

| Serious adverse events | Visonac cream with PDT | Vehicle cream with PDT | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 53 (0.00%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | 0 | 0 | |

Frequency threshold for reporting non-serious adverse events: 1 %

| Non-serious adverse events | Visonac cream with PDT | Vehicle cream with PDT | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 48 / 100 (48.00%) | 14 / 53 (26.42%) | |
| Injury, poisoning and procedural complications | | | |
| Joint sprain | | | |
| subjects affected / exposed | 2 / 100 (2.00%) | 0 / 53 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Concussion | | | |
| subjects affected / exposed | 1 / 100 (1.00%) | 1 / 53 (1.89%) | |
| occurrences (all) | 1 | 1 | |
| Nervous system disorders | | | |

| | | | |
|---|---|---|---|
| Headache | | | |
| subjects affected / exposed | 3 / 100 (3.00%) | 3 / 53 (5.66%) | |
| occurrences (all) | 3 | 3 | |
| General disorders and administration site conditions | | | |
| Pyrexia | | | |
| subjects affected / exposed | 2 / 100 (2.00%) | 0 / 53 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Gastrointestinal disorders | | | |
| Nausea | | | |
| subjects affected / exposed | 3 / 100 (3.00%) | 0 / 53 (0.00%) | |
| occurrences (all) | 3 | 0 | |
| Vomiting | | | |
| subjects affected / exposed | 2 / 100 (2.00%) | 0 / 53 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Nasal congestion | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 2 / 53 (3.77%) | |
| occurrences (all) | 0 | 2 | |
| Cough | | | |
| subjects affected / exposed | 1 / 100 (1.00%) | 1 / 53 (1.89%) | |
| occurrences (all) | 1 | 1 | |
| Skin and subcutaneous tissue disorders | | | |
| Pain of skin | | | |
| subjects affected / exposed | 17 / 100 (17.00%) | 0 / 53 (0.00%) | |
| occurrences (all) | 32 | 0 | |
| Skin burning sensation | | | |
| subjects affected / exposed | 15 / 100 (15.00%) | 0 / 53 (0.00%) | |
| occurrences (all) | 22 | 0 | |
| Pruritus | | | |
| subjects affected / exposed | 8 / 100 (8.00%) | 1 / 53 (1.89%) | |
| occurrences (all) | 18 | 1 | |
| Erythema | | | |
| subjects affected / exposed | 4 / 100 (4.00%) | 0 / 53 (0.00%) | |
| occurrences (all) | 4 | 0 | |
| Rash | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 2 / 100 (2.00%) | 1 / 53 (1.89%) | |
| occurrences (all) | 2 | 1 | |
| Scab | | | |
| subjects affected / exposed | 2 / 100 (2.00%) | 0 / 53 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Skin hyperpigmentation | | | |
| subjects affected / exposed | 2 / 100 (2.00%) | 0 / 53 (0.00%) | |
| occurrences (all) | 3 | 0 | |
| Swelling face | | | |
| subjects affected / exposed | 1 / 100 (1.00%) | 1 / 53 (1.89%) | |
| occurrences (all) | 1 | 1 | |
| Dermatitis | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 1 / 53 (1.89%) | |
| occurrences (all) | 0 | 1 | |
| Skin mass | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 1 / 53 (1.89%) | |
| occurrences (all) | 0 | 2 | |
| Musculoskeletal and connective tissue disorders | | | |
| Back pain | | | |
| subjects affected / exposed | 2 / 100 (2.00%) | 0 / 53 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Infections and infestations | | | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 3 / 100 (3.00%) | 0 / 53 (0.00%) | |
| occurrences (all) | 3 | 0 | |
| Gastroenteritis | | | |
| subjects affected / exposed | 2 / 100 (2.00%) | 0 / 53 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 2 / 100 (2.00%) | 0 / 53 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Staphylococcal infection | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 1 / 53 (1.89%) | |
| occurrences (all) | 0 | 1 | |
| Tooth abscess | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 100 (0.00%) | 1 / 53 (1.89%) | |
| occurrences (all) | 0 | 1 | |
| Conjunctivitis bacterial | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 1 / 53 (1.89%) | |
| occurrences (all) | 0 | 1 | |

## 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

### Online references

http://www.ncbi.nlm.nih.gov/pubmed/26663215