



## 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
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#### 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)	EMA-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:

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**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:

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**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:

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**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:

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**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
<b>Arm title</b>	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

<b>Arm title</b>	Vehicle cream and PDT
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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

<b>Number of subjects in period 1</b>	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
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Reporting group description:

Test product and red light illumination

Reporting group title	Vehicle cream and PDT
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Reporting group description:

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 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 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:	
Test product and red light illumination	
Reporting group title	Vehicle cream and PDT
Reporting group description:	
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:	
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:	
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 <sup>[1]</sup>
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
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End point description:

End point type	Secondary
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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
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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 <sup>[2]</sup>
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
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End point description:

End point type	Secondary
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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**

<b>Statistical analysis title</b>	Percent change in facial non-inflam. lesion counts
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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 <sup>[3]</sup>
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.
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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

<b>Statistical analysis title</b>	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:
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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
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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
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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
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End point description:

End point type	Secondary
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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 <sup>[4]</sup>
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
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End point description:

End point type	Secondary
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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
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End point description:

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

End point type	Other pre-specified
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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
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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
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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
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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
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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
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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
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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
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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
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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
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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
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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
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	12.1
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### Reporting groups

Reporting group title	Visonac cream with PDT
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Reporting group description:

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

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

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

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported

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### Online references

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