Clinical trial results:
LEO 90100 aerosol foam compared to calcipotriol plus betamethasone dipropionate gel in subjects with psoriasis vulgaris

Due to the EudraCT – Results system being out of service between 31 July 2015 and 12 January 2016, these results have been published in compliance with revised timelines.

Summary

EudraCT number	2013-004686-14
Trial protocol	FR
Global end of trial date	04 March 2015

Results information

Result version number	v1 (current)
This version publication date	17 July 2016
First version publication date	17 July 2016

Trial information

Trial identification

Sponsor protocol code	LP0053-1003

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02132936
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	LEO Pharma A/S
Sponsor organisation address	Industriparken 55, Ballerup, Denmark, 2750
Public contact	Clinical Trial Disclosure Manager, LEO Pharma A/S, 45 44945888, ctr.disclosure@leo-pharma.com
Scientific contact	Clinical Trial Disclosure Manager, LEO Pharma A/S, 45 44945888, ctr.disclosure@leo-pharma.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	11 September 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	04 March 2015
Global end of trial reached?	Yes
Global end of trial date	04 March 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To compare the efficacy of treatment with LEO 90100 at Week 4 to that of calcipotriol plus betamethasone dipropionate (BDP) gel at Week 8 in subjects with psoriasis vulgaris

Protection of trial subjects:

NA

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	30 June 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	United Kingdom: 173
Country: Number of subjects enrolled	France: 122
Country: Number of subjects enrolled	United States: 168
Worldwide total number of subjects	463
EEA total number of subjects	295

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)	0
Adults (18-64 years)	341
From 65 to 84 years	121
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

The first subject was enrolled on 30-Jun-2014 and the last subject completed the trial (last visit, including followup) on 04-Mar-2015.

Pre-assignment

Screening details:

504 subjects from 41 centres in the UK (15 centres), the US (15 centres) and France (11 centres) were enrolled into the trial.
41 enrolled subjects were not randomised due to the following reasons: screening failures (29 subjects); AE (1); protocol deviation (1); lost to follow-up (2); withdrawal by subject (3); other reasons (5).

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Single blind
Roles blinded	Investigator[1]

Blinding implementation details:

The trial was investigator-blinded. As 2 of the treatments were in an aerosol foam formulation and 2 were in a gel formulation, the subjects knew if they received aerosol foam or gel but did not know if they received active treatment or vehicle. Furthermore, the trial medication was handed out to the subjects by a designated person (a study coordinator) so the investigator did not know which IP the subject received.

Arms

Are arms mutually exclusive?	Yes
Arm title	LEO 90100 aerosol foam

Arm description:

Calcipotriol (as hydrate) 50 mcg/g and betamethasone 0.5 mg/g (as dipropionate), 60 g per can

Arm type	Experimental
Investigational medicinal product name	LEO 90100
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cutaneous foam
Routes of administration	Topical use

Dosage and administration details:

The investigational product (IP) was applied to psoriasis vulgaris affected areas on the trunk, arms and legs once daily for up to 12 weeks.

Arm title	Aerosol Foam Vehicle

Arm description:

Aerosol foam vehicle, 60 g per can

Arm type	Placebo
Investigational medicinal product name	Aerosol foam vehicle
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cutaneous foam
Routes of administration	Topical use

Dosage and administration details:

The IP was applied to psoriasis vulgaris affected areas on the trunk, arms and legs once daily for up to 12 weeks.

Arm title	Calcipotriol BDP Gel

Arm description:

Calcipotriol BDP gel, containing calcipotriol (as hydrate) 50 mcg/g and betamethasone 0.5 mg/g (as dipropionate), 60 g per bottle

Arm type	Active comparator
Investigational medicinal product name	Calcipotriol BDP Gel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Gel
Routes of administration	Topical use

Dosage and administration details:

The IP was applied to psoriasis vulgaris affected areas on the trunk, arms and legs once daily for up to 12 weeks.

Arm title	Gel Vehicle

Arm description:

Gel vehicle, 60 g per bottle

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

Dosage and administration details:

The IP was applied to psoriasis vulgaris affected areas on the trunk, arms and legs once daily for up to 12 weeks.

Notes:

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

Justification: The trial was investigator-blinded to ensure unbiased efficacy assessment.
Subjects knew if they were treated with a foam or gel formulation but did not know if they received active treatment or vehicle.

Number of subjects in period 1	LEO 90100 aerosol foam	Aerosol Foam Vehicle	Calcipotriol BDP Gel
Started	185	47	188
Completed	175	38	174
Not completed	10	9	14
Consent withdrawn by subject	2	1	-
Subject withdrew consent	-	-	2
Adverse event, non-fatal	3	1	3
Lost to follow-up	2	2	5
Lack of efficacy	1	5	4
Protocol deviation	2	-	-

Number of subjects in period 1	Gel Vehicle
Started	43
Completed	29
Not completed	14
Consent withdrawn by subject	4
Subject withdrew consent	-
Adverse event, non-fatal	-

Lost to follow-up	1
Lack of efficacy	9
Protocol deviation	-

Baseline characteristics

Reporting groups	
Reporting group title	LEO 90100 aerosol foam
Reporting group description:	
Calcipotriol (as hydrate) 50 mcg/g and betamethasone 0.5 mg/g (as dipropionate), 60 g per can	
Reporting group title	Aerosol Foam Vehicle
Reporting group description:	
Aerosol foam vehicle, 60 g per can	
Reporting group title	Calcipotriol BDP Gel
Reporting group description:	
Calcipotriol BDP gel, containing calcipotriol (as hydrate) 50 mcg/g and betamethasone 0.5 mg/g (as dipropionate), 60 g per bottle	
Reporting group title	Gel Vehicle
Reporting group description:	
Gel vehicle, 60 g per bottle	

Reporting group values	LEO 90100 aerosol foam	Aerosol Foam Vehicle	Calcipotriol BDP Gel
Number of subjects	185	47	188
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)	0	0	0
Adults (18-64 years)	137	37	134
From 65-84 years	48	10	53
85 years and over	0	0	1
Gender categorical Units: Subjects			
Female	59	18	74
Male	126	29	114

Reporting group values	Gel Vehicle	Total	
Number of subjects	43	463	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	33	341	

From 65-84 years	10	121	
85 years and over	0	1	

Gender categorical Units: Subjects			
Female	17	168	
Male	26	295	

End points

End points reporting groups

Reporting group title	LEO 90100 aerosol foam
Reporting group description:	
Calcipotriol (as hydrate) 50 mcg/g and betamethasone 0.5 mg/g (as dipropionate), 60 g per can	
Reporting group title	Aerosol Foam Vehicle
Reporting group description:	
Aerosol foam vehicle, 60 g per can	
Reporting group title	Calcipotriol BDP Gel
Reporting group description:	
Calcipotriol BDP gel, containing calcipotriol (as hydrate) 50 mcg/g and betamethasone 0.5 mg/g (as dipropionate), 60 g per bottle	
Reporting group title	Gel Vehicle
Reporting group description:	
Gel vehicle, 60 g per bottle	

Primary: Treatment Success According to the PGA

End point title	Treatment Success According to the PGA[1]
End point description:	
To compare the efficacy of treatment of LEO 90100 at Week 4 to that of calcipotriol BDP gel at Week 8 in subjects with psoriasis vulgaris. The severity of psoriasis vulgaris on the trunk and limbs was assessed using the Physician's Global Assessment of disease severity (PGA). A five-point scale (clear, almost clear, mild, moderate, and severe) was used. 'Treatment success' was defined as achieving 'clear' or 'almost clear' for subjects with at least 'moderate' disease at baseline and 'clear' for subjects with 'mild' disease at baseline.	
End point type	Primary
End point timeframe:	
Week 4 for LEO 90100 and Week 8 for calcipotriol BDP gel	

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The statistical analysis of the primary endpoint was planned and performed to compare the 2 active treatments.

End point values	LEO 90100 aerosol foam	Calcipotriol BDP Gel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	185	188		
Units: Percentage of subjects				
number (not applicable)	38.3	22.5		

Statistical analyses

Statistical analysis title	Treatment Success According to the PGA
Statistical analysis description:	
Mantel-Haenszel odds of treatment success in LEO 90100 group relative to calcipotriol BDP gel group, adjusted for pooled centre and baseline PGA. Multiple imputation was used to handle missing PGA values.	

Comparison groups	LEO 90100 aerosol foam v Calcipotriol BDP Gel
Number of subjects included in analysis	373
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	2.55
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.46
upper limit	4.46

Secondary: Subjects With PASI 75 at Week 4 for LEO 90100 and at Week 8 for Calcipotriol BDP Gel

End point title	Subjects With PASI 75 at Week 4 for LEO 90100 and at Week 8 for Calcipotriol BDP Gel[2]

End point description:

Subjects with PASI 75 (a 75% reduction in the modified Psoriasis Area and Severity Index) at Week 4 for LEO 90100 and at Week 8 for calcipotriol BDP gel.

End point type	Secondary

End point timeframe:

Week 4 for LEO 90100 and Week 8 for calcipotriol BDP gel

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The statistical analysis of this secondary endpoint was planned and performed for the 2 active treatments.

End point values	LEO 90100 aerosol foam	Calcipotriol BDP Gel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	185	188		
Units: Percentage of subjects				
number (not applicable)	52.1	34.6		

Statistical analyses

Statistical analysis title	Subjects With PASI 75

Statistical analysis description:

Mantel-Haenszel odds of having PASI 75 in LEO 90100 group relative to calcipotriol BDP gel group, adjusted for pooled centre and baseline PGA.
Multiple imputation was used to handle missing data.

Comparison groups	LEO 90100 aerosol foam v Calcipotriol BDP Gel

Number of subjects included in analysis	373
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.001
Method	Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	2.18
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.37
upper limit	3.47

Secondary: Time to 'Treatment Success' According to PGA.

End point title	Time to 'Treatment Success' According to PGA.[3]

End point description:

Definition for 'treatment success' is given under the primary endpoint.
Time to treatment success was calculated as the number of weeks from baseline to the visit where the subject first achieved treatment success.

LEO 90100 (n=185)
Time to treatment success (median): 6 weeks
Lower quartile: 4
Upper quartile: NA (could not be estimated as less than 75% of subjects achieved treatment success)

Calcipotriol BDP gel (n=188)
Time to treatment success (median): NA (could not be estimated for the group as less than 50% of subjects achieved treatment success)
Lower quartile: 6
Upper quartile: NA (could not be estimated as less than 75% of subjects achieved treatment success)

In the table below, measure type is set to 'number' instead of 'median', and precision type is set to 'not applicable' instead of 'inter-quartile range', as the database does not accept NA values for intra-quartile range to a median number.

End point type	Secondary

End point timeframe:

Baseline to Week 12

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The statistical analysis of this secondary endpoint was planned and performed for the 2 active treatments.

End point values	LEO 90100 aerosol foam	Calcipotriol BDP Gel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	185	188		
Units: Weeks				
number (not applicable)	6	0		

Statistical analyses

Statistical analysis title	Time to 'Treatment Success' According to PGA.
Comparison groups	Calcipotriol BDP Gel v LEO 90100 aerosol foam
Number of subjects included in analysis	373
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.97
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.46
upper limit	2.65

Secondary: Change in Itch as Assessed on a VAS Scale (LEO 90100 vs. the Foam Vehicle Group)

End point title	Change in Itch as Assessed on a VAS Scale (LEO 90100 vs. the Foam Vehicle Group)[4]

End point description:

Maximum itch during the previous 24 hours was assessed on a Visual Analogue Scale (VAS) - range from 0 (no itch at all) to 100 mm (worst itch one could imagine).

End point type	Secondary

End point timeframe:

Baseline to Week 4

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The statistical analysis of this secondary endpoint was planned and performed to compare LEO 90100 with its vehicle.

End point values	LEO 90100 aerosol foam	Aerosol Foam Vehicle		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	185	47		
Units: Units on a scale				
arithmetic mean (confidence interval 95%)	-30.5 (-33.4 to -27.5)	-15.9 (-21.3 to 10.5)		

Statistical analyses

Statistical analysis title	Change in Itch (LEO 90100 vs. the Foam Vehicle)
Comparison groups	LEO 90100 aerosol foam v Aerosol Foam Vehicle

Number of subjects included in analysis	232
Analysis specification	Pre-specified
Analysis type	superiority[5]
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-14.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-20.64
upper limit	-8.55

Notes:

[5] - Mean change in itch adjusted for pooled centre, baseline PGA and baseline itch. Multiple imputation used for missing data.

Secondary: Change in Itch as Assessed on a VAS Scale From Baseline to Week 4 (LEO 90100) vs. Week 8 (Calcipotriol BDP Gel).

End point title	Change in Itch as Assessed on a VAS Scale From Baseline to Week 4 (LEO 90100) vs. Week 8 (Calcipotriol BDP Gel).[6]

End point description:

Maximum itch during the previous 24 hours was assessed on a Visual Analogue Scale - range from 0 (no itch at all) to 100 mm (worst itch one could imagine).

End point type	Secondary

End point timeframe:

Baseline to Week 4 for LEO 90100 and Baseline to Week 8 for calcipotriol BDP gel

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The statistical analysis of this secondary endpoint was planned and performed for the 2 active treatments.

End point values	LEO 90100 aerosol foam	Calcipotriol BDP Gel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	185	188		
Units: Units on a scale				
arithmetic mean (confidence interval 95%)	-30.5 (-33.4 to -27.5)	-28.5 (-31.4 to -25.6)		

Statistical analyses

Statistical analysis title	Change in Itch (LEO 90100 vs. Calcipotriol BDP Ge)

Statistical analysis description:

Mean change in itch adjusted for pooled centre, baseline PGA and baseline itch. Multiple imputation used for missing data.

Comparison groups	LEO 90100 aerosol foam v Calcipotriol BDP Gel

Number of subjects included in analysis	373
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.33
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-1.93
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.78
upper limit	1.93

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Day 0 until week 12	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	15.1

Reporting groups	
Reporting group title	LEO 90100
Reporting group description: -	
Reporting group title	Aerosol Foam Vehicle
Reporting group description: -	
Reporting group title	Calcipotriol BDP Gel
Reporting group description: -	
Reporting group title	Gel Vehicle
Reporting group description: -	

Serious adverse events	LEO 90100	Aerosol Foam Vehicle	Calcipotriol BDP Gel
Total subjects affected by serious adverse events			
subjects affected / exposed	8 / 185 (4.32%)	0 / 47 (0.00%)	3 / 188 (1.60%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Prostate cancer			
subjects affected / exposed	1 / 185 (0.54%)	0 / 47 (0.00%)	0 / 188 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Post procedural haemorrhage			
subjects affected / exposed	0 / 185 (0.00%)	0 / 47 (0.00%)	1 / 188 (0.53%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Cardiac failure congestive			

subjects affected / exposed	1 / 185 (0.54%)	0 / 47 (0.00%)	0 / 188 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Ischaemic stroke			
subjects affected / exposed	0 / 185 (0.00%)	0 / 47 (0.00%)	1 / 188 (0.53%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 185 (0.54%)	0 / 47 (0.00%)	0 / 188 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	0 / 185 (0.00%)	0 / 47 (0.00%)	0 / 188 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Psoriasis			
subjects affected / exposed	1 / 185 (0.54%)	0 / 47 (0.00%)	0 / 188 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Type 2 diabetes mellitus			
subjects affected / exposed	0 / 185 (0.00%)	0 / 47 (0.00%)	1 / 188 (0.53%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Gel Vehicle		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 43 (2.33%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			

Prostate cancer			
subjects affected / exposed	0 / 43 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Post procedural haemorrhage			
subjects affected / exposed	0 / 43 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Cardiac failure congestive			
subjects affected / exposed	0 / 43 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Ischaemic stroke			
subjects affected / exposed	0 / 43 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 43 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	1 / 43 (2.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Psoriasis			
subjects affected / exposed	0 / 43 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			

Type 2 diabetes mellitus			
subjects affected / exposed	0 / 43 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 2 %

Non-serious adverse events	LEO 90100	Aerosol Foam Vehicle	Calcipotriol BDP Gel
Total subjects affected by non-serious adverse events			
subjects affected / exposed	77 / 185 (41.62%)	25 / 47 (53.19%)	60 / 188 (31.91%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Colon adenoma			
subjects affected / exposed	0 / 185 (0.00%)	0 / 47 (0.00%)	0 / 188 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Haematoma			
subjects affected / exposed	0 / 185 (0.00%)	0 / 47 (0.00%)	0 / 188 (0.00%)
occurrences (all)	0	0	0
Hypertension			
subjects affected / exposed	2 / 185 (1.08%)	0 / 47 (0.00%)	7 / 188 (3.72%)
occurrences (all)	2	0	7
General disorders and administration site conditions			
Application site pain			
subjects affected / exposed	0 / 185 (0.00%)	1 / 47 (2.13%)	0 / 188 (0.00%)
occurrences (all)	0	1	0
Application site pruritus			
subjects affected / exposed	1 / 185 (0.54%)	2 / 47 (4.26%)	1 / 188 (0.53%)
occurrences (all)	1	2	1
Feeling cold			
subjects affected / exposed	0 / 185 (0.00%)	1 / 47 (2.13%)	0 / 188 (0.00%)
occurrences (all)	0	1	0
Influenza like illness			
subjects affected / exposed	3 / 185 (1.62%)	0 / 47 (0.00%)	2 / 188 (1.06%)
occurrences (all)	3	0	2
Respiratory, thoracic and mediastinal disorders			

Cough			
subjects affected / exposed	1 / 185 (0.54%)	1 / 47 (2.13%)	2 / 188 (1.06%)
occurrences (all)	1	1	2
Nasal congestion			
subjects affected / exposed	0 / 185 (0.00%)	1 / 47 (2.13%)	0 / 188 (0.00%)
occurrences (all)	0	1	0
Pulmonary congestion			
subjects affected / exposed	0 / 185 (0.00%)	1 / 47 (2.13%)	0 / 188 (0.00%)
occurrences (all)	0	1	0
Sinus congestion			
subjects affected / exposed	0 / 185 (0.00%)	1 / 47 (2.13%)	0 / 188 (0.00%)
occurrences (all)	0	1	0
Investigations			
Vitamin D decreased			
subjects affected / exposed	2 / 185 (1.08%)	1 / 47 (2.13%)	3 / 188 (1.60%)
occurrences (all)	2	1	3
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 185 (0.00%)	0 / 47 (0.00%)	1 / 188 (0.53%)
occurrences (all)	0	0	1
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 185 (0.00%)	1 / 47 (2.13%)	0 / 188 (0.00%)
occurrences (all)	0	1	0
Atrial fibrillation			
subjects affected / exposed	0 / 185 (0.00%)	0 / 47 (0.00%)	0 / 188 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	2 / 185 (1.08%)	2 / 47 (4.26%)	1 / 188 (0.53%)
occurrences (all)	2	2	1
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	0 / 185 (0.00%)	0 / 47 (0.00%)	0 / 188 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			

subjects affected / exposed	4 / 185 (2.16%)	0 / 47 (0.00%)	2 / 188 (1.06%)
occurrences (all)	4	0	2
Gastrooesophageal reflux disease			
subjects affected / exposed	2 / 185 (1.08%)	1 / 47 (2.13%)	1 / 188 (0.53%)
occurrences (all)	2	1	1
Nausea			
subjects affected / exposed	2 / 185 (1.08%)	0 / 47 (0.00%)	2 / 188 (1.06%)
occurrences (all)	2	0	2
Gastroentirits			
subjects affected / exposed	1 / 185 (0.54%)	1 / 47 (2.13%)	1 / 188 (0.53%)
occurrences (all)	1	1	1
Skin and subcutaneous tissue disorders			
Blister			
subjects affected / exposed	1 / 185 (0.54%)	1 / 47 (2.13%)	0 / 188 (0.00%)
occurrences (all)	1	1	0
Dermatitis contact			
subjects affected / exposed	0 / 185 (0.00%)	1 / 47 (2.13%)	0 / 188 (0.00%)
occurrences (all)	0	1	0
Dry skin			
subjects affected / exposed	1 / 185 (0.54%)	1 / 47 (2.13%)	0 / 188 (0.00%)
occurrences (all)	1	1	0
Erythema			
subjects affected / exposed	1 / 185 (0.54%)	1 / 47 (2.13%)	0 / 188 (0.00%)
occurrences (all)	1	1	0
Pruritus			
subjects affected / exposed	5 / 185 (2.70%)	1 / 47 (2.13%)	2 / 188 (1.06%)
occurrences (all)	6	1	2
Psoriasis			
subjects affected / exposed	4 / 185 (2.16%)	1 / 47 (2.13%)	7 / 188 (3.72%)
occurrences (all)	4	1	8
Renal and urinary disorders			
Renal failure chronic			
subjects affected / exposed	0 / 185 (0.00%)	1 / 47 (2.13%)	1 / 188 (0.53%)
occurrences (all)	0	1	1
Musculoskeletal and connective tissue disorders			

Back pain			
subjects affected / exposed	5 / 185 (2.70%)	1 / 47 (2.13%)	3 / 188 (1.60%)
occurrences (all)	5	1	3
Joint swelling			
subjects affected / exposed	0 / 185 (0.00%)	0 / 47 (0.00%)	1 / 188 (0.53%)
occurrences (all)	0	0	1
Infections and infestations			
Cellulitis			
subjects affected / exposed	0 / 185 (0.00%)	0 / 47 (0.00%)	0 / 188 (0.00%)
occurrences (all)	0	0	0
Intertrigo candida			
subjects affected / exposed	0 / 185 (0.00%)	1 / 47 (2.13%)	0 / 188 (0.00%)
occurrences (all)	0	1	0
Lower respiratory tract infection			
subjects affected / exposed	4 / 185 (2.16%)	0 / 47 (0.00%)	1 / 188 (0.53%)
occurrences (all)	4	0	1
Nail infection			
subjects affected / exposed	0 / 185 (0.00%)	0 / 47 (0.00%)	0 / 188 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	7 / 185 (3.78%)	0 / 47 (0.00%)	4 / 188 (2.13%)
occurrences (all)	7	0	4
Sinusitis			
subjects affected / exposed	2 / 185 (1.08%)	0 / 47 (0.00%)	3 / 188 (1.60%)
occurrences (all)	2	0	3
Tooth abscess			
subjects affected / exposed	1 / 185 (0.54%)	1 / 47 (2.13%)	1 / 188 (0.53%)
occurrences (all)	1	1	1
Upper respiratory tract infection			
subjects affected / exposed	5 / 185 (2.70%)	1 / 47 (2.13%)	9 / 188 (4.79%)
occurrences (all)	6	1	9
Metabolism and nutrition disorders			
Vitamin D deficiency			
subjects affected / exposed	6 / 185 (3.24%)	0 / 47 (0.00%)	5 / 188 (2.66%)
occurrences (all)	6	0	5

Non-serious adverse events	Gel Vehicle		

Total subjects affected by non-serious adverse events subjects affected / exposed	28 / 43 (65.12%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps) Colon adenoma subjects affected / exposed occurrences (all)	1 / 43 (2.33%) 1		
Vascular disorders Haematoma subjects affected / exposed occurrences (all) Hypertension subjects affected / exposed occurrences (all)	 1 / 43 (2.33%) 1 0 / 43 (0.00%) 0		
General disorders and administration site conditions Application site pain subjects affected / exposed occurrences (all) Application site pruritus subjects affected / exposed occurrences (all) Feeling cold subjects affected / exposed occurrences (all) Influenza like illness subjects affected / exposed occurrences (all)	 1 / 43 (2.33%) 1 1 / 43 (2.33%) 1 0 / 43 (0.00%) 0 1 / 43 (2.33%) 1		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) Nasal congestion subjects affected / exposed occurrences (all) Pulmonary congestion subjects affected / exposed occurrences (all)	 1 / 43 (2.33%) 1 0 / 43 (0.00%) 0 0 / 43 (0.00%) 0		

Sinus congestion subjects affected / exposed occurrences (all)	0 / 43 (0.00%) 0		
Investigations Vitamin D decreased subjects affected / exposed occurrences (all)	1 / 43 (2.33%) 1		
Injury, poisoning and procedural complications Fall subjects affected / exposed occurrences (all)	1 / 43 (2.33%) 1		
Cardiac disorders Angina pectoris subjects affected / exposed occurrences (all) Atrial fibrillation subjects affected / exposed occurrences (all)	0 / 43 (0.00%) 0 1 / 43 (2.33%) 1		
Nervous system disorders Headache subjects affected / exposed occurrences (all)	1 / 43 (2.33%) 1		
Gastrointestinal disorders Abdominal pain upper subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all) Gastrooesophageal reflux disease subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all) Gastroentirits	1 / 43 (2.33%) 1 2 / 43 (4.65%) 2 0 / 43 (0.00%) 0 1 / 43 (2.33%) 1		

subjects affected / exposed	0 / 43 (0.00%)		
occurrences (all)	0		
Skin and subcutaneous tissue disorders			
Blister			
subjects affected / exposed	0 / 43 (0.00%)		
occurrences (all)	0		
Dermatitis contact			
subjects affected / exposed	0 / 43 (0.00%)		
occurrences (all)	0		
Dry skin			
subjects affected / exposed	0 / 43 (0.00%)		
occurrences (all)	0		
Erythema			
subjects affected / exposed	0 / 43 (0.00%)		
occurrences (all)	0		
Pruritus			
subjects affected / exposed	0 / 43 (0.00%)		
occurrences (all)	0		
Psoriasis			
subjects affected / exposed	0 / 43 (0.00%)		
occurrences (all)	0		
Renal and urinary disorders			
Renal failure chronic			
subjects affected / exposed	0 / 43 (0.00%)		
occurrences (all)	0		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	2 / 43 (4.65%)		
occurrences (all)	2		
Joint swelling			
subjects affected / exposed	1 / 43 (2.33%)		
occurrences (all)	1		
Infections and infestations			
Cellulitis			
subjects affected / exposed	1 / 43 (2.33%)		
occurrences (all)	1		

Intertrigo candida subjects affected / exposed occurrences (all)	0 / 43 (0.00%) 0		
Lower respiratory tract infection subjects affected / exposed occurrences (all)	1 / 43 (2.33%) 1		
Nail infection subjects affected / exposed occurrences (all)	1 / 43 (2.33%) 1		
Nasopharyngitis subjects affected / exposed occurrences (all)	2 / 43 (4.65%) 2		
Sinusitis subjects affected / exposed occurrences (all)	1 / 43 (2.33%) 1		
Tooth abscess subjects affected / exposed occurrences (all)	1 / 43 (2.33%) 1		
Upper respiratory tract infection subjects affected / exposed occurrences (all)	2 / 43 (4.65%) 2		
Metabolism and nutrition disorders Vitamin D deficiency subjects affected / exposed occurrences (all)	2 / 43 (4.65%) 2		

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

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

NA

Notes: