Clinical trial results:
A Phase 2a, proof of concept trial, testing twice daily application of LEO 124249 ointment 30mg/g in the treatment of mild to moderate inverse psoriasis

Summary

EudraCT number	2015-002098-40
Trial protocol	DE
Global end of trial date	20 September 2016

Results information

Result version number	v1 (current)
This version publication date	14 October 2017
First version publication date	14 October 2017

Trial information

Trial identification

Sponsor protocol code	LP0133-1182

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02695940
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, disclosure@leo-pharma.com
Scientific contact	Clinical Trial Disclosure Manager, LEO Pharma A/S, +45 44945888, 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	20 September 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	20 September 2016
Global end of trial reached?	Yes
Global end of trial date	20 September 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To compare the efficacy of twice daily application of LEO 124249 ointment 30 mg/g and LEO 124249 ointment vehicle for 6 weeks in the treatment of subjects with mild to moderate inverse psoriasis.

Protection of trial subjects:

The clinical trial was conducted to conform to the principles of the Declaration of Helsinki as adopted by the 18th World Medical Association General Assembly, 1964, and subsequent amendments. All subjects received written and verbal information concerning the clinical trial. This information emphasised that participation in the clinical trial was voluntary and that the subject could withdraw from the clinical trial at any time and for any reason. All subjects were given an opportunity to ask questions and were given sufficient time to consider before consenting.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	22 February 2016
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: 69
Worldwide total number of subjects	69
EEA total number of subjects	69

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)	69
From 65 to 84 years	0

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

110 subjects from 11 sites in Germany were screened into the trial. The first subject was enrolled on 11-Mar-2016, and the last subject completed the trial on 20-Sep-2016

Pre-assignment

Screening details:

Screening assessment occurred up to 28 days prior to baseline. 41 out of 110 subjects were not randomised due to the following reasons: screening failure (33 subjects), recruitment stop due to over recruitment (7 subjects), and voluntary withdrawal of consent by the subject prior to randomisation (1 subject). 69 subjects were randomised.

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	Investigator, Subject

Arms

Are arms mutually exclusive?	Yes
Arm title	LEO 124249 30mg/g

Arm description: -

Arm type	Experimental
Investigational medicinal product name	LEO 124249 30mg/g
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Ointment
Routes of administration	Topical use

Dosage and administration details:

A thin layer covering the affected area corresponding to 1.0mg/cm2 of LEO 124249 ointment 30mg/g was to be applied twice daily. Depending on the size of the affected areas, a maximum of 4% BSA or 720cm2 could be treated, corresponding to a maximum of 720mg ointment per application. IMP had to be applied morning and evening (approximately 12 hours apart, minimum 8 hours apart) with the exception of Day 1 (start of treatment), where 2 doses were to be administered regardless of timing; one at the site visit, and one administered by the subject at home in the evening.

Arm title	Vehicle

Arm description: -

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

Dosage and administration details:

A thin layer covering the affected area corresponding to 1.0mg/cm2 of LEO 124249 ointment vehicle was to be applied twice daily.
Depending on the size of the affected areas, a maximum of 4% BSA or 720cm2 could be treated, corresponding to a maximum of 720mg ointment per application. IMP had to be applied morning and evening (approximately 12 hours apart, minimum 8 hours apart) with the exception of Day 1 (start of treatment), where 2 doses were to be administered regardless of timing; one at the site visit, and one administered by the subject at home in the evening.

Number of subjects in period 1	LEO 124249 30mg/g	Vehicle
Started	45	24
Completed	39	21
Not completed	6	3
Consent withdrawn by subject	3	2
Adverse event, non-fatal	1	1
Lack of efficacy	2	-

Baseline characteristics

Reporting groups

Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	69	69	
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)	69	69	
From 65-84 years	0	0	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	27	27	
Male	42	42	

End points

End points reporting groups

Reporting group title	LEO 124249 30mg/g
Reporting group description: -	
Reporting group title	Vehicle
Reporting group description: -	

Primary: The total sign score (TSS) at end of treatment (Week 6)

End point title	The total sign score (TSS) at end of treatment (Week 6)

End point description:

The severity of the inverse psoriasis was recorded for each clinical sign redness, thickness and scaliness. For each sign, a single score reflecting the average severity of all inverse psoriasis lesions were determined according to the scale below of 0 to 4.
1) Redness '0 -4' denoted none to very severe erythema, very dark red erythema
2) Thickness '0-4' denoted none, no plaque elevation to very severe, very thick plaque with sharp edge and
3) Scaliness '0-4' denoted none, no scaling to very severe, very thick coarse scales, possibly fissured

End point type	Primary

End point timeframe:

From screening (28 days before baseline) to Week 6 (end of treatment). TSS was assessed at regular intervals including baseline, Week 1, Week 2, and Week 4.

End point values	LEO 124249 30mg/g	Vehicle		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	43	24		
Units: Scores on a scale				
arithmetic mean (confidence interval 95%)	4.1 (3.5 to 4.7)	4.2 (3.4 to 5)		

Statistical analyses

Statistical analysis title	Total Sign Score at Week 6 (LOCF)

Statistical analysis description:

The comparison between treatment groups was done by means of an analysis of covariance (ANCOVA) model with treatment and pooled site as factors and baseline TSS as covariate.

Comparison groups	LEO 124249 30mg/g v Vehicle
Number of subjects included in analysis	67
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.89
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.7

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.09
upper limit	0.95

Secondary: For Physician's Global Assessment (PGA), the number of subjects achieving controlled disease

End point title	For Physician's Global Assessment (PGA), the number of subjects achieving controlled disease

End point description:

For Physician's global assessment (PGA), the number of subjects reaching controlled disease was defined as follows:
- Subjects classified as having at least 'moderate' disease at baseline who achieved 'clear' or 'almost clear' disease severity were considered to have controlled disease.
- Subjects classified at baseline as having 'mild' disease had to achieve 'clear' to be considered having controlled disease.

End point type	Secondary

End point timeframe:

From screening (28 days prior to baseline) to end of treatment (Week 6)

End point values	LEO 124249 30mg/g	Vehicle		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	43	24		
Units: Number of subjects				
Controlled disease	4	3		
Non-controlled disease	35	18		

Statistical analyses

Statistical analysis title	Controlled disease according to PGA at Week 6

Statistical analysis description:

The proportion of subjects with controlled disease according to Physician's Global Assessment at week 6 was compared between treatment groups using a Cochran-Mantel-Haenszel test adjusting for pooled site. Odds ratio, 95% CI and p-value presented.

Comparison groups	LEO 124249 30mg/g v Vehicle
Number of subjects included in analysis	67
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	0.57

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.12
upper limit	2.76

Secondary: Clinical sign score for redness for inverse psoriasis: (score 0 to 4)

End point title	Clinical sign score for redness for inverse psoriasis: (score 0 to 4)

End point description:

End point type	Secondary

End point timeframe:

From screening (28 days prior to baseline) to end of treatment (Week 6)

End point values	LEO 124249 30mg/g	Vehicle		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	43	24		
Units: Scores on a scale				
arithmetic mean (confidence interval 95%)	1.9 (1.6 to 2.1)	1.9 (1.6 to 2.2)		

Statistical analyses

Statistical analysis title	Redness at Week 6

Statistical analysis description:

Differences between treatment groups at end of treatment (Week 6) for redness was estimated using an ANCOVA model with treatment and pooled site as factors and baseline value as covariate.

Comparison groups	Vehicle v LEO 124249 30mg/g
Number of subjects included in analysis	67
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.91
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.44
upper limit	0.39

Secondary: Clinical sign score for thickness for inverse psoriasis: (score 0 to 4)	
End point title	Clinical sign score for thickness for inverse psoriasis: (score 0 to 4)

End point description:

End point type	Secondary

End point timeframe:

From screening (28 days prior to baseline) to end of treatment (Week 6)

End point values	LEO 124249 30mg/g	Vehicle		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	43	24		
Units: On a scale of scores				
arithmetic mean (confidence interval 95%)	1.2 (1 to 1.5)	1.3 (0.9 to 1.6)		

Statistical analyses

Statistical analysis title	Thickness at Week 6

Statistical analysis description:

Differences between treatment groups at end of treatment (Week 6) for thickness was estimated using an ANCOVA model with treatment and pooled site as factors and baseline value as covariate.

Comparison groups	LEO 124249 30mg/g v Vehicle
Number of subjects included in analysis	67
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.78
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.48
upper limit	0.36

Secondary: Clinical sign score for scaliness for inverse psoriasis: (score 0 to 4)	
End point title	Clinical sign score for scaliness for inverse psoriasis: (score 0 to 4)

End point description:

End point type	Secondary

End point timeframe:

From screening (28 days prior to baseline) to end of treatment (Week 6)

End point values	LEO 124249 30mg/g	Vehicle		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	43	24		
Units: Scores on a scale				
arithmetic mean (confidence interval 95%)	0.8 (0.6 to 1.1)	0.9 (0.5 to 1.2)		

Statistical analyses

Statistical analysis title	Scaliness at Week 6

Statistical analysis description:

Differences between treatment groups at end of treatment (Week 6) for scaliness was estimated using an ANCOVA model with treatment and pooled site as factors and baseline value as covariate.

Comparison groups	Vehicle v LEO 124249 30mg/g
Number of subjects included in analysis	67
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.77
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.47
upper limit	0.35

Secondary: Size of treatment area of inverse psoriasis

End point title	Size of treatment area of inverse psoriasis

End point description:

End point type	Secondary

End point timeframe:

From screening (28 days prior to baseline) to end of treatment (Week 6)

End point values	LEO 124249 30mg/g	Vehicle		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	43	24		
Units: score on a scale				
arithmetic mean (confidence interval 95%)	73.9 (60.1 to 87.7)	81.3 (62.4 to 100.2)		

Statistical analyses

Statistical analysis title	Size of treatment area of inverse psoriasis Week 6

Statistical analysis description:

Differences between treatment groups at end of treatment (Week 6) for the size of the treatment area was estimated using an ANCOVA model with treatment and pooled site as factors and baseline value as covariate.

Comparison groups	LEO 124249 30mg/g v Vehicle
Number of subjects included in analysis	67
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.53
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-7.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-31.03
upper limit	16.17

Secondary: For Patient's Global Assessment (PaGA), the number of subjects reaching controlled disease

End point title	For Patient's Global Assessment (PaGA), the number of subjects reaching controlled disease

End point description:

For Patient's global assessment (PaGA), the number of subjects reaching controlled disease defined as follows:

- Subjects classified as having at least ‘moderate’ disease at baseline who achieved ‘clear’ or ‘very mild’ disease severity were considered to have controlled disease.
- Subjects classified at baseline as having ‘mild’ disease had to achieve ‘clear’ to be considered having controlled disease.

End point type	Secondary

End point timeframe:

From baseline to end of treatment (Week 6)

End point values	LEO 124249 30mg/g	Vehicle		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	43	24		
Units: Number of subjects				
Controlled disease	5	1		
Non-controlled disease	34	20		

Statistical analyses

Statistical analysis title	Controlled disease according to PaGA Week 6

Statistical analysis description:

For PaGA, the proportion of subjects with controlled disease at end of treatment (Week 6) was compared between treatments using the Cochran-Mantel-Haenzel test adjusting for pooled site. The odds ratio (odds of controlled disease for LEO 124249 ointment 30mg/g relative to that of LEO 124249 ointment vehicle), CI for the odds ratio and the p-value presented.

Comparison groups	LEO 124249 30mg/g v Vehicle
Number of subjects included in analysis	67
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.43
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	2
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.33
upper limit	11.97

Secondary: Dermatology Life Quality Index (DLQI) questionnaire

End point title	Dermatology Life Quality Index (DLQI) questionnaire

End point description:

End point type	Secondary

End point timeframe:

From baseline to end of treatment (Week 6)

End point values	LEO 124249 30mg/g	Vehicle		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	43	24		
Units: Quality of life index score				
arithmetic mean (confidence interval 95%)	3.8 (2.9 to 4.7)	4.6 (3.3 to 5.8)		

Statistical analyses

Statistical analysis title	Total DLQI score at Week 6

Statistical analysis description:

Differences between treatments in DLQI score at end of treatment (Week 6) were analysed using an ANCOVA model with treatment and pooled site as factors and baseline value as covariate.

Comparison groups	LEO 124249 30mg/g v Vehicle
Number of subjects included in analysis	67
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.35
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.74
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.31
upper limit	0.83

Secondary: Treatment Satisfaction Questionnaire for Medication (TSQM II)

End point title	Treatment Satisfaction Questionnaire for Medication (TSQM II)

End point description:

End point type	Secondary

End point timeframe:

At end of treatment (Week 6)

End point values	LEO 124249 30mg/g	Vehicle		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	43	24		
Units: Score on a scale				
arithmetic mean (confidence interval 95%)				
Effectiveness	56.4 (47.2 to 65.5)	56.3 (44 to 68.6)		
Side effects	97.6 (95.2 to 99.9)	99.3 (96.2 to 102.5)		
Convenience	78.5 (72.5 to 84.4)	76 (67.8 to 84.2)		

Global satisfaction	65 (56.1 to 74)	52.2 (40 to 64.5)		

Statistical analyses

Statistical analysis title	TSQM derived scores at Week 6 - Effectiveness
Statistical analysis description:	
Differences in derived TSQM scores at end of treatment (Week 6) were analysed using an ANCOVA model with treatment and pooled site as factors.	
Comparison groups	LEO 124249 30mg/g v Vehicle
Number of subjects included in analysis	67
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.99
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	0.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	-15.4
upper limit	15.56

Statistical analysis title	TSQM derived scores at Week 6 - Side Effects
Statistical analysis description:	
Differences in derived TSQM scores at end of treatment (Week 6) were analysed using an ANCOVA model with treatment and pooled site as factors.	
Comparison groups	LEO 124249 30mg/g v Vehicle
Number of subjects included in analysis	67
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.37
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-1.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.7
upper limit	2.16

Statistical analysis title	TSQM derived scores at Week 6 - Convenience
Statistical analysis description:	
Differences in derived TSQM scores at end of treatment (Week 6) were analysed using an ANCOVA	

model with treatment and pooled site as factors.

Comparison groups	LEO 124249 30mg/g v Vehicle
Number of subjects included in analysis	67
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.63
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	2.48
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.74
upper limit	12.7

Statistical analysis title	TSQM derived scores at Week 6 -Global Satisfaction

Statistical analysis description:

Differences in derived TSQM scores at end of treatment (Week 6) were analysed using an ANCOVA model with treatment and pooled site as factors.

Comparison groups	LEO 124249 30mg/g v Vehicle
Number of subjects included in analysis	67
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.099
Method	ANCOVA
Parameter estimate	Mean difference (net)
Point estimate	12.82
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.49
upper limit	28.13

Adverse events

Adverse events information	
Timeframe for reporting adverse events: From screening (28 days prior to baseline) to follow-up (14±2 days after end of treatment, Week 6)	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	19.0
Reporting groups	
Reporting group title	LEO 124249 30mg/g
Reporting group description: -	
Reporting group title	LEO 124249 ointment vehicle
Reporting group description: -	

Serious adverse events	LEO 124249 30mg/g	LEO 124249 ointment vehicle	
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 45 (4.44%)	0 / 24 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Pancreatic carcinoma			
subjects affected / exposed	1 / 45 (2.22%)	0 / 24 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Coronary artery disease			
subjects affected / exposed	1 / 45 (2.22%)	0 / 24 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	LEO 124249 30mg/g	LEO 124249 ointment vehicle	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	19 / 45 (42.22%)	8 / 24 (33.33%)	

Investigations			
Blood creatine phosphokinase increased			
subjects affected / exposed	1 / 45 (2.22%)	0 / 24 (0.00%)	
occurrences (all)	1	0	
Blood lactate dehydrogenase increased			
subjects affected / exposed	1 / 45 (2.22%)	0 / 24 (0.00%)	
occurrences (all)	1	0	
Electrocardiogram T wave amplitude decreased			
subjects affected / exposed	1 / 45 (2.22%)	0 / 24 (0.00%)	
occurrences (all)	1	0	
Injury, poisoning and procedural complications			
Overdose			
subjects affected / exposed	6 / 45 (13.33%)	2 / 24 (8.33%)	
occurrences (all)	13	2	
Contusion			
subjects affected / exposed	1 / 45 (2.22%)	0 / 24 (0.00%)	
occurrences (all)	1	0	
Sunburn			
subjects affected / exposed	1 / 45 (2.22%)	0 / 24 (0.00%)	
occurrences (all)	1	0	
Cardiac disorders			
Atrioventricular block first degree			
subjects affected / exposed	1 / 45 (2.22%)	0 / 24 (0.00%)	
occurrences (all)	1	0	
Sinus bradycardia			
subjects affected / exposed	1 / 45 (2.22%)	0 / 24 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 45 (2.22%)	1 / 24 (4.17%)	
occurrences (all)	1	1	
Nerve root compression			
subjects affected / exposed	0 / 45 (0.00%)	1 / 24 (4.17%)	
occurrences (all)	0	1	
General disorders and administration site conditions			

Application site erythema subjects affected / exposed occurrences (all)	0 / 45 (0.00%) 0	2 / 24 (8.33%) 9	
Application site pain subjects affected / exposed occurrences (all)	3 / 45 (6.67%) 3	1 / 24 (4.17%) 2	
Application site pruritus subjects affected / exposed occurrences (all)	1 / 45 (2.22%) 1	2 / 24 (8.33%) 3	
Application site hypertrichosis subjects affected / exposed occurrences (all)	0 / 45 (0.00%) 0	1 / 24 (4.17%) 1	
Eye disorders Eyelid oedema subjects affected / exposed occurrences (all)	0 / 45 (0.00%) 0	1 / 24 (4.17%) 1	
Gastrointestinal disorders Lip erosion subjects affected / exposed occurrences (all)	1 / 45 (2.22%) 1	0 / 24 (0.00%) 0	
Toothache subjects affected / exposed occurrences (all)	1 / 45 (2.22%) 1	0 / 24 (0.00%) 0	
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	1 / 45 (2.22%) 1	0 / 24 (0.00%) 0	
Skin and subcutaneous tissue disorders Psoriasis subjects affected / exposed occurrences (all)	1 / 45 (2.22%) 1	1 / 24 (4.17%) 1	
Skin fissures subjects affected / exposed occurrences (all)	1 / 45 (2.22%) 1	0 / 24 (0.00%) 0	
Infections and infestations			

Nasopharyngitis			
subjects affected / exposed	6 / 45 (13.33%)	0 / 24 (0.00%)	
occurrences (all)	7	0	
Cystitis			
subjects affected / exposed	0 / 45 (0.00%)	1 / 24 (4.17%)	
occurrences (all)	0	1	
Erysipelas			
subjects affected / exposed	1 / 45 (2.22%)	0 / 24 (0.00%)	
occurrences (all)	1	0	
Fungal infection			
subjects affected / exposed	0 / 45 (0.00%)	1 / 24 (4.17%)	
occurrences (all)	0	1	
Tonsillitis			
subjects affected / exposed	1 / 45 (2.22%)	0 / 24 (0.00%)	
occurrences (all)	1	0	
Urinary tract infection			
subjects affected / exposed	0 / 45 (0.00%)	1 / 24 (4.17%)	
occurrences (all)	0	1	
Metabolism and nutrition disorders			
Hyperlipidaemia			
subjects affected / exposed	1 / 45 (2.22%)	0 / 24 (0.00%)	
occurrences (all)	1	0	

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