Clinical trial results:
LEO 90100 twice weekly maintenance regimen for psoriasis vulgaris

Summary

EudraCT number	2016-000556-95
Trial protocol	GB FR PL
Global end of trial date	27 June 2019

Results information

Result version number	v1 (current)
This version publication date	01 July 2020
First version publication date	01 July 2020

Trial information

Trial identification

Sponsor protocol code	LP0053-1004

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02899962
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 Disclosure Specialist, LEO Pharma A/S, LEO Pharma A/S, 45 4494 5888, disclosure@leo-pharma.com
Scientific contact	Clinical Disclosure Specialist, LEO Pharma A/S, LEO Pharma A/S, 45 4494 5888, 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	26 November 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	27 June 2019
Global end of trial reached?	Yes
Global end of trial date	27 June 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective was to evaluate the efficacy of a twice weekly maintenance regimen with LEO 90100 compared to vehicle in the prevention of relapse in subjects with psoriasis vulgaris.

Protection of trial subjects:

This clinical trial was conducted in accordance with the revision, current at the start of the trial, of the World Medical Association’s Declaration of Helsinki – Ethical Principles for Medical Research Involving Human Subjects. 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. Subjects' signed and dated informed consent to participate in the clinical trial were obtained prior to any trial related activities being carried out in accordance with ICH Good Clinical Practice (GCP) Section 4.8 and all applicable laws and regulations. Overdosage with calcipotriol may be associated with hypercalcaemia, and clinically important hypercalcaemia could be managed at the investigator’s discretion with rehydration, biphosphonate administration or according to local instructions. Overdosage with betamethasone dipropionate may result in suppression of the pituitary adrenal function, and could be treated symptomatically at the investigator's discretion. There is a risk of allergic hypersensitivity reactions with administration of Cortrosyn®/Synacthen®. Prior to the injection of Cortrosyn®/Synacthen®, the physician administering the injection was prepared to treat any possible hypersensitivity reactions.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	31 October 2016
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Poland: 60
Country: Number of subjects enrolled	United Kingdom: 79
Country: Number of subjects enrolled	France: 61
Country: Number of subjects enrolled	Germany: 59
Country: Number of subjects enrolled	United States: 228
Country: Number of subjects enrolled	Canada: 163
Worldwide total number of subjects	650
EEA total number of subjects	259

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)	516
From 65 to 84 years	134
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Adults with psoriasis on body: Subj. not performing HPA axis test: Plaque psoriasis ≥2% BSA, ≥mild severity; Subj. performing HPA axis test: Plaque psoriasis ≥10% BSA, ≥ moderate severity, normal HPA-axis function 722 screened, 650 assigned to treatment, 52 screening failures, 15 withdrew consent, 2 lost to follow-up, 2 other reasons, 1 AE

Period 1

Period 1 title	Open-label phase
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	LEO 90100

Arm description: -

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

Dosage and administration details:

LEO 90100 is formulated as an aerosol foam formulation containing calcipotriol 50 mcg/g (as hydrate) and betamethasone 0.5 mg/g (as dipropionate). LEO 90100 was applied once daily on psoriasis lesions on the body. The maximum weekly use of LEO 91000 is estimated at 100 g per week (which corresponds to 15 g per day) for once-daily treatment with treatment duration of 4 weeks.

Number of subjects in period 1	LEO 90100
Started	650
Completed	623
Not completed	27
Consent withdrawn by subject	7
Adverse event, non-fatal	2
Other reasons	9
Lost to follow-up	9

Period 2

Period 2 title	Maintenance phase
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Blinding implementation details:

The packaging and labelling of the IMPs contained no evidence of the identity of IMPs. It was not considered possible to differentiate between the IMPs solely by sensory evaluation. No effects of the IMPs which would reveal the identity of the individual treatment allocations were expected. Consequently, it was expected that the subjects and the site staff remained unaware of the individual treatment assignment during the conduct of the clinical trial.

Arms

Are arms mutually exclusive?	Yes
Arm title	LEO 90100

Arm description:

LEO 90100 was to be applied twice-weekly 3 or 4 days apart on specific days. If an application was missed, the medication was to be applied as soon as subject remembered. The next application was to be made at the next scheduled dosing date. Upon confirmation of relapse, LEO 90100 for 4 weeks once daily was applied.

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

Dosage and administration details:

LEO 90100 is formulated as an aerosol foam formulation containing calcipotriol 50 mcg/g (as hydrate) and betamethasone 0.5 mg/g (as dipropionate). LEO 90100 was applied twice weekly on psoriasis lesions on the body with a maximum weekly use of 30 g (15 g per day) for twice weekly treatment with treatment duration of up to 52 weeks.

Investigational medicinal product name	LEO 90100 rescue medication
Investigational medicinal product code	
Other name	Enstilar®
Pharmaceutical forms	Cutaneous foam
Routes of administration	Topical use

Dosage and administration details:

Rescue medication: If subjects experienced a confirmed relapse (PGA≥2; i.e. at least ‘mild’) during the maintenance phase, they were to be provided with rescue medication. LEO 90100 is formulated as an aerosol foam formulation containing calcipotriol 50 mcg/g (as hydrate) and betamethasone 0.5 mg/g (as dipropionate). LEO 90100 was applied once daily on psoriasis lesions on the body: 100 g per week (15 g per day) for once-daily treatment with treatment duration of 4 weeks.

Arm title	Vehicle

Arm description:

Vehicle was to be applied twice-weekly 3 or 4 days apart on specific days. If an application was missed, the medication was to be applied as soon as subject remembered. The next application was to be made at the next scheduled dosing date. Upon confirmation of relapse, LEO 90100 for 4 weeks once daily was applied.

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

Dosage and administration details:

Aerosol foam vehicle contains the same ingredients as LEO 90100 except the active ingredients (calcipotriol and betamethasone). The vehicle was applied twice weekly on psoriasis lesions on the body with a maximum weekly use of 30 g (15 g per day) for twice weekly treatment with treatment duration of up to 52 weeks.

Investigational medicinal product name	LEO 90100 rescue medication
Investigational medicinal product code	
Other name	Enstilar®
Pharmaceutical forms	Cutaneous foam
Routes of administration	Topical use

Dosage and administration details:

Rescue medication: If subjects experienced a confirmed relapse (PGA≥2; i.e. at least 'mild') during the maintenance phase, they were to be provided with rescue medication. LEO 90100 is formulated as an aerosol foam formulation containing calcipotriol 50 mcg/g (as hydrate) and betamethasone 0.5 mg/g (as dipropionate). LEO 90100 was applied once daily psoriasis lesions on the body with a maximum 100 g per week (15 g per day) for once-daily treatment with treatment duration of 4 weeks.

Number of subjects in period 2[1]	LEO 90100	Vehicle
Started	272	273
Completed	131	120
Not completed	141	153
Adverse event, serious fatal	-	1
Consent withdrawn by subject	30	36
Adverse event, non-fatal	2	1
Other	9	13
No treatment success after initial 4 weeks	3	2
Subjects not clear/almost clear after rescue med	65	70
Lost to follow-up	12	14
Lack of efficacy	20	16

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: Subjects who did not achieve treatment success according to PGA scale were not randomized into the maintenance phase. In addition, among subjects randomized to maintenance phase, 24 had not achieved treatment success and therefore they were randomized in error.

Baseline characteristics

Reporting groups	
Reporting group title	Open-label phase

Reporting group description: -

Reporting group values	Open-label phase	Total	
Number of subjects	650	650	
Age categorical Units: Subjects			
Age continuous Units: years arithmetic mean standard deviation	 51.8 ± 14.2	 -	
Gender categorical Units: Subjects			
Female	226	226	
Male	424	424	
PGA at baseline Units: Subjects			
Mild	83	83	
Moderate	509	509	
Severe	58	58	
m-PASI at baseline Units: units on scale arithmetic mean full range (min-max)	 7.7 2.0 to 32.4	 -	
Body surface area			
Extent of psoriasis affecting body surface area			
Units: Percentage arithmetic mean full range (min-max)	 8.2 1.0 to 38.0	 -	

End points

End points reporting groups

Reporting group title	LEO 90100
Reporting group description: -	
Reporting group title	LEO 90100

Reporting group description:

LEO 90100 was to be applied twice-weekly 3 or 4 days apart on specific days. If an application was missed, the medication was to be applied as soon as subject remembered. The next application was to be made at the next scheduled dosing date. Upon confirmation of relapse, LEO 90100 for 4 weeks once daily was applied.

Reporting group title	Vehicle

Reporting group description:

Vehicle was to be applied twice-weekly 3 or 4 days apart on specific days. If an application was missed, the medication was to be applied as soon as subject remembered. The next application was to be made at the next scheduled dosing date. Upon confirmation of relapse, LEO 90100 for 4 weeks once daily was applied.

Primary: Time to first relapse

End point title	Time to first relapse

End point description:

Time to first relapse (at least 'mild' according to the Physician's Global Assessment of disease severity [PGA]). A five-point scale (clear, almost clear, mild, moderate, and severe) of PGA was used.

End point type	Primary

End point timeframe:

From the start of maintenance phase after randomisation until subjects experienced first relapse or end of treatment (Week 56 or early withdrawal)

End point values	LEO 90100	Vehicle		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	256	265		
Units: days				
median (confidence interval 95%)	56 (34 to 59)	30 (29 to 31)		

Statistical analyses

Statistical analysis title	Primary analysis

Statistical analysis description:

The primary endpoint was time to first relapse during the maintenance phase, where relapse was an exacerbation of psoriasis defined as a PGA of at least 'mild'. This was calculated as the number of days from randomisation to the day where the subject had the first relapse confirmed. For subjects who either did not encounter a relapse or were withdrawn from the trial, the number of days was treated as a censored observation at the day of end of trial visit.

Comparison groups	LEO 90100 v Vehicle

Number of subjects included in analysis	521
Analysis specification	Pre-specified
Analysis type	superiority[1]
P-value	< 0.001
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.57
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.47
upper limit	0.69

Notes:

[1] - The primary endpoint was analysed using a Cox proportional hazards model with treatment group, pooled sites, and disease severity at maintenance baseline (as determined by the PGA) as factors. Maintenance baseline (Week 4) was used in the model as compared to baseline at Week 0

Secondary: Proportion of days in remission

End point title	Proportion of days in remission

End point description:

The proportion of days in remission (‘clear’ or ‘almost clear’ according to the PGA) during the maintenance phase was compared between LEO 90100 and vehicle

End point type	Secondary

End point timeframe:

52 weeks in the maintenance phase

End point values	LEO 90100	Vehicle		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	256	265		
Units: Percentage				
arithmetic mean (standard deviation)	70.2 (± 21.7)	60.8 (± 20.1)		

Statistical analyses

Statistical analysis title	Analysis of proportion of days in remission

Statistical analysis description:

The number of days in remission was calculated as the sum of days where the subject was in remission periods. The proportion of days in remission was calculated as the number of days in remission divided by the length of the maintenance phase in days.

Comparison groups	LEO 90100 v Vehicle
Number of subjects included in analysis	521
Analysis specification	Pre-specified
Analysis type	superiority[2]
P-value	< 0.001
Method	ANOVA
Parameter estimate	Mean difference (net)
Point estimate	0.11

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.08
upper limit	0.14

Notes:

[2] - Multiple imputation of data for withdrawn subjects was done using 100 imputations. In order not to favour any treatment arm, the imputation approach depended on whether the subject's reason for withdrawal potentially was related to IMP or not. For the imputation, the length of the maintenance phase was assumed to be 52 weeks, corresponding to 364 days.

Secondary: Number of relapses

End point title	Number of relapses

End point description:

To compare the number of relapses during the maintenance phase between LEO 90100 and vehicle

End point type	Secondary

End point timeframe:

52 weeks in the maintenance phase

End point values	LEO 90100	Vehicle		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	256	265		
Units: Numbers				
arithmetic mean (standard deviation)	2.0 (± 1.7)	3.1 (± 2.2)		

Statistical analyses

Statistical analysis title	Analysis of number of relapses

Statistical analysis description:

The number of relapses was calculated as the sum of confirmed relapses for each subject.

Comparison groups	LEO 90100 v Vehicle
Number of subjects included in analysis	521
Analysis specification	Pre-specified
Analysis type	superiority[3]
P-value	< 0.001
Method	Poisson regression
Parameter estimate	rate ratio
Point estimate	0.54
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.46
upper limit	0.63

Notes:

[3] - The number of relapses was analysed using a Poisson regression model with treatment group, pooled sites, and disease severity at maintenance baseline as factors, subject as random effect, and time at risk as an offset. Maintenance baseline was used in the model as compared to baseline

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Week 0 until end of 52-week maintenance phase	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	19

Reporting groups	
Reporting group title	LEO 90100 maintenance
Reporting group description:	
Subjects who received LEO 90100 (once daily for 4 weeks) in the open-label phase and randomised to receive LEO 90100 (twice weekly for up to 52 weeks) in the maintenance phase with rescue medication LEO 90100 (once daily for 4 weeks) provided upon confirmation of a relapse	
Reporting group title	Vehicle maintenance
Reporting group description:	
Subjects who received LEO 90100 (once daily for 4 weeks) in the open-label phase and randomised to receive Vehicle (twice weekly for up to 52 weeks) in the maintenance phase with rescue medication LEO 90100 (once daily for 4 weeks) provided upon confirmation of a relapse	
Reporting group title	LEO 90100 open-label
Reporting group description:	
Subjects who received LEO 90100 (once daily for 4 weeks) in the open-label phase. The same subjects were randomised into LEO 90100 or vehicle in the maintenance phase	

Serious adverse events	LEO 90100 maintenance	Vehicle maintenance	LEO 90100 open-label
Total subjects affected by serious adverse events			
subjects affected / exposed	14 / 272 (5.15%)	11 / 273 (4.03%)	4 / 650 (0.62%)
number of deaths (all causes)	0	1	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 / 272 (0.37%)	0 / 273 (0.00%)	1 / 650 (0.15%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Arterial stenosis			
subjects affected / exposed	2 / 272 (0.74%)	0 / 273 (0.00%)	0 / 650 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertension			

subjects affected / exposed	1 / 272 (0.37%)	0 / 273 (0.00%)	0 / 650 (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
Venous thrombosis			
subjects affected / exposed	0 / 272 (0.00%)	1 / 273 (0.37%)	0 / 650 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	1 / 272 (0.37%)	0 / 273 (0.00%)	0 / 650 (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
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	1 / 272 (0.37%)	0 / 273 (0.00%)	0 / 650 (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
Respiratory, thoracic and mediastinal disorders			
Pneumothorax			
subjects affected / exposed	0 / 272 (0.00%)	1 / 273 (0.37%)	0 / 650 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	0 / 272 (0.00%)	1 / 273 (0.37%)	0 / 650 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Intentional overdose			
subjects affected / exposed	0 / 272 (0.00%)	1 / 273 (0.37%)	1 / 650 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 4	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gun shot wound			

subjects affected / exposed	0 / 272 (0.00%)	1 / 273 (0.37%)	0 / 650 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Cardiac disorders			
Myocardial ischaemia			
subjects affected / exposed	1 / 272 (0.37%)	0 / 273 (0.00%)	0 / 650 (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
Coronary artery occlusion			
subjects affected / exposed	1 / 272 (0.37%)	0 / 273 (0.00%)	0 / 650 (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
Acute myocardial infarction			
subjects affected / exposed	1 / 272 (0.37%)	0 / 273 (0.00%)	0 / 650 (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
Atrial fibrillation			
subjects affected / exposed	1 / 272 (0.37%)	0 / 273 (0.00%)	0 / 650 (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
Mitral valve incompetence			
subjects affected / exposed	0 / 272 (0.00%)	1 / 273 (0.37%)	0 / 650 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	1 / 272 (0.37%)	0 / 273 (0.00%)	1 / 650 (0.15%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	1 / 272 (0.37%)	0 / 273 (0.00%)	0 / 650 (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

Gastrointestinal disorders			
Alcoholic pancreatitis			
subjects affected / exposed	0 / 272 (0.00%)	1 / 273 (0.37%)	0 / 650 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal obstruction			
subjects affected / exposed	0 / 272 (0.00%)	1 / 273 (0.37%)	0 / 650 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis			
subjects affected / exposed	1 / 272 (0.37%)	0 / 273 (0.00%)	0 / 650 (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
Musculoskeletal and connective tissue disorders			
Myositis			
subjects affected / exposed	0 / 272 (0.00%)	0 / 273 (0.00%)	1 / 650 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Pneumonia			
subjects affected / exposed	0 / 272 (0.00%)	1 / 273 (0.37%)	0 / 650 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atypical pneumonia			
subjects affected / exposed	1 / 272 (0.37%)	0 / 273 (0.00%)	0 / 650 (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
Appendicitis			
subjects affected / exposed	0 / 272 (0.00%)	1 / 273 (0.37%)	0 / 650 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocarditis			

subjects affected / exposed	0 / 272 (0.00%)	1 / 273 (0.37%)	0 / 650 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Electrolyte imbalance			
subjects affected / exposed	1 / 272 (0.37%)	0 / 273 (0.00%)	0 / 650 (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

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

Non-serious adverse events	LEO 90100 maintenance	Vehicle maintenance	LEO 90100 open-label
Total subjects affected by non-serious adverse events			
subjects affected / exposed	129 / 272 (47.43%)	128 / 273 (46.89%)	112 / 650 (17.23%)
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	5 / 272 (1.84%)	0 / 273 (0.00%)	0 / 650 (0.00%)
occurrences (all)	5	0	0
Ligament sprain			
subjects affected / exposed	1 / 272 (0.37%)	4 / 273 (1.47%)	1 / 650 (0.15%)
occurrences (all)	2	4	1
Joint injury			
subjects affected / exposed	3 / 272 (1.10%)	0 / 273 (0.00%)	0 / 650 (0.00%)
occurrences (all)	3	0	0
Laceration			
subjects affected / exposed	2 / 272 (0.74%)	3 / 273 (1.10%)	1 / 650 (0.15%)
occurrences (all)	2	3	1
Contusion			
subjects affected / exposed	2 / 272 (0.74%)	3 / 273 (1.10%)	1 / 650 (0.15%)
occurrences (all)	2	3	1
Vascular disorders			
Hypertension			
subjects affected / exposed	4 / 272 (1.47%)	3 / 273 (1.10%)	6 / 650 (0.92%)
occurrences (all)	4	3	6
Nervous system disorders			

Sciatica			
subjects affected / exposed	4 / 272 (1.47%)	3 / 273 (1.10%)	0 / 650 (0.00%)
occurrences (all)	4	3	0
Dizziness			
subjects affected / exposed	3 / 272 (1.10%)	0 / 273 (0.00%)	1 / 650 (0.15%)
occurrences (all)	4	0	1
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	3 / 272 (1.10%)	0 / 273 (0.00%)	1 / 650 (0.15%)
occurrences (all)	3	0	1
Eye disorders			
Cataract			
subjects affected / exposed	3 / 272 (1.10%)	0 / 273 (0.00%)	0 / 650 (0.00%)
occurrences (all)	4	0	0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 272 (0.37%)	3 / 273 (1.10%)	2 / 650 (0.31%)
occurrences (all)	1	3	2
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 272 (0.00%)	3 / 273 (1.10%)	0 / 650 (0.00%)
occurrences (all)	0	3	0
Skin and subcutaneous tissue disorders			
Rebound psoriasis			
subjects affected / exposed	4 / 272 (1.47%)	12 / 273 (4.40%)	0 / 650 (0.00%)
occurrences (all)	4	12	0
Psoriasis			
subjects affected / exposed	1 / 272 (0.37%)	7 / 273 (2.56%)	3 / 650 (0.46%)
occurrences (all)	1	7	3
Actinic keratosis			
subjects affected / exposed	3 / 272 (1.10%)	0 / 273 (0.00%)	0 / 650 (0.00%)
occurrences (all)	3	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	4 / 272 (1.47%)	6 / 273 (2.20%)	3 / 650 (0.46%)
occurrences (all)	4	6	4

Back pain			
subjects affected / exposed	6 / 272 (2.21%)	4 / 273 (1.47%)	4 / 650 (0.62%)
occurrences (all)	7	4	4
Pain in extremity			
subjects affected / exposed	4 / 272 (1.47%)	2 / 273 (0.73%)	3 / 650 (0.46%)
occurrences (all)	4	2	3
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	16 / 272 (5.88%)	15 / 273 (5.49%)	7 / 650 (1.08%)
occurrences (all)	17	24	7
Nasopharyngitis			
subjects affected / exposed	22 / 272 (8.09%)	19 / 273 (6.96%)	7 / 650 (1.08%)
occurrences (all)	23	24	7
Influenza			
subjects affected / exposed	7 / 272 (2.57%)	3 / 273 (1.10%)	2 / 650 (0.31%)
occurrences (all)	7	3	2
Urinary tract infection			
subjects affected / exposed	3 / 272 (1.10%)	6 / 273 (2.20%)	2 / 650 (0.31%)
occurrences (all)	3	6	2
Bronchitis			
subjects affected / exposed	2 / 272 (0.74%)	5 / 273 (1.83%)	1 / 650 (0.15%)
occurrences (all)	2	5	1
Sinusitis			
subjects affected / exposed	5 / 272 (1.84%)	2 / 273 (0.73%)	2 / 650 (0.31%)
occurrences (all)	5	3	2
Gastroenteritis			
subjects affected / exposed	4 / 272 (1.47%)	2 / 273 (0.73%)	3 / 650 (0.46%)
occurrences (all)	4	2	3
Folliculitis			
subjects affected / exposed	4 / 272 (1.47%)	2 / 273 (0.73%)	2 / 650 (0.31%)
occurrences (all)	4	2	2
Lower respiratory tract infection			
subjects affected / exposed	3 / 272 (1.10%)	3 / 273 (1.10%)	0 / 650 (0.00%)
occurrences (all)	3	3	0
Metabolism and nutrition disorders			

Vitamin D deficiency subjects affected / exposed occurrences (all)	1 / 272 (0.37%) 1	2 / 273 (0.73%) 2	36 / 650 (5.54%) 36

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
19 August 2016	The amendment was made to implement advice from the Food and Drug Administration (FDA) and the Danish Medicines Agency (DKMA). The following important changes were made: - Updates to the inclusion/exclusion criteria. - Criteria for entering the maintenance phase was changed from "a PGA score of clear or almost clear" to "a PGA score of clear or almost clear with at least a 2-step improvement". Correspondingly the number of subjects to be enrolled has been increased. - Clarification that subjects were to apply IMP to areas of trunk and/or limbs where lesions have cleared and also to new lesions. Upon relapse, subjects were instructed to apply IMP on affected areas once-daily for up to 4 weeks.
14 December 2016	This amendment was made to describe a new treatment principle for non-active lesions during relapse treatment: - Clarification that only the active areas were to be treated with rescue medication upon relapse and the non-active psoriasis areas were to be treated with maintenance treatment. The following other important change were made: - Addition of an 8-week follow-up period at the end of the maintenance period.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported