Clinical trial results:
LEO 32731 for the treatment of moderate to severe psoriasis vulgaris
A phase 2a proof of concept study comparing an oral tablet formulation of LEO 32731 with a corresponding placebo tablet in patients with moderate to severe psoriasis vulgaris.
A multi-centre, prospective, randomized, double-blind, 2-arm, placebo-controlled, parallel-group study with 16 weeks twice times daily oral treatment.

Summary

EudraCT number	2015-005279-25
Trial protocol	DE
Global end of trial date	06 July 2017

Results information

Result version number	v1 (current)
This version publication date	17 October 2018
First version publication date	17 October 2018

Trial information

Trial identification

Sponsor protocol code	LP0058-1072

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02888236
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, +45 44945888, disclosure@leo-pharma.com
Scientific contact	Clinical Disclosure Specialist, 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	01 February 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	06 July 2017
Global end of trial reached?	Yes
Global end of trial date	06 July 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To investigate the efficacy of LEO 32731 30 mg compared with that of placebo after 16 weeks of oral treatment of psoriasis vulgaris.

Protection of trial subjects:

This 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 the amendment from Somerset West, South Africa, October 1996. All subjects received written and verbal information concerning the clinical trial. Subjects were asked to consent that their personal data were recorded, collected, processed and could be transferred to other countries in accordance with any national legislation regulating privacy and data protection.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 July 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: 36
Worldwide total number of subjects	36
EEA total number of subjects	36

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)	36
From 65 to 84 years	0

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

50 subjects were screened and 14 subjects were screening failures. 36 subjects were randomised: 18 to each treatment. The randomised subjects were enrolled at 7 trial sites in Germany.

Pre-assignment

Screening details:

Key inclusion criteria:
Moderate to severe psoriasis vulgaris with or without psoriatic arthritis (maximum 4 joints with active arthritis) for ≥6 months prior to screening.
Men, or women of non-childbearing potential.

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

Blinding implementation details:

The packaging and labelling of the IMPs contained no evidence of their identity. It was not considered possible to differentiate between the IMPs solely by sensory evaluation.

Arms

Are arms mutually exclusive?	Yes
Arm title	LEO 32731 30 mg

Arm description:

Subjects received twice daily treatment for 16 weeks: a 1-week dose escalation followed by 15 weeks of full dose treatment.

Arm type	Experimental
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Each dose consisted of 3 tablets, including 1 or 2 placebo tablets in combination with 1 or 2 LEO 32731 tablets, supplied at a strength of 10 mg or 30 mg.
Subjects were dosed twice daily as follows: Days 1–3: 1 tablet LEO 32731 10 mg + 2 placebo tablets; Days 4–6: 2 tablets LEO 32731 10 mg + 1 placebo tablet; Day 7–Week 16 : 1 tablet LEO 32731 30 mg + 2 placebo tablets.

Investigational medicinal product name	LEO 32731
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Each dose consisted of 3 tablets, including 1 or 2 placebo tablets in combination with 1 or 2 LEO 32731 tablets, supplied at a strength of 10 mg or 30 mg.
Subjects were dosed twice daily as follows: Days 1–3: 1 tablet LEO 32731 10 mg + 2 placebo tablets; Days 4–6: 2 tablets LEO 32731 10 mg + 1 placebo tablet; Day 7–Week 16 : 1 tablet LEO 32731 30 mg + 2 placebo tablets.

Arm title	Placebo

Arm description:

Subjects received twice daily treatment for 16 weeks.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received 3 placebo tablets twice daily for 16 weeks.

Number of subjects in period 1	LEO 32731 30 mg	Placebo
Started	18	18
Completed	8	9
Not completed	10	9
Consent withdrawn by subject	1	-
Adverse event, non-fatal	9	3
Lost to follow-up	-	1
Lack of efficacy	-	5

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	36	36	
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)	36	36	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous Units: years			
median	46.5		
full range (min-max)	20 to 61	-	
Gender categorical Units: Subjects			
Female	3	3	
Male	33	33	

End points

End points reporting groups

Reporting group title	LEO 32731 30 mg
Reporting group description:	
Subjects received twice daily treatment for 16 weeks: a 1-week dose escalation followed by 15 weeks of full dose treatment.	
Reporting group title	Placebo
Reporting group description:	
Subjects received twice daily treatment for 16 weeks.	

Primary: PASI at Week 16

End point title	PASI at Week 16
End point description:	
The PASI score is an investigator assessment that grades the extent and severity of psoriatic involvement for each of four body regions (head and neck, upper extremities, trunk, and lower extremities) using a 7-point scale for extent of involvement in each body region and 5-point scales for severity of each of the clinical signs redness, thickness, and scaliness in each body region.	
End point type	Primary
End point timeframe:	
At Week 16	

End point values	LEO 32731 30 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18[1]	18[2]		
Units: Score on a scale				
least squares mean (confidence interval 95%)	7.1 (4.3 to 9.9)	13.1 (10.3 to 15.9)		

Notes:

[1] - Based on last observation carried forward (LOCF)

[2] - Based on last observation carried forward (LOCF)

Statistical analyses

Statistical analysis title	ANCOVA with LOCF
Statistical analysis description:	
Based on an analysis of covariance (ANCOVA) model with treatment and site as factors and baseline value as covariate.	
Comparison groups	LEO 32731 30 mg v Placebo
Number of subjects included in analysis	36
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.005
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-6

Confidence interval	
level	95 %
sides	2-sided
lower limit	-10
upper limit	-2

Secondary: PGA treatment success at Week 16

End point title	PGA treatment success at Week 16

End point description:

Physician’s Global Assessment of disease severity (PGA) is done on a 5-point ordinal scale and represents the average lesion severity on the trunk, limbs, and scalp. The assessment is based on the condition of the disease at the time of evaluation. Treatment success according to PGA is defined as reaching either of the 2 lowest points on the ordinal scale: 'clear' or 'almost clear'

End point type	Secondary

End point timeframe:

At Week 16

End point values	LEO 32731 30 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18[3]	18[4]		
Units: Subjects	7	1		

Notes:

[3] - Based on LOCF

[4] - Based on LOCF

Statistical analyses

Statistical analysis title	Logistic regression with LOCF

Statistical analysis description:

Adjusted for pooled site.

Comparison groups	LEO 32731 30 mg v Placebo
Number of subjects included in analysis	36
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.032 [5]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	12.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.7
upper limit	256.1

Notes:

[5] - Wald test; test for the hypothesis of odds ratio (LEO 32731 30 mg relative to placebo) equal to 1

Secondary: Itch NRS at Week 16

End point title	Itch NRS at Week 16

End point description:

Subject assessment of the maximal intensity of itch during the previous 24 hours on a numeric rating scale (NRS) ranging from 0 (no itch at all) to 10 (worst itch imaginable).

End point type	Secondary

End point timeframe:

At Week 16

End point values	LEO 32731 30 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18[6]	18[7]		
Units: Score on a scale				
least squares mean (confidence interval 95%)	3.4 (1.8 to 5.1)	5.7 (4.1 to 7.3)		

Notes:

[6] - Based on LOCF

[7] - Based on LOCF

Statistical analyses

Statistical analysis title	ANCOVA with LOCF

Statistical analysis description:

Based on an ANCOVA model with treatment and site as factors and baseline value as covariate.

Comparison groups	LEO 32731 30 mg v Placebo
Number of subjects included in analysis	36
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.053
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-2.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.6
upper limit	0

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were reported from the time informed consent was signed until the end of trial.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.0

Reporting groups

Reporting group title	LEO 32731 30 mg

Reporting group description:

All subjects who received at least 1 dose of trial medication and for whom safety data were available post-baseline.

Reporting group title	Placebo

Reporting group description:

All subjects who received at least 1 dose of trial medication and for whom safety data were available post-baseline

Serious adverse events	LEO 32731 30 mg	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 18 (11.11%)	1 / 18 (5.56%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
General disorders and administration site conditions			
Condition aggravated	Additional description: Relating to pre-existing Scheuermann's disease.		
subjects affected / exposed	0 / 18 (0.00%)	1 / 18 (5.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Ureterolithiasis			
subjects affected / exposed	1 / 18 (5.56%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Erysipelas			
subjects affected / exposed	1 / 18 (5.56%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	LEO 32731 30 mg	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	17 / 18 (94.44%)	16 / 18 (88.89%)	
Vascular disorders			
Haematoma			
subjects affected / exposed	0 / 18 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Hot flush			
subjects affected / exposed	1 / 18 (5.56%)	0 / 18 (0.00%)	
occurrences (all)	1	0	
Hypertension			
subjects affected / exposed	0 / 18 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	2 / 18 (11.11%)	0 / 18 (0.00%)	
occurrences (all)	2	0	
Pain			
subjects affected / exposed	1 / 18 (5.56%)	1 / 18 (5.56%)	
occurrences (all)	1	1	
Face oedema			
subjects affected / exposed	1 / 18 (5.56%)	0 / 18 (0.00%)	
occurrences (all)	1	0	
Feeling cold			
subjects affected / exposed	1 / 18 (5.56%)	0 / 18 (0.00%)	
occurrences (all)	1	0	
Influenza like illness			
subjects affected / exposed	1 / 18 (5.56%)	0 / 18 (0.00%)	
occurrences (all)	1	0	
Peripheral swelling			

subjects affected / exposed	0 / 18 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Thirst			
subjects affected / exposed	0 / 18 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	2 / 18 (11.11%)	2 / 18 (11.11%)	
occurrences (all)	2	2	
Thinking abnormal			
subjects affected / exposed	2 / 18 (11.11%)	0 / 18 (0.00%)	
occurrences (all)	2	0	
Depressed mood			
subjects affected / exposed	1 / 18 (5.56%)	0 / 18 (0.00%)	
occurrences (all)	1	0	
Sleep disorder			
subjects affected / exposed	1 / 18 (5.56%)	0 / 18 (0.00%)	
occurrences (all)	1	0	
Investigations			
Red blood cell sedimentation rate increased			
subjects affected / exposed	3 / 18 (16.67%)	3 / 18 (16.67%)	
occurrences (all)	4	4	
C-reactive protein increased			
subjects affected / exposed	2 / 18 (11.11%)	1 / 18 (5.56%)	
occurrences (all)	3	4	
Alanine aminotransferase increased			
subjects affected / exposed	2 / 18 (11.11%)	0 / 18 (0.00%)	
occurrences (all)	3	0	
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 18 (5.56%)	0 / 18 (0.00%)	
occurrences (all)	1	0	
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 18 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Weight decreased			

subjects affected / exposed	1 / 18 (5.56%)	0 / 18 (0.00%)	
occurrences (all)	1	0	
Injury, poisoning and procedural complications			
Joint injury			
subjects affected / exposed	0 / 18 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Muscle strain			
subjects affected / exposed	1 / 18 (5.56%)	0 / 18 (0.00%)	
occurrences (all)	1	0	
Soft tissue injury			
subjects affected / exposed	0 / 18 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Wound			
subjects affected / exposed	0 / 18 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Cardiac disorders			
Palpitations			
subjects affected / exposed	1 / 18 (5.56%)	0 / 18 (0.00%)	
occurrences (all)	1	0	
Tachycardia			
subjects affected / exposed	1 / 18 (5.56%)	0 / 18 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			
Headache			
subjects affected / exposed	5 / 18 (27.78%)	2 / 18 (11.11%)	
occurrences (all)	7	2	
Dizziness			
subjects affected / exposed	4 / 18 (22.22%)	0 / 18 (0.00%)	
occurrences (all)	5	0	
Dysaesthesia			
subjects affected / exposed	0 / 18 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Hypoaesthesia			
subjects affected / exposed	1 / 18 (5.56%)	0 / 18 (0.00%)	
occurrences (all)	1	0	
Migraine			

subjects affected / exposed	1 / 18 (5.56%)	0 / 18 (0.00%)	
occurrences (all)	1	0	
Blood and lymphatic system disorders			
Lymphopenia			
subjects affected / exposed	1 / 18 (5.56%)	1 / 18 (5.56%)	
occurrences (all)	1	1	
Ear and labyrinth disorders			
Hypoacusis			
subjects affected / exposed	1 / 18 (5.56%)	0 / 18 (0.00%)	
occurrences (all)	1	0	
Tinnitus			
subjects affected / exposed	0 / 18 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Vertigo			
subjects affected / exposed	1 / 18 (5.56%)	0 / 18 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	11 / 18 (61.11%)	1 / 18 (5.56%)	
occurrences (all)	16	1	
Diarrhoea			
subjects affected / exposed	9 / 18 (50.00%)	0 / 18 (0.00%)	
occurrences (all)	12	0	
Vomiting			
subjects affected / exposed	3 / 18 (16.67%)	1 / 18 (5.56%)	
occurrences (all)	5	1	
Abdominal pain			
subjects affected / exposed	3 / 18 (16.67%)	1 / 18 (5.56%)	
occurrences (all)	4	1	
Abdominal pain upper			
subjects affected / exposed	2 / 18 (11.11%)	1 / 18 (5.56%)	
occurrences (all)	4	1	
Flatulence			
subjects affected / exposed	2 / 18 (11.11%)	1 / 18 (5.56%)	
occurrences (all)	3	2	
Abdominal discomfort			

subjects affected / exposed	2 / 18 (11.11%)	0 / 18 (0.00%)	
occurrences (all)	3	0	
Toothache			
subjects affected / exposed	1 / 18 (5.56%)	1 / 18 (5.56%)	
occurrences (all)	1	2	
Dyspepsia			
subjects affected / exposed	1 / 18 (5.56%)	1 / 18 (5.56%)	
occurrences (all)	1	1	
Faeces soft			
subjects affected / exposed	1 / 18 (5.56%)	0 / 18 (0.00%)	
occurrences (all)	1	0	
Frequent bowel movements			
subjects affected / exposed	1 / 18 (5.56%)	0 / 18 (0.00%)	
occurrences (all)	1	0	
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 18 (5.56%)	0 / 18 (0.00%)	
occurrences (all)	1	0	
Haemorrhoidal haemorrhage			
subjects affected / exposed	1 / 18 (5.56%)	0 / 18 (0.00%)	
occurrences (all)	1	0	
Paraesthesia oral			
subjects affected / exposed	1 / 18 (5.56%)	0 / 18 (0.00%)	
occurrences (all)	1	0	
Skin and subcutaneous tissue disorders			
Hyperhidrosis			
subjects affected / exposed	2 / 18 (11.11%)	1 / 18 (5.56%)	
occurrences (all)	2	1	
Prurigo			
subjects affected / exposed	0 / 18 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	2	
Pruritus			
subjects affected / exposed	0 / 18 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Psoriasis			
subjects affected / exposed	0 / 18 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	

Seborrhoeic dermatitis			
subjects affected / exposed	0 / 18 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Renal and urinary disorders			
Glycosuria			
subjects affected / exposed	2 / 18 (11.11%)	0 / 18 (0.00%)	
occurrences (all)	2	0	
Haematuria			
subjects affected / exposed	0 / 18 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Pollakiuria			
subjects affected / exposed	0 / 18 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	2 / 18 (11.11%)	2 / 18 (11.11%)	
occurrences (all)	2	2	
Muscle spasms			
subjects affected / exposed	1 / 18 (5.56%)	1 / 18 (5.56%)	
occurrences (all)	1	1	
Joint swelling			
subjects affected / exposed	0 / 18 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Muscle tightness			
subjects affected / exposed	1 / 18 (5.56%)	0 / 18 (0.00%)	
occurrences (all)	1	0	
Myalgia			
subjects affected / exposed	1 / 18 (5.56%)	0 / 18 (0.00%)	
occurrences (all)	1	0	
Osteoarthritis			
subjects affected / exposed	0 / 18 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Pain in extremity			
subjects affected / exposed	1 / 18 (5.56%)	0 / 18 (0.00%)	
occurrences (all)	1	0	
Tenosynovitis			

subjects affected / exposed	0 / 18 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	5 / 18 (27.78%)	5 / 18 (27.78%)	
occurrences (all)	5	6	
Gastroenteritis			
subjects affected / exposed	1 / 18 (5.56%)	1 / 18 (5.56%)	
occurrences (all)	1	1	
Bronchitis			
subjects affected / exposed	1 / 18 (5.56%)	0 / 18 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal infection			
subjects affected / exposed	0 / 18 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Gingivitis			
subjects affected / exposed	1 / 18 (5.56%)	0 / 18 (0.00%)	
occurrences (all)	1	0	
Pulpitis dental			
subjects affected / exposed	1 / 18 (5.56%)	0 / 18 (0.00%)	
occurrences (all)	1	0	
Rhinitis			
subjects affected / exposed	1 / 18 (5.56%)	0 / 18 (0.00%)	
occurrences (all)	1	0	
Soft tissue infection			
subjects affected / exposed	1 / 18 (5.56%)	0 / 18 (0.00%)	
occurrences (all)	1	0	
Tonsillitis			
subjects affected / exposed	1 / 18 (5.56%)	0 / 18 (0.00%)	
occurrences (all)	1	0	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	2 / 18 (11.11%)	0 / 18 (0.00%)	
occurrences (all)	3	0	
Hypertriglyceridaemia			

subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	0 / 18 (0.00%) 0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
06 June 2016	Before any subjects were screened, the protocol was amended to address objections from the regulatory authority and the central IEC, and to take into account new findings on the tolerability of LEO 32731 that emerged from another phase 1 trial. The trial design was changed as follows: The maximum dose of LEO 32731 was reduced from 50 mg twice daily to 30 mg twice daily, and the number of trial arms was reduced from 4 to 2. According the original protocol, subjects were to be randomised to twice daily doses of 30 mg, 40 mg, or 50 mg LEO 32731 or placebo in a 1:1:1:1 ratio. According to the amended protocol, subjects were randomised to twice daily doses of 30 mg LEO 32731 or placebo in a 1:1 ratio. As a consequence, the number of subjects to be randomised was reduced from 72 to 36, and the percentage of subjects to be treated with LEO 32731 was reduced from 75% to 50%.
21 December 2016	During the trial conduct, the protocol was amended to allow trial sites to include more subjects. The maximum number of subjects per trial site was increased from 8 subjects to approximately one third of the total number of subjects to be randomised (that is, approximately one third of 36). This change was based on the following considerations: - Evaluation of the recruitment estimates for each trial site did not indicate that one site would be dominating the recruitment. - The planned analysis method for the primary endpoint, PASI at Week 16, allowed for low subject numbers per trial site (should this happen as a result of some sites recruiting more than 8 subjects), as long as each treatment arm was represented at each site, which was expected to be fulfilled.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported