Clinical trial results:
Topical Aprepitant in Prurigo Patients (iTAPP)

An exploratory phase IIa trial with topically applied aprepitant in patients with prurigo

Summary

EudraCT number	2013-000410-38
Trial protocol	DE
Global end of trial date	28 July 2014

Results information

Result version number	v1 (current)
This version publication date	19 February 2016
First version publication date	22 July 2015

Trial information

Trial identification

Sponsor protocol code	LP0066-1019

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01963793
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	LEO Pharma A/S
Sponsor organisation address	Industriparken 55, Ballerup, Denmark,
Public contact	Clinical Trial Disclosure Manager, LEO Pharma A/S, 0045 44945888, ctr.disclosure@Leo-pharma.com
Scientific contact	Clinical Trial Disclosure Manager, LEO Pharma A/S, 0045 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	28 July 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	28 July 2014
Global end of trial reached?	Yes
Global end of trial date	28 July 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To investigate the efficacy of topical treatment with aprepitant on pruritus compared to placebo, after 4 weeks of treatment

Protection of trial subjects:

n/a

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	12 November 2013
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: 20
Worldwide total number of subjects	20
EEA total number of subjects	20

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)	18
From 65 to 84 years	2
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

23 subjects were enrolled in the trial and 3 were screening failures, the remaining 20 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

Blinding implementation details:

Subjects were treated with aprepitant on one extremity and vehicle gel on the other 1:1 thus acting as their own intra-individual controls
10 subjects: LEFT: aprepitant 10 mg/g gel , RIGHT: vehicle gel
and
10 subjects: LEFT: vehicle gel RIGHT: aprepitant 10 mg/g gel

Arms

Are arms mutually exclusive?	No
Arm title	Aprepitant 10 mg/g gel

Arm description:

20 subjects treated with aprepitant 10mg/g gel on either left or right extremity

Arm type	Experimental
Investigational medicinal product name	Aprepitant 10mg/g gel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Gel
Routes of administration	Topical use

Dosage and administration details:

Subjects were treated with aprepitant 10mg/g gel twice daily for four weeks (28 days).

Arm title	Vehicle gel

Arm description:

20 subjects were treated with vehicle gel on either left or right extremity

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

Dosage and administration details:

Subjects were treated with vehicle gel twice daily for 4 weeks (28 days)

Number of subjects in period 1	Aprepitant 10 mg/g gel	Vehicle gel
Started	20	20
Completed	20	20

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial
Reporting group description:	
All 20 randomised subjects were divided into two groups 1:1 10 with LEFT: aprepitant 10 mg/g gel and RIGHT: vehicle gel and 10 with LEFT: vehicle gel and RIGHT: aprepitant 10 mg/g gel	

Reporting group values	Overall trial	Total	
Number of subjects	20	20	
Age categorical Units: Subjects			
Adults (18-64 years)	18	18	
From 65-84 years	2	2	
Age continuous Units: years			
arithmetic mean	62.8		
full range (min-max)	45 to 81	-	
Gender categorical Units: Subjects			
Female	13	13	
Male	7	7	
Duration of Prurigo			
Subjects' medical history of prurigo			
Units: Months			
arithmetic mean	185		
full range (min-max)	14 to 816	-	

End points

End points reporting groups

Reporting group title	Aprepitant 10 mg/g gel
Reporting group description:	
20 subjects treated with aprepitant 10mg/g gel on either left or right extremity	
Reporting group title	Vehicle gel
Reporting group description:	
20 subjects were treated with vehicle gel on either left or right extremity	

Primary: Comparison of subjects' VAS assessements of pruritus at end of treatment

End point title	Comparison of subjects' VAS assessements of pruritus at end of treatment
End point description:	
Subjects' assessments of itch at end of treatment by use of a Visual Analogue Scale (VAS)	
End point type	Primary
End point timeframe:	
1-28 days (4 weeks)	

End point values	Aprepitant 10 mg/g gel	Vehicle gel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	20		
Units: Intensity of itch				
least squares mean (confidence interval 95%)	19.7 (9.5 to 29.8)	21.2 (11.1 to 31.4)		

Statistical analyses

Statistical analysis title	Subjects assessment of prutitus - end of treatment

Statistical analysis description:

The primary efficacy endpoint was compared between areas treated with aprepitant and vehicle. According to the clinical study protocol the comparison was to be done by means of a paired t-test on change from baseline. Instead, a mixed model was applied because this method allows for the correct adjustment of baseline values and also utilises the benefits of the left-right design inherent in the paired t-test.

Comparison groups	Aprepitant 10 mg/g gel v Vehicle gel
Number of subjects included in analysis	40
Analysis specification	Post-hoc
Analysis type	other[1]
P-value	= 0.58
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-1.51

Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.12
upper limit	4.11

Notes:

[1] - For the analysis of the primary efficacy endpoint (VAS assessments of pruritus at end of treatment (Day 28) for areas treated with aprepitant and vehicle) a mixed model with treatment and baseline pruritus as fixed effects and subject as random effect was used.

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Entire trial period (1-28 days)

Adverse event reporting additional description:

The trial was conducted as left/right intra-individual control and thus the subjects acted as their own controls, so each subject appear twice in the reporting of adverse events (one for each treatment area) and adverse events deemed unrelated to treatment (e.g. outside treatment area) were designated "treatment not defined".

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	16.0

Reporting groups

Reporting group title	Aprepitant gel

Reporting group description:

10 subjects treated on the right extremity
10 subjects treated on the left extremity

Reporting group title	Vehicle gel

Reporting group description:

Vehicle group:
10 subjects treated on the right extremity
10 subjects treated on the left extremity

Reporting group title	Treatment not defined

Reporting group description:

This group was created to include adverse events that were deemed unrelated to treatment with either aprepitant gel or vehicle gel (e.g adverse events outside the treatment area)

Serious adverse events	Aprepitant gel	Vehicle gel	Treatment not defined
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

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

Non-serious adverse events	Aprepitant gel	Vehicle gel	Treatment not defined
Total subjects affected by non-serious adverse events			
subjects affected / exposed	11 / 20 (55.00%)	15 / 20 (75.00%)	10 / 20 (50.00%)
Vascular disorders			

Flushing			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Hot flush			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Surgical and medical procedures			
Wound treatment			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			
Paraesthesia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	2 / 20 (10.00%)
occurrences (all)	0	0	2
General disorders and administration site conditions			
Application site discolouration			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Application site discomfort			
subjects affected / exposed	1 / 20 (5.00%)	2 / 20 (10.00%)	0 / 20 (0.00%)
occurrences (all)	4	3	0
Application site erythema			
subjects affected / exposed	1 / 20 (5.00%)	1 / 20 (5.00%)	0 / 20 (0.00%)
occurrences (all)	5	6	0
Application site haemorrhage			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Application site nodule			
subjects affected / exposed	1 / 20 (5.00%)	1 / 20 (5.00%)	0 / 20 (0.00%)
occurrences (all)	1	2	0
Application site pain			
subjects affected / exposed	8 / 20 (40.00%)	11 / 20 (55.00%)	0 / 20 (0.00%)
occurrences (all)	36	67	0
Application site paraesthesia			
subjects affected / exposed	1 / 20 (5.00%)	2 / 20 (10.00%)	0 / 20 (0.00%)
occurrences (all)	1	3	0

Application site pruritus			
subjects affected / exposed	1 / 20 (5.00%)	1 / 20 (5.00%)	0 / 20 (0.00%)
occurrences (all)	1	2	0
Application site urticaria			
subjects affected / exposed	2 / 20 (10.00%)	1 / 20 (5.00%)	0 / 20 (0.00%)
occurrences (all)	4	5	0
Application site vesicles			
subjects affected / exposed	1 / 20 (5.00%)	1 / 20 (5.00%)	0 / 20 (0.00%)
occurrences (all)	1	1	0
Fatigue			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	2
Eye disorders			
Visual impairment			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			
Dysphonia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Sneezing			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
Dermatitis allergic			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	2 / 20 (10.00%)
occurrences (all)	0	0	2
Erythema			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	4
Rash			
subjects affected / exposed	1 / 20 (5.00%)	1 / 20 (5.00%)	0 / 20 (0.00%)
occurrences (all)	1	1	0
Skin burning sensation			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	0 / 20 (0.00%)
occurrences (all)	0	1	0

Urticaria			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	13
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Restlessness			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	2
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Bursitis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	2
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	3 / 20 (15.00%)
occurrences (all)	0	0	3
Postoperative wound infection			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Wound infection			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Metabolism and nutrition disorders			
Hypercholesterolaemia			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	0 / 20 (0.00%)
occurrences (all)	0	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