



## Clinical trial results:

**A phase 3 study comparing an ointment containing calcipotriol 25 mcg/g plus hydrocortisone 10 mg/g (LEO 80190 ointment) with hydrocortisone 10 mg/g ointment, both applied once daily in the treatment of psoriasis vulgaris on the face and intertriginous areas**

**(Calcipotriol Plus Hydrocortisone in Paediatric Patients (Aged 6 to 17 Years) with Psoriasis Vulgaris on the Face and on the Intertriginous Areas)**

## Summary

EudraCT number	2009-010963-18
Trial protocol	DE FR
Global end of trial date	08 June 2010

## Results information

Result version number	v1 (current)
This version publication date	01 February 2016
First version publication date	22 July 2015

## Trial information

### Trial identification

Sponsor protocol code	LEO80190-O25
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### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01007591
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, 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)	Yes
EMA paediatric investigation plan number(s)	EMA-000277-PIP01-08
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?	Yes
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Notes:

## Results analysis stage

Analysis stage	Final
Date of interim/final analysis	08 June 2010
Is this the analysis of the primary completion data?	Yes
Primary completion date	08 June 2010
Global end of trial reached?	Yes
Global end of trial date	08 June 2010
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

To compare the efficacy of once daily treatment for up to 8 weeks of an ointment containing calcipotriol 25 mcg/g plus hydrocortisone 10 mg/g (LEO 80190 ointment) with an ointment containing hydrocortisone 10 mg/g in paediatric patients with psoriasis vulgaris on the face.

Protection of trial subjects:

Not applicable

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	13 October 2009
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	France: 16
Country: Number of subjects enrolled	Germany: 16
Country: Number of subjects enrolled	Canada: 8
Worldwide total number of subjects	40
EEA total number of subjects	32

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)	21

Adolescents (12-17 years)	19
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

Before randomization the study participants entered a washout period.

### 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	Subject, Investigator

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	Calcipotriol 25 mcg/g plus hydrocortisone 10 mg/g ointment

Arm description:

the 10 mg/g ointment is the LEO 80910 ointment

Arm type	Experimental
Investigational medicinal product name	LEO 80190 ointment
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Ointment
Routes of administration	Cutaneous use

Dosage and administration details:

Calcipotriol 25 mcg/g plus hydrocortisone 10 mg/g (LEO 80190 ointment) applied once daily in the treatment of psoriasis vulgaris on the face and intertriginous areas for 8 weeks (56 days)

<b>Arm title</b>	Hydrocortisone 10 mg/g Ointment
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Arm description: -

Arm type	Active comparator
Investigational medicinal product name	Hydrocortisone 1% Ointment
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Ointment
Routes of administration	Cutaneous use

Dosage and administration details:

Hydrocortisone 10 mg/g (LEO 80190 ointment) applied once daily in the treatment of psoriasis vulgaris on the face and intertriginous areas for 8 weeks

Number of subjects in period 1	Calcipotriol 25 mcg/g plus hydrocortisone 10 mg/g ointment	Hydrocortisone 10 mg/g Ointment
Started	27	13
Completed	26	12
Not completed	1	1
Voluntary	-	1

Adverse event, non-fatal	1	-
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## Baseline characteristics

### Reporting groups

Reporting group title	Calcipotriol 25 mcg/g plus hydrocortisone 10 mg/g ointment
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Reporting group description:

the 10 mg/g ointment is the LEO 80910 ointment

Reporting group title	Hydrocortisone 10 mg/g Ointment
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Reporting group description: -

Reporting group values	Calcipotriol 25 mcg/g plus hydrocortisone 10 mg/g ointment	Hydrocortisone 10 mg/g Ointment	Total
Number of subjects	27	13	40
Age categorical Units: Subjects			
Children (2-11 years)	14	7	21
Adolescents (12-17 years)	13	6	19
Age continuous Units: years			
arithmetic mean	11.8	11.6	
full range (min-max)	6 to 17	6 to 17	-
Gender categorical Units: Subjects			
Female	19	7	26
Male	8	6	14

## End points

### End points reporting groups

Reporting group title	Calcipotriol 25 mcg/g plus hydrocortisone 10 mg/g ointment
Reporting group description:	the 10 mg/g ointment is the LEO 80910 ointment
Reporting group title	Hydrocortisone 10 mg/g Ointment
Reporting group description:	-

### Primary: The percent change in Psoriasis Area and Severity Index (PASI) of the face from baseline to week 8

End point title	The percent change in Psoriasis Area and Severity Index (PASI) of the face from baseline to week 8
End point description:	This study only used the PASI subscale evaluating the face
End point type	Primary
End point timeframe:	8 weeks

End point values	Calcipotriol 25 mcg/g plus hydrocortisone 10 mg/g ointment	Hydrocortisone 10 mg/g Ointment		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27	13		
Units: Percentage change in PASI week 8				
arithmetic mean (standard deviation)	-60.8 (± 51.1)	-54.2 (± 59.2)		

### Statistical analyses

Statistical analysis title	Analysis 1
Comparison groups	Calcipotriol 25 mcg/g plus hydrocortisone 10 mg/g ointment v Hydrocortisone 10 mg/g Ointment
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.75 <sup>[1]</sup>
Method	ANOVA

Notes:

[1] - There was no statistical difference between the treatment groups (mean difference -6.02; 95% CI: -43.7, 31.7)

### Secondary: The percentage change in PASI of the face from baseline to week 4

End point title	The percentage change in PASI of the face from baseline to
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End point description:

This study only used the PASI subscale evaluating the face

End point type

Secondary

End point timeframe:

4 weeks

<b>End point values</b>	Calcipotriol 25 mcg/g plus hydrocortisone 10 mg/g ointment	Hydrocortisone 10 mg/g Ointment		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27	13		
Units: Percentage change in PASI week 4				
arithmetic mean (standard deviation)	-54.8 (± 33.8)	54.9 (± 37.3)		

### Statistical analyses

<b>Statistical analysis title</b>	Analysis 1
Comparison groups	Calcipotriol 25 mcg/g plus hydrocortisone 10 mg/g ointment v Hydrocortisone 10 mg/g Ointment
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.97 [2]
Method	ANOVA

Notes:

[2] - There was no statistically significant difference between the treatment groups (mean difference -0.43; 95% CI: -24.3 to 23.4)

### Secondary: Subjects with "controlled disease" according to the Investigator's Global Assessment (IGA) of disease severity of the face at week 8

End point title	Subjects with "controlled disease" according to the Investigator's Global Assessment (IGA) of disease severity of the face at week 8
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End point description:

End point type

Secondary

End point timeframe:

8 weeks



<b>End point values</b>	Calcipotriol 25 mcg/g plus hydrocortisone 10 mg/g ointment	Hydrocortisone 10 mg/g Ointment		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27	13		
Units: Number of Subjects	13	7		

## Statistical analyses

<b>Statistical analysis title</b>	Analysis 1
Statistical analysis description:	
Test for homogeneity of odds ratios across age group using Breslow-Day test. The Breslow-Day test for homogeneity of the odds ratios across age group were performed using a significance level of 10%.	
Comparison groups	Calcipotriol 25 mcg/g plus hydrocortisone 10 mg/g ointment v Hydrocortisone 10 mg/g Ointment
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0425 <sup>[3]</sup>
Method	Breslow-Day test
Parameter estimate	Odds ratio (OR)
Point estimate	1.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.4
upper limit	4.7

Notes:

[3] - There was a significant effect of age; this is considered due to the small numbers in the age subgroups.

<b>Statistical analysis title</b>	Analysis 2
Comparison groups	Calcipotriol 25 mcg/g plus hydrocortisone 10 mg/g ointment v Hydrocortisone 10 mg/g Ointment
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.67 <sup>[4]</sup>
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	1.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.4
upper limit	4.7

Notes:

[4] - Treatment comparison by Cochran-Mantel-Haenszel test adjusted for age group. There was no significant difference between the treatments.

**Secondary: The percentage change in Total Sign Score (TSS) of the intertriginous areas from baseline to week 8**

End point title	The percentage change in Total Sign Score (TSS) of the intertriginous areas from baseline to week 8
End point description:	
End point type	Secondary
End point timeframe:	8 weeks

<b>End point values</b>	Calcipotriol 25 mcg/g plus hydrocortisone 10 mg/g ointment	Hydrocortisone 10 mg/g Ointment		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	4		
Units: Percentage change in TSS week 8				
arithmetic mean (standard deviation)	-56.6 (± 38.2)	-93.2 (± 8.2)		

**Statistical analyses**

<b>Statistical analysis title</b>	Analysis 1
Comparison groups	Calcipotriol 25 mcg/g plus hydrocortisone 10 mg/g ointment v Hydrocortisone 10 mg/g Ointment
Number of subjects included in analysis	11
Analysis specification	Pre-specified
Analysis type	other <sup>[5]</sup>
P-value	= 0.072 <sup>[6]</sup>
Method	ANOVA

Notes:

[5] - They analysis of these secondary response criteria was to use the Hochberg correction to account for multiplicity.

[6] - There was no statistically significant difference between the treatment groups (mean difference 40.58; 95% CI: -4.8 to 86.0).

**Secondary: Subjects with "controlled disease" according to the IGA of disease severity of the intertriginous areas at week 8**

End point title	Subjects with "controlled disease" according to the IGA of disease severity of the intertriginous areas at week 8
End point description:	
End point type	Secondary
End point timeframe:	8 weeks

<b>End point values</b>	Calcipotriol 25 mcg/g plus hydrocortisone 10 mg/g ointment	Hydrocortisone 10 mg/g Ointment		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	4		
Units: Number of Subjects	2	4		

## Statistical analyses

<b>Statistical analysis title</b>	Analysis 1
Statistical analysis description:	
Test for homogeneity of odds ratios across age group using Breslow-Day test. The Breslow-Day test for homogeneity of the odds ratios across age group were performed using a significance level of 10%.	
Comparison groups	Calcipotriol 25 mcg/g plus hydrocortisone 10 mg/g ointment v Hydrocortisone 10 mg/g Ointment
Number of subjects included in analysis	11
Analysis specification	Pre-specified
Analysis type	superiority
Method	Breslow-Day test
Parameter estimate	Odds ratio (OR)
Point estimate	6.54
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.9
upper limit	50

<b>Statistical analysis title</b>	Analysis 2
Statistical analysis description:	
Treatment comparison by Cochran-Mantel-Haenszel test adjusted for age group.	
Comparison groups	Calcipotriol 25 mcg/g plus hydrocortisone 10 mg/g ointment v Hydrocortisone 10 mg/g Ointment
Number of subjects included in analysis	11
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.059 <sup>[7]</sup>
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	6.54
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.9
upper limit	50

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Notes:

[7] - There was no significant difference between the treatments.

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

8 weeks

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	6.1
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### Reporting groups

Reporting group title	Calcipotriol 25 mcg/g plus hydrocortisone 10 mg/g ointment
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Reporting group description:

the 10 mg/g ointment is the LEO 80910 ointment

Reporting group title	Hydrocortisone 10 mg/g Ointment
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Reporting group description: -

Serious adverse events	Calcipotriol 25 mcg/g plus hydrocortisone 10 mg/g ointment	Hydrocortisone 10 mg/g Ointment	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 27 (0.00%)	0 / 13 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

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

Non-serious adverse events	Calcipotriol 25 mcg/g plus hydrocortisone 10 mg/g ointment	Hydrocortisone 10 mg/g Ointment	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	17 / 27 (62.96%)	9 / 13 (69.23%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Skin papilloma			
subjects affected / exposed	0 / 27 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Injury, poisoning and procedural complications			
Joint sprain			

subjects affected / exposed occurrences (all)	1 / 27 (3.70%) 1	0 / 13 (0.00%) 0	
Nervous system disorders Headache subjects affected / exposed occurrences (all)	3 / 27 (11.11%) 9	1 / 13 (7.69%) 1	
General disorders and administration site conditions Application site burning subjects affected / exposed occurrences (all)  Influenza like illness subjects affected / exposed occurrences (all)  Pyrexia subjects affected / exposed occurrences (all)	1 / 27 (3.70%) 4  1 / 27 (3.70%) 1  1 / 27 (3.70%) 1	0 / 13 (0.00%) 0  0 / 13 (0.00%) 0  0 / 13 (0.00%) 0	
Ear and labyrinth disorders Ear pain subjects affected / exposed occurrences (all)	1 / 27 (3.70%) 1	0 / 13 (0.00%) 0	
Eye disorders Conjunctivitis subjects affected / exposed occurrences (all)	1 / 27 (3.70%) 1	1 / 13 (7.69%) 1	
Reproductive system and breast disorders Pruritus genital subjects affected / exposed occurrences (all)  Dysmenorrhoea subjects affected / exposed occurrences (all)	0 / 27 (0.00%) 0  1 / 27 (3.70%) 1	1 / 13 (7.69%) 1  0 / 13 (0.00%) 0	
Gastrointestinal disorders Abdominal pain subjects affected / exposed occurrences (all)  Abdominal pain upper	2 / 27 (7.41%) 3	0 / 13 (0.00%) 0	

subjects affected / exposed occurrences (all)	1 / 27 (3.70%) 1	0 / 13 (0.00%) 0	
Nausea subjects affected / exposed occurrences (all)	1 / 27 (3.70%) 1	0 / 13 (0.00%) 0	
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	1 / 27 (3.70%) 1	0 / 13 (0.00%) 0	
Pharyngolaryngeal pain subjects affected / exposed occurrences (all)	3 / 27 (11.11%) 3	2 / 13 (15.38%) 2	
Skin and subcutaneous tissue disorders Erythema subjects affected / exposed occurrences (all)	2 / 27 (7.41%) 3	0 / 13 (0.00%) 0	
Nail dystrophy subjects affected / exposed occurrences (all)	1 / 27 (3.70%) 1	0 / 13 (0.00%) 0	
Psoriasis subjects affected / exposed occurrences (all)	3 / 27 (11.11%) 6	0 / 13 (0.00%) 0	
Rash scaly subjects affected / exposed occurrences (all)	1 / 27 (3.70%) 1	0 / 13 (0.00%) 0	
Skin burning sensation subjects affected / exposed occurrences (all)	1 / 27 (3.70%) 2	0 / 13 (0.00%) 0	
Skin irritation subjects affected / exposed occurrences (all)	1 / 27 (3.70%) 1	0 / 13 (0.00%) 0	
Musculoskeletal and connective tissue disorders Pain in extremity subjects affected / exposed occurrences (all)	1 / 27 (3.70%) 1	0 / 13 (0.00%) 0	
Infections and infestations			

Acute tonsillitis			
subjects affected / exposed	1 / 27 (3.70%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Bladder infection			
subjects affected / exposed	1 / 27 (3.70%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Bronchitis			
subjects affected / exposed	1 / 27 (3.70%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Gastroenteritis			
subjects affected / exposed	2 / 27 (7.41%)	0 / 13 (0.00%)	
occurrences (all)	2	0	
Herpes simplex			
subjects affected / exposed	1 / 27 (3.70%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Influenza			
subjects affected / exposed	1 / 27 (3.70%)	2 / 13 (15.38%)	
occurrences (all)	1	2	
Nasopharyngitis			
subjects affected / exposed	5 / 27 (18.52%)	2 / 13 (15.38%)	
occurrences (all)	6	2	
Pharyngitis streptococcal			
subjects affected / exposed	1 / 27 (3.70%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Tonsillitis			
subjects affected / exposed	1 / 27 (3.70%)	0 / 13 (0.00%)	
occurrences (all)	1	0	



## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
10 September 2009	Definition of the contraceptive methods considered adequate for the study and an indication of the possible need for ongoing assessment of birth control methods and sexual contact during the study.  Guidance on the use of concomitant therapies for psoriasis  Details of unacceptable treatment efficacy for the withdrawal criteria

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported