



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 |
|-----------------------|--------------|

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 |
|--|-----|

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 |
|------------------------------|-----|

| | |
|------------------|--|
| Arm title | 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)

| | |
|------------------|---------------------------------|
| Arm title | Hydrocortisone 10 mg/g Ointment |
|------------------|---------------------------------|

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 | - |
|--------------------------|---|---|

Baseline characteristics

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: -

| 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 ^[1] |
| 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 |
|-----------------|--|

End point description:

This study only used the PASI subscale evaluating the face

End point type

Secondary

End point timeframe:

4 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 4 | | | | |
| arithmetic mean (standard deviation) | -54.8 (± 33.8) | 54.9 (± 37.3) | | |

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 | = 0.97 ^[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 |
|-----------------|--|

End point description:

End point type

Secondary

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: Number of Subjects | 13 | 7 | | |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | 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 ^[3] |
| 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.

| | |
|---|--|
| Statistical analysis title | 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 ^[4] |
| 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 |

| | | | | |
|--|--|---------------------------------|--|--|
| 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 | 7 | 4 | | |
| Units: Percentage change in TSS week 8 | | | | |
| arithmetic mean (standard deviation) | -56.6 (± 38.2) | -93.2 (± 8.2) | | |

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 | 11 |
| Analysis specification | Pre-specified |
| Analysis type | other ^[5] |
| P-value | = 0.072 ^[6] |
| 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 |

| | | | | |
|-----------------------------|--|---------------------------------|--|--|
| 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 | 7 | 4 | | |
| Units: Number of Subjects | 2 | 4 | | |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | 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 |

| | |
|--|--|
| Statistical analysis title | 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 ^[7] |
| 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 |

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 |
|-----------------|------------|

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|-----|
| Dictionary version | 6.1 |
|--------------------|-----|

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: -

| 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:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported