



Clinical trial results:

Double-blind, randomised clinical study comparing efficacy and safety of Calcipotriol 50 µg/g_Betamethasone 0.5 mg/g Gel (Test) vs. Daivobet (R) Gel (Reference) vs. Vehicle in patients with scalp psoriasis.

Summary

| | |
|--------------------------|------------------|
| EudraCT number | 2016-001106-42 |
| Trial protocol | DE |
| Global end of trial date | 27 November 2017 |

Results information

| | |
|--------------------------------|--------------|
| Result version number | v1 (current) |
| This version publication date | 15 May 2020 |
| First version publication date | 15 May 2020 |

Trial information

Trial identification

| | |
|-----------------------|--------------------|
| Sponsor protocol code | 16-01/CalciBet-Gel |
|-----------------------|--------------------|

Additional study identifiers

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

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | Dermapharm AG |
| Sponsor organisation address | Lil-Dagover Ring 7, Gruenwald, Germany, 82031 |
| Public contact | Clinical Research Department, Dermapharm AG, Clinicaltrials.Dermapharm@dermapharm.com |
| Scientific contact | Clinical Research Department, Dermapharm AG, Clinicaltrials.Dermapharm@dermapharm.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 | 23 April 2018 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 27 November 2017 |
| Global end of trial reached? | Yes |
| Global end of trial date | 27 November 2017 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

Evaluation of the efficacy and safety of a new gel containing 50 µg/g calcipotriol and 0.5 mg/g betamethasone vs. the reference product Daivobet®Gel vs. vehicle in patients with psoriasis of the scalp. The study aimed to show non-inferiority of the test preparation as compared to Daivobet® Gel and superiority of both active medications over the vehicle.

Protection of trial subjects:

The study was conducted in accordance with the principles of ICH GCP, the declaration of Helsinki, as well as all other applicable ethical and legal requirements. The reference product is already registered and commercially available for years in Europe. For the purpose of approval the efficacy and safety of this medicinal product has already been proven in clinical trials. An patient with lack of efficacy and/or deterioration of symptoms could stop treatment with study drug at any moment based on the clinical judgment of the investigator and/or on his/ her own request and without giving reasons. The planned procedures within the trial represented no special risk to the patients as, apart from blood sampling for laboratory safety evaluations, there were no further invasive procedures planned.

Background therapy: -

Evidence for comparator: -

| | |
|---|-------------------|
| Actual start date of recruitment | 01 September 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: 234 |
| Worldwide total number of subjects | 234 |
| EEA total number of subjects | 234 |

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) | 165 |
| From 65 to 84 years | 69 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

Multi-centric study in Germany; first volunteer enrolled: 06-Dec-2016; date of last completion: 27-Nov-2017

Pre-assignment

Screening details:

Diagnosis and main criteria for inclusion:

Women and men ≥ 18 years of age; diagnosis of "scalp psoriasis vulgaris" involving at least 20% of the total scalp area; activity parameters erythema, scaling, induration and pruritus (assessed on a scale from 0 to 3): sum score of all four parameters ≥ 6 and scaling + erythema ≥ 4 and scaling ≥ 2

Period 1

| | |
|------------------------------|--|
| Period 1 title | Treatment period (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator, Monitor, Data analyst |

Blinding implementation details:

The bottles containing the study medications were neutral white. The labels on the bottles were identical for all three preparations. All three study medications were indistinguishable with respect to visual characteristics.

Arms

| | |
|------------------------------|-----|
| Are arms mutually exclusive? | Yes |
|------------------------------|-----|

| | |
|------------------|--------------|
| Arm title | Test product |
|------------------|--------------|

Arm description: -

| | |
|--|------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Calcipotriol Combi Gel |
| Investigational medicinal product code | D05AX52 |
| Other name | |
| Pharmaceutical forms | Gel |
| Routes of administration | Cutaneous use |

Dosage and administration details:

1 to 4 g per day, once daily

| | |
|------------------|-------------------|
| Arm title | Reference product |
|------------------|-------------------|

Arm description: -

| | |
|--|-------------------|
| Arm type | Active comparator |
| Investigational medicinal product name | Daivobet Gel |
| Investigational medicinal product code | D05AX52 |
| Other name | |
| Pharmaceutical forms | Gel |
| Routes of administration | Cutaneous use |

Dosage and administration details:

1 to 4 g per day, once daily

| | |
|------------------|---------|
| Arm title | Vehicle |
|------------------|---------|

Arm description: -

| | |
|----------|---------|
| Arm type | Placebo |
|----------|---------|

| | |
|--|---------------|
| Investigational medicinal product name | Vehicle |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Gel |
| Routes of administration | Cutaneous use |

Dosage and administration details:

1 to 4 g per day, once daily

| Number of subjects in period 1 | Test product | Reference product | Vehicle |
|---------------------------------------|--------------|-------------------|---------|
| Started | 79 | 74 | 81 |
| Completed | 73 | 72 | 75 |
| Not completed | 6 | 2 | 6 |
| Adverse event, non-fatal | 3 | - | 3 |
| Lost to follow-up | - | - | 1 |
| Healing | 3 | 2 | - |
| Lack of efficacy | - | - | 2 |

Baseline characteristics

Reporting groups

| | |
|-----------------------|------------------|
| Reporting group title | Treatment period |
|-----------------------|------------------|

Reporting group description: -

| Reporting group values | Treatment period | Total | |
|---|------------------|-------|--|
| Number of subjects | 234 | 234 | |
| 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) | 165 | 165 | |
| From 65-84 years | 69 | 69 | |
| 85 years and over | 0 | 0 | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 138 | 138 | |
| Male | 96 | 96 | |

End points

End points reporting groups

| | |
|--------------------------------|-------------------|
| Reporting group title | Test product |
| Reporting group description: - | |
| Reporting group title | Reference product |
| Reporting group description: - | |
| Reporting group title | Vehicle |
| Reporting group description: - | |

Primary: Primary endpoint

| | |
|---|------------------|
| End point title | Primary endpoint |
| End point description: Change of the modified Total Severity Sign Score (mTSS), defined as the sum of the score values of the four activity parameters erythema, scaling, induration and pruritus. | |
| End point type | Primary |
| End point timeframe: Baseline to end of week 4 (EOT) | |

| End point values | Test product | Reference product | Vehicle | |
|---|---------------------|---------------------|---------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 71 | 67 | 81 | |
| Units: sum of score values | | | | |
| arithmetic mean (confidence interval 95%) | 7.45 (7.07 to 7.84) | 7.67 (7.28 to 8.07) | 3.76 (3.21 to 4.32) | |

Statistical analyses

| | |
|--|----------------------------------|
| Statistical analysis title | Therapeutic equivalence |
| Statistical analysis description: The non-inferiority limit was set to $\Delta = 1.5$ in the study protocol. The corresponding test was carried out one-sided with $\alpha = 0.025$. Statistical proof of non-inferiority is attained if the lower limit of the two-sided 95% confidence interval (CI) for $\mu_{\text{Test}} - \mu_{\text{Reference}}$ is larger than $-\Delta = -1.5$. Analysis of covariance (ANCOVA) with baseline adjustment was applied as testing procedure. | |
| Comparison groups | Test product v Reference product |
| Number of subjects included in analysis | 138 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -0.22 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.77 |
| upper limit | 0.33 |

| | |
|--|--|
| Statistical analysis title | Superiority of test product to vehicle |
| Statistical analysis description: | |
| The analysis was intended to provide supportive evidence with regard to assay sensitivity. | |
| Comparison groups | Test product v Vehicle |
| Number of subjects included in analysis | 152 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 |
| Method | ANCOVA |

| | |
|---|---|
| Statistical analysis title | Superiority of reference product to vehicle |
| Statistical analysis description: | |
| This analysis was intended to provide supportive evidence to assay sensitivity. | |
| Comparison groups | Reference product v Vehicle |
| Number of subjects included in analysis | 148 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 |
| Method | ANCOVA |

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From baseline to the last visit (EOT, 4 weeks)

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|-----------------|----------------|
| Assessment type | Non-systematic |
|-----------------|----------------|

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 20.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|--------------|
| Reporting group title | Test product |
|-----------------------|--------------|

Reporting group description: -

| | |
|-----------------------|-------------------|
| Reporting group title | Reference product |
|-----------------------|-------------------|

Reporting group description: -

| | |
|-----------------------|---------|
| Reporting group title | Vehicle |
|-----------------------|---------|

Reporting group description: -

| Serious adverse events | Test product | Reference product | Vehicle |
|---|----------------|-------------------|----------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | 0 / 74 (0.00%) | 0 / 81 (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: 0.05 %

| Non-serious adverse events | Test product | Reference product | Vehicle |
|---|------------------|-------------------|----------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 17 / 79 (21.52%) | 15 / 74 (20.27%) | 8 / 81 (9.88%) |
| Investigations | | | |
| Cortisol decreased | | | |
| subjects affected / exposed | 1 / 79 (1.27%) | 0 / 74 (0.00%) | 0 / 81 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Cortisol increased | | | |
| subjects affected / exposed | 1 / 79 (1.27%) | 1 / 74 (1.35%) | 0 / 81 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Gamma-glutamyltransferase increased | | | |

| | | | |
|--|---------------------|---------------------|---------------------|
| subjects affected / exposed occurrences (all) | 0 / 79 (0.00%) 0 | 0 / 74 (0.00%) 0 | 1 / 81 (1.23%) 1 |
| Injury, poisoning and procedural complications | | | |
| Arthropod sting | | | |
| subjects affected / exposed | 1 / 79 (1.27%) | 0 / 74 (0.00%) | 0 / 81 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Joint dislocation | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | 1 / 74 (1.35%) | 0 / 81 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Road traffic accident | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | 1 / 74 (1.35%) | 0 / 81 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Nervous system disorders | | | |
| Burning sensation | | | |
| subjects affected / exposed | 1 / 79 (1.27%) | 0 / 74 (0.00%) | 0 / 81 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Headache | | | |
| subjects affected / exposed | 2 / 79 (2.53%) | 2 / 74 (2.70%) | 0 / 81 (0.00%) |
| occurrences (all) | 2 | 2 | 0 |
| Migraine | | | |
| subjects affected / exposed | 2 / 79 (2.53%) | 0 / 74 (0.00%) | 0 / 81 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Radiculopathy | | | |
| subjects affected / exposed | 1 / 79 (1.27%) | 0 / 74 (0.00%) | 0 / 81 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Sciatica | | | |
| subjects affected / exposed | 1 / 79 (1.27%) | 0 / 74 (0.00%) | 0 / 81 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Blood and lymphatic system disorders | | | |
| Thrombocytopenia | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | 1 / 74 (1.35%) | 0 / 81 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| General disorders and administration site conditions | | | |
| Application site dermatitis | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | 0 / 74 (0.00%) | 1 / 81 (1.23%) |
| occurrences (all) | 0 | 0 | 1 |

| | | | |
|--|---------------------|---------------------|---------------------|
| Application site dryness subjects affected / exposed occurrences (all) | 1 / 79 (1.27%) 1 | 0 / 74 (0.00%) 0 | 0 / 81 (0.00%) 0 |
| Application site joint discomfort subjects affected / exposed occurrences (all) | 1 / 79 (1.27%) 1 | 0 / 74 (0.00%) 0 | 0 / 81 (0.00%) 0 |
| Application site laceration subjects affected / exposed occurrences (all) | 1 / 79 (1.27%) 1 | 0 / 74 (0.00%) 0 | 0 / 81 (0.00%) 0 |
| Application site pain subjects affected / exposed occurrences (all) | 0 / 79 (0.00%) 0 | 1 / 74 (1.35%) 1 | 0 / 81 (0.00%) 0 |
| Eye disorders Eczema eyelids subjects affected / exposed occurrences (all) | 0 / 79 (0.00%) 0 | 0 / 74 (0.00%) 0 | 1 / 81 (1.23%) 1 |
| Gastrointestinal disorders Constipation subjects affected / exposed occurrences (all) | 1 / 79 (1.27%) 1 | 0 / 74 (0.00%) 0 | 0 / 81 (0.00%) 0 |
| Respiratory, thoracic and mediastinal disorders Rhinitis allergic subjects affected / exposed occurrences (all) | 1 / 79 (1.27%) 1 | 0 / 74 (0.00%) 0 | 0 / 81 (0.00%) 0 |
| Skin and subcutaneous tissue disorders Alopecia subjects affected / exposed occurrences (all) | 1 / 79 (1.27%) 1 | 0 / 74 (0.00%) 0 | 0 / 81 (0.00%) 0 |
| Erythema subjects affected / exposed occurrences (all) | 1 / 79 (1.27%) 1 | 0 / 74 (0.00%) 0 | 0 / 81 (0.00%) 0 |
| Psoriasis subjects affected / exposed occurrences (all) | 0 / 79 (0.00%) 0 | 0 / 74 (0.00%) 0 | 1 / 81 (1.23%) 1 |
| Rash papular | | | |

| | | | |
|--|---------------------|---------------------|---------------------|
| subjects affected / exposed occurrences (all) | 1 / 79 (1.27%) 1 | 0 / 74 (0.00%) 0 | 0 / 81 (0.00%) 0 |
| Seborrhoea subjects affected / exposed occurrences (all) | 2 / 79 (2.53%) 2 | 2 / 74 (2.70%) 2 | 2 / 81 (2.47%) 2 |
| Endocrine disorders Glucocorticoid deficiency subjects affected / exposed occurrences (all) | 0 / 79 (0.00%) 0 | 1 / 74 (1.35%) 1 | 0 / 81 (0.00%) 0 |
| Infections and infestations Eczema impetiginous subjects affected / exposed occurrences (all) | 0 / 79 (0.00%) 0 | 1 / 74 (1.35%) 1 | 0 / 81 (0.00%) 0 |
| Furuncle subjects affected / exposed occurrences (all) | 1 / 79 (1.27%) 1 | 0 / 74 (0.00%) 0 | 0 / 81 (0.00%) 0 |
| Nasopharyngitis subjects affected / exposed occurrences (all) | 2 / 79 (2.53%) 2 | 5 / 74 (6.76%) 5 | 1 / 81 (1.23%) 1 |
| Oral candidiasis subjects affected / exposed occurrences (all) | 0 / 79 (0.00%) 0 | 0 / 74 (0.00%) 0 | 1 / 81 (1.23%) 1 |
| Oral herpes subjects affected / exposed occurrences (all) | 0 / 79 (0.00%) 0 | 1 / 74 (1.35%) 1 | 0 / 81 (0.00%) 0 |
| Otitis externa subjects affected / exposed occurrences (all) | 0 / 79 (0.00%) 0 | 1 / 74 (1.35%) 1 | 0 / 81 (0.00%) 0 |
| Otitis media subjects affected / exposed occurrences (all) | 0 / 79 (0.00%) 0 | 0 / 74 (0.00%) 0 | 1 / 81 (1.23%) 1 |
| Root canal infection subjects affected / exposed occurrences (all) | 0 / 79 (0.00%) 0 | 1 / 74 (1.35%) 1 | 0 / 81 (0.00%) 0 |
| Upper respiratory tract infection | | | |

| | | | |
|--------------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 1 / 79 (1.27%) | 0 / 74 (0.00%) | 0 / 81 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Vulvovaginal mycotic infection | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | 0 / 74 (0.00%) | 1 / 81 (1.23%) |
| occurrences (all) | 0 | 0 | 1 |

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

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

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|------|
| None |
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Notes: