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 Δ = 1.5 in the study protocol. The correspond-ing test was carried out one-sided with α = 0.025. Statistical proof of non-inferiority is attained if the lower limit of the two-sided 95% confidence interval (CI) for μTest - μReference is larger than -Δ = -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)	
Assessment type	Non-systematic
Dictionary used	
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	0 / 79 (0.00%)	0 / 74 (0.00%)	1 / 81 (1.23%)
occurrences (all)	0	0	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	1 / 79 (1.27%)	0 / 74 (0.00%)	0 / 81 (0.00%)
occurrences (all)	1	0	0
Application site joint discomfort			
subjects affected / exposed	1 / 79 (1.27%)	0 / 74 (0.00%)	0 / 81 (0.00%)
occurrences (all)	1	0	0
Application site laceration			
subjects affected / exposed	1 / 79 (1.27%)	0 / 74 (0.00%)	0 / 81 (0.00%)
occurrences (all)	1	0	0
Application site pain			
subjects affected / exposed	0 / 79 (0.00%)	1 / 74 (1.35%)	0 / 81 (0.00%)
occurrences (all)	0	1	0
Eye disorders			
Eczema eyelids			
subjects affected / exposed	0 / 79 (0.00%)	0 / 74 (0.00%)	1 / 81 (1.23%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	1 / 79 (1.27%)	0 / 74 (0.00%)	0 / 81 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
Rhinitis allergic			
subjects affected / exposed	1 / 79 (1.27%)	0 / 74 (0.00%)	0 / 81 (0.00%)
occurrences (all)	1	0	0
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	1 / 79 (1.27%)	0 / 74 (0.00%)	0 / 81 (0.00%)
occurrences (all)	1	0	0
Erythema			
subjects affected / exposed	1 / 79 (1.27%)	0 / 74 (0.00%)	0 / 81 (0.00%)
occurrences (all)	1	0	0
Psoriasis			
subjects affected / exposed	0 / 79 (0.00%)	0 / 74 (0.00%)	1 / 81 (1.23%)
occurrences (all)	0	0	1
Rash papular			

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

None

Notes: