Clinical trial results:
Double blind, randomized, clinical study to compare the efficacy and safety of betamethasone 0,05%_salicyclic acid 2% solution vs. Diprosalic solution vs. vehicle for the treatment of psoriasis capitis

Summary

EudraCT number	2010-024033-24
Trial protocol	DE
Global end of trial date	15 October 2013

Results information

Result version number	v1 (current)
This version publication date	14 February 2016
First version publication date	14 February 2016

Trial information

Trial identification

Sponsor protocol code	11-01/BSal-L

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, 82031, Germany, Gruenwald
Public contact	Head of clinical department, Dermapharm AG, 0049 08964186-0,
Scientific contact	Head of clinical department, Dermapharm AG, 0049 08964186-0,

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 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	15 October 2013
Global end of trial reached?	Yes
Global end of trial date	15 October 2013
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 0,05% betamethasone 2% salicylic acid solution vs. the originator Diprosalic solution (licensed) vs. vehicle in patients with psoriasis of the scalp

Protection of trial subjects:

There were no specific measures necessary.

Background therapy:

There was no background therapy.

Evidence for comparator:

The trial aimed to show non-inferiority with regard to the comparator in order to obtain a generic marketing authorization for the test product.

Actual start date of recruitment	29 June 2011
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: 225
Worldwide total number of subjects	225
EEA total number of subjects	225

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)	143
From 65 to 84 years	72
85 years and over	10

Subject disposition

Recruitment

Recruitment details:

All study centres in Germany
First patient first visit: 04 July 2011
Last patient last visit: 15 October 2013

Pre-assignment

Screening details:

Main criteria for inclusion:
Women and men ≥ 18 years of age
Diagnosis of "scalp psoriasis" according to generally accepted criteria
Affection of at least 20% of the scalp
Affection of up to 50% or, in case of progression of psoriasis vulgaris during the last four weeks, up to 30% of the body surface
Score values as specified in the protocol

Period 1

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

Blinding implementation details:

All study preparations were indistinguishable in terms of appearance and were filled in white bottles of identical appearance.

Arms

Are arms mutually exclusive?	Yes
Arm title	BetaSal Solution

Arm description:

Test product

Arm type	Experimental
Investigational medicinal product name	Betamethasone 0.05%_Salicylic Acid 2% Solution
Investigational medicinal product code	D07XC01
Other name	
Pharmaceutical forms	Cutaneous solution
Routes of administration	Cutaneous use

Dosage and administration details:

Twice per day. Total dose depends on the extent of the area to be treated.

Arm title	Diprosalic Solution

Arm description:

Reference product

Arm type	Active comparator
Investigational medicinal product name	Diprosalic
Investigational medicinal product code	D07XC01
Other name	
Pharmaceutical forms	Cutaneous solution
Routes of administration	Cutaneous use

Dosage and administration details:

Twice per day. Total dose depends on the extent of the area to be treated.

Arm title	Vehicle

Arm description: -	
Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cutaneous solution
Routes of administration	Cutaneous use

Dosage and administration details:

Twice per day. Total amount depends on the area to be treated.

Number of subjects in period 1	BetaSal Solution	Diprosalic Solution	Vehicle
Started	75	77	73
Completed	72	74	69
Not completed	3	3	4
Adverse event, non-fatal	1	-	1
Technical-logistic reasons	1	-	-
Pregnancy	-	1	-
Lost to follow-up	1	-	-
Low cortisol values	-	1	-
Lack of efficacy	-	1	3

Period 2

Period 2 title	Follow-up Period
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Investigator, Monitor, Subject

Blinding implementation details:

No treatment in the follow-up period.

Arms

Are arms mutually exclusive?	Yes
Arm title	BetaSal Solution

Arm description:

Test product

Arm type	Experimental
Investigational medicinal product name	Betamethasone 0.05%_Salicylic Acid 2% Solution
Investigational medicinal product code	D07XC01
Other name	
Pharmaceutical forms	Cutaneous solution
Routes of administration	Cutaneous use

Dosage and administration details:
Twice per day. Total dose depends on the extent of the area to be treated.

Arm title	Diprosalic Solution
Arm description: Reference product	
Arm type	Active comparator
Investigational medicinal product name	Diprosalic
Investigational medicinal product code	D07XC01
Other name	
Pharmaceutical forms	Cutaneous solution
Routes of administration	Cutaneous use

Dosage and administration details:
Twice per day. Total dose depends on the extent of the area to be treated.

Arm title	Vehicle
Arm description: -	
Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cutaneous solution
Routes of administration	Cutaneous use

Dosage and administration details:
Twice per day. Total amount depends on the area to be treated.

Number of subjects in period 2	BetaSal Solution	Diprosalic Solution	Vehicle
Started	72	74	69
Completed	70	71	62
Not completed	2	3	7
Consent withdrawn by subject	1	1	-
Lost to follow-up	1	1	2
Lack of efficacy	-	1	5

Baseline characteristics

Reporting groups

Reporting group title	Treatment Period

Reporting group description: -

Reporting group values	Treatment Period	Total	
Number of subjects	225	225	
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)	0	0	
From 65-84 years	0	0	
85 years and over	0	0	
Adults (18 years and above)	225	225	
Age continuous Units: years			
arithmetic mean	55.7		
full range (min-max)	20 to 92	-	
Gender categorical			
Total number of subjects			
Units: Subjects			
Female	137	137	
Male	88	88	

Subject analysis sets

Subject analysis set title	ITT
Subject analysis set type	Intention-to-treat

Subject analysis set description:

includes all patients of the safety data who comply with the study diagnosis (according to the associated inclusion criterion) and provide the baseline value and at least one post baseline value under treatment

Subject analysis set title	PP
Subject analysis set type	Per protocol

Subject analysis set description:

includes all patients of the ITT data set who do not exhibit any major protocol violations

Subject analysis set title	Safety data
Subject analysis set type	Safety analysis

Subject analysis set description:

comprises all patients who had administered the study medication at least once

Reporting group values	ITT	PP	Safety data
Number of subjects	225	210	225
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	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)	0		
From 65-84 years	0		
85 years and over	0		
Adults (18 years and above)	225		
Age continuous Units: years			
arithmetic mean	55.7		
full range (min-max)	20 to 92		
Gender categorical			
Total number of subjects			
Units: Subjects			
Female	137	126	137
Male	88	84	88

End points

End points reporting groups

Reporting group title	BetaSal Solution
Reporting group description: Test product	
Reporting group title	Diprosalic Solution
Reporting group description: Reference product	
Reporting group title	Vehicle
Reporting group description: -	
Reporting group title	BetaSal Solution
Reporting group description: Test product	
Reporting group title	Diprosalic Solution
Reporting group description: Reference product	
Reporting group title	Vehicle
Reporting group description: -	
Subject analysis set title	ITT
Subject analysis set type	Intention-to-treat
Subject analysis set description: includes all patients of the safety data who comply with the study diagnosis (according to the associated inclusion criterion) and provide the baseline value and at least one post baseline value under treatment	
Subject analysis set title	PP
Subject analysis set type	Per protocol
Subject analysis set description: includes all patients of the ITT data set who do not exhibit any major protocol violations	
Subject analysis set title	Safety data
Subject analysis set type	Safety analysis
Subject analysis set description: comprises all patients who had administered the study medication at least once	

Primary: Treatment effect

End point title	Treatment effect
End point description: change of the sum score, defined as the sum of the score values of the individual activity parameters erythema, desquamation, thickening and pruritus, calculated as "value at visit 1 minus value at visit 4"	
End point type	Primary
End point timeframe: start of treatment (visit 1) and end of treatment (visit 4)	

End point values	BetaSal Solution	Diprosalic Solution	Vehicle	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	68	71	71	
Units: sum score values				
median (full range (min-max))	6 (1 to 11)	6 (-1 to 11)	2 (-2 to 10)	

Statistical analyses

Statistical analysis title	Analysis of efficacy

Statistical analysis description:

Non-inferiority test (one-sided test) with alpha = 2.5% (t-test model) and beta = 20%, based on the PP data set. The Non-Inferiority limit was set to 1.5

Comparison groups	Diprosalic Solution v BetaSal Solution
Number of subjects included in analysis	139
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	Mean difference (final values)
Point estimate	0.35
Confidence interval	
level	Other: 97.5 %
sides	1-sided
lower limit	-0.36

Other pre-specified: Superiority of Test over Vehicle

End point title	Superiority of Test over Vehicle[1]

End point description:

change of the sum score, defined as the sum of the score values of the individual activity parameters erythema, desquamation, thickening and pruritus, calculated as "value at visit 1 minus value at visit 4"

End point type	Other pre-specified

End point timeframe:

start of treatment (visit 1) and end of treatment (visit 4)

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The statistical analysis for this end point served as verification of the assay sensitivity and had to be done individually for each active preparation in accordance with CPMP/EWP/908/99.

End point values	BetaSal Solution	Vehicle		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	75	73		
Units: sum score values				
number (not applicable)	5.9	2.27		

Statistical analyses

Statistical analysis title	Sensitivity analysis

Statistical analysis description:

Superiority of Test over Vehicle for the primary efficacy variable

Comparison groups	BetaSal Solution v Vehicle
Number of subjects included in analysis	148
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANCOVA

Other pre-specified: Superiority of Reference over Vehicle

End point title	Superiority of Reference over Vehicle[2]

End point description:

change of the sum score, defined as the sum of the score values of the individual activity parameters erythema, desquamation, thickening and pruritus, calculated as "value at visit 1 minus value at visit 4"

End point type	Other pre-specified

End point timeframe:

start of treatment (visit 1) and end of treatment (visit 4)

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: The statistical analysis for this end point served as verification of the assay sensitivity and had to be done individually for each active preparation in accordance with CPMP/EWP/908/99.

End point values	Diprosalic Solution	Vehicle		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	77	73		
Units: sum score values				
number (not applicable)	5.37	2.29		

Statistical analyses

Statistical analysis title	Sensitivity analysis
Comparison groups	Diprosalic Solution v Vehicle
Number of subjects included in analysis	150
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANCOVA

Adverse events

Adverse events information	
Timeframe for reporting adverse events: from the inclusion visit (visit 0) to the final visit (visit 5)	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	16.1

Reporting groups	
Reporting group title	BetaSal Solution
Reporting group description: Treatment arm with test product	
Reporting group title	Diprosalic Solution
Reporting group description: Treatment arm with reference product	
Reporting group title	Vehicle
Reporting group description: Treatment arm with placebo	

Serious adverse events	BetaSal Solution	Diprosalic Solution	Vehicle
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 75 (0.00%)	2 / 77 (2.60%)	0 / 73 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Alcohol poisoning			
subjects affected / exposed	0 / 75 (0.00%)	1 / 77 (1.30%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Urinary tract infection staphylococcal			
subjects affected / exposed	0 / 75 (0.00%)	1 / 77 (1.30%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 0.05 %

Non-serious adverse events	BetaSal Solution	Diprosalic Solution	Vehicle
Total subjects affected by non-serious adverse events			
subjects affected / exposed	12 / 75 (16.00%)	10 / 77 (12.99%)	13 / 73 (17.81%)
Investigations			
Blood glucose increased			
subjects affected / exposed	1 / 75 (1.33%)	2 / 77 (2.60%)	0 / 73 (0.00%)
occurrences (all)	1	2	0
Blood creatinine increased			
subjects affected / exposed	0 / 75 (0.00%)	1 / 77 (1.30%)	0 / 73 (0.00%)
occurrences (all)	0	1	0
Blood bilirubin increased			
subjects affected / exposed	0 / 75 (0.00%)	1 / 77 (1.30%)	0 / 73 (0.00%)
occurrences (all)	0	1	0
Blood cortisol increased			
subjects affected / exposed	1 / 75 (1.33%)	0 / 77 (0.00%)	2 / 73 (2.74%)
occurrences (all)	1	0	2
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Skin papilloma			
subjects affected / exposed	1 / 75 (1.33%)	0 / 77 (0.00%)	0 / 73 (0.00%)
occurrences (all)	1	0	0
Seborrhoeic keratosis			
subjects affected / exposed	1 / 75 (1.33%)	0 / 77 (0.00%)	0 / 73 (0.00%)
occurrences (all)	1	0	0
Injury, poisoning and procedural complications			
Arthropod sting			
subjects affected / exposed	0 / 75 (0.00%)	1 / 77 (1.30%)	0 / 73 (0.00%)
occurrences (all)	0	1	0
Arthropod bite			
subjects affected / exposed	1 / 75 (1.33%)	1 / 77 (1.30%)	0 / 73 (0.00%)
occurrences (all)	1	2	0
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 75 (1.33%)	0 / 77 (0.00%)	1 / 73 (1.37%)
occurrences (all)	1	0	1
General disorders and administration site conditions			

Application site pain			
subjects affected / exposed	0 / 75 (0.00%)	0 / 77 (0.00%)	2 / 73 (2.74%)
occurrences (all)	0	0	2
Application site pruritus			
subjects affected / exposed	0 / 75 (0.00%)	0 / 77 (0.00%)	1 / 73 (1.37%)
occurrences (all)	0	0	1
Application site dryness			
subjects affected / exposed	0 / 75 (0.00%)	0 / 77 (0.00%)	1 / 73 (1.37%)
occurrences (all)	0	0	1
Eye disorders			
Conjunctivitis			
subjects affected / exposed	1 / 75 (1.33%)	0 / 77 (0.00%)	0 / 73 (0.00%)
occurrences (all)	1	0	0
Conjunctivitis allergic			
subjects affected / exposed	0 / 75 (0.00%)	0 / 77 (0.00%)	1 / 73 (1.37%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	0 / 75 (0.00%)	1 / 77 (1.30%)	0 / 73 (0.00%)
occurrences (all)	0	1	0
Diarrhoea			
subjects affected / exposed	0 / 75 (0.00%)	1 / 77 (1.30%)	0 / 73 (0.00%)
occurrences (all)	0	1	0
Skin and subcutaneous tissue disorders			
Angioedema			
subjects affected / exposed	0 / 75 (0.00%)	0 / 77 (0.00%)	1 / 73 (1.37%)
occurrences (all)	0	0	1
Hyperkeratosis			
subjects affected / exposed	1 / 75 (1.33%)	0 / 77 (0.00%)	0 / 73 (0.00%)
occurrences (all)	1	0	0
Skin tightness			
subjects affected / exposed	0 / 75 (0.00%)	0 / 77 (0.00%)	1 / 73 (1.37%)
occurrences (all)	0	0	1
Eczema			
subjects affected / exposed	1 / 75 (1.33%)	0 / 77 (0.00%)	0 / 73 (0.00%)
occurrences (all)	1	0	0
Rosacea			

subjects affected / exposed	0 / 75 (0.00%)	0 / 77 (0.00%)	1 / 73 (1.37%)
occurrences (all)	0	0	1
Dermatitis			
subjects affected / exposed	0 / 75 (0.00%)	1 / 77 (1.30%)	0 / 73 (0.00%)
occurrences (all)	0	1	0
Skin burning sensation			
subjects affected / exposed	1 / 75 (1.33%)	0 / 77 (0.00%)	0 / 73 (0.00%)
occurrences (all)	1	0	0
Polymorphic light eruption			
subjects affected / exposed	0 / 75 (0.00%)	1 / 77 (1.30%)	0 / 73 (0.00%)
occurrences (all)	0	1	0
Renal and urinary disorders			
Hydronephrosis			
subjects affected / exposed	0 / 75 (0.00%)	1 / 77 (1.30%)	0 / 73 (0.00%)
occurrences (all)	0	1	0
Cystitis noninfective			
subjects affected / exposed	1 / 75 (1.33%)	0 / 77 (0.00%)	0 / 73 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal and connective tissue disorders			
Trigger finger			
subjects affected / exposed	0 / 75 (0.00%)	0 / 77 (0.00%)	1 / 73 (1.37%)
occurrences (all)	0	0	1
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	2 / 75 (2.67%)	1 / 77 (1.30%)	2 / 73 (2.74%)
occurrences (all)	2	1	2
Gastroenteritis			
subjects affected / exposed	0 / 75 (0.00%)	1 / 77 (1.30%)	0 / 73 (0.00%)
occurrences (all)	0	1	0
Bronchitis			
subjects affected / exposed	0 / 75 (0.00%)	0 / 77 (0.00%)	1 / 73 (1.37%)
occurrences (all)	0	0	1
Metabolism and nutrition disorders			
Hyperglycaemia			
subjects affected / exposed	0 / 75 (0.00%)	1 / 77 (1.30%)	0 / 73 (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