Clinical trial results:
A multi-center, randomized, double-blind, phase II trial with intraindividual comparison to assess superiority of Soventol HydroCort 1% cream versus vehicle on lesional skin in patients with mild atopic eczema, seborrheic eczema or stasis dermatitis and to assess safety of Soventol HydroCort 1% cream

Summary

EudraCT number	2013-000715-25
Trial protocol	DE
Global end of trial date	26 November 2013

Results information

Result version number	v1 (current)
This version publication date	09 September 2016
First version publication date	09 September 2016

Trial information

Trial identification

Sponsor protocol code	6520-9170-07

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	MEDICE Arzneimittel Pütter GmbH & Co. KG
Sponsor organisation address	Kuhloweg 37, Iserlohn, Germany, 58638
Public contact	Medical Department, MEDICE Arzneimittel Pütter GmbH & Co. KG, +49 023719370, info@medice.de
Scientific contact	Medical Department, MEDICE Arzneimittel Pütter GmbH & Co. KG, +49 023719370, info@medice.de

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	26 November 2013
Is this the analysis of the primary completion data?	Yes
Primary completion date	26 November 2013
Global end of trial reached?	Yes
Global end of trial date	26 November 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the superiority of Soventol HydroCort 1% cream versus vehicle and to assess safety of Soventol HydroCort 1% cream

Protection of trial subjects:

A specific treatment was to be discontinued if a treatment area showed worsening effects after one week of treatment. Since the appearance of the skin disease was described by several criteria (edema/papulation, oozing/crusts, excoriations, scaling and lichenification) discontinuation of special test areas were to be determined at the discretion of the investigator

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	19 August 2013
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: 50
Worldwide total number of subjects	50
EEA total number of subjects	50

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)	45
From 65 to 84 years	5
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The participants were selected via advertisements and from the patient pool of the 4 selected trial centers.

Pre-assignment

Screening details:

50 patients were enrolled in this clinical trial and were with normal trial completion. There were no dropouts. For this trial, a total of 51 patients were screened (1 screening failure) of which 50 patients were randomized.

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	Investigator, Monitor, Data analyst, Carer, Assessor, Subject

Arms

Are arms mutually exclusive?	No
Arm title	Soventol HydroCort 1% Cream

Arm description:

1% Hydrocortisone Cream

Arm type	Experimental
Investigational medicinal product name	1% Hydrocortisone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cream
Routes of administration	Cutaneous use

Dosage and administration details:

Up to 3 FTUs corresponding to approximately 1.5 g of the IMPs Soventol HydroCort 1 % cream and the active ingredient-free vehicle were applied to the respective treatment areas three times daily (morning, noon and evening) over a 2-week treatment period by the patient. The applied IMPs were distributed equally in the test areas using finger stalls. The time between the 2 applications should have included minimum 3 hours and maximum 18 hours. The application times were documented in the patient diaries. On trial Day 1 the application of the IMPs was demonstrated to the patient at the trial center. The first treatment (Day 1) as well as one treatment on Days 4 and 8, each were carried out at the trial center.

Arm title	Placebo

Arm description:

Active ingrediant free vehicle to IMP

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cream
Routes of administration	Cutaneous use

Dosage and administration details:

Up to 3 FTUs corresponding to approximately 1.5 g of the IMPs Soventol HydroCort 1 % cream and the active ingredient-free vehicle were applied to the respective treatment areas three times daily (morning, noon and evening) over a 2-week treatment period by the patient. The applied IMPs were distributed equally in the test areas using finger stalls. The time between the 2 applications should have included minimum 3 hours and maximum 18 hours. The application times were documented in the patient

diaries. On trial Day 1 the application of the IMPs was demonstrated to the patient at the trial center. The first treatment (Day 1) as well as one treatment on Days 4 and 8, each were carried out at the trial center.

Number of subjects in period 1	Soventol HydroCort 1% Cream	Placebo
Started	50	50
Completed	50	50

Baseline characteristics

Reporting groups

Reporting group title	overall trial

Reporting group description: -

Reporting group values	overall trial	Total	
Number of subjects	50	50	
Age categorical Units: Subjects			
Adults (18-64 years)	45	45	
From 65-84 years	5	5	
Gender categorical Units: Subjects			
Female	28	28	
Male	22	22	

Subject analysis sets

Subject analysis set title	Safety set (SES)
Subject analysis set type	Safety analysis

Subject analysis set description:

The SES comprised of all patients who received any IMP at least once. All safety analyses were based on the SES.

Subject analysis set title	Full analysis set (FAS)
Subject analysis set type	Full analysis

Subject analysis set description:

The FAS included all randomized patients who received at least one dose of IMP, and had at least one post-baseline assessment. The ITT analysis was based on the FAS.

Subject analysis set title	Valid case set (VSC)
Subject analysis set type	Per protocol

Subject analysis set description:

The VCS included all patients of the FAS without any major protocol deviation.

Reporting group values	Safety set (SES)	Full analysis set (FAS)	Valid case set (VSC)
Number of subjects	50	50	49
Age categorical Units: Subjects			
Adults (18-64 years)	45	45	44
From 65-84 years	5	5	5
Gender categorical Units: Subjects			
Female	28	28	27
Male	22	22	22

End points

End points reporting groups

Reporting group title	Soventol HydroCort 1% Cream
Reporting group description:	
1% Hydrocortisone Cream	
Reporting group title	Placebo
Reporting group description:	
Active ingrediant free vehicle to IMP	
Subject analysis set title	Safety set (SES)
Subject analysis set type	Safety analysis
Subject analysis set description:	
The SES comprised of all patients who received any IMP at least once. All safety analyses were based on the SES.	
Subject analysis set title	Full analysis set (FAS)
Subject analysis set type	Full analysis
Subject analysis set description:	
The FAS included all randomized patients who received at least one dose of IMP, and had at least one post-baseline assessment. The ITT analysis was based on the FAS.	
Subject analysis set title	Valid case set (VSC)
Subject analysis set type	Per protocol
Subject analysis set description:	
The VCS included all patients of the FAS without any major protocol deviation.	

Primary: Erythema Scores - AUC comparison (Full analysis set)

End point title	Erythema Scores - AUC comparison (Full analysis set)
End point description:	
The primary aim of superiority of IMP vs. the vehicle to IMP was evaluated with respect to the area under the time curve (AUC) of baseline corrected erythema scores determined applying the linear trapezoidal rule over the whole experimental phase. Treatment success resulted in a decrease in erythema score, corresponding to a negative baseline corrected AUC.	
End point type	Primary
End point timeframe:	
The severity of the lesions was clinically assessed by the investigator on Days 1, 4, 8 and 15	

End point values	Soventol HydroCort 1% Cream	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	50		
Units: AUC				
arithmetic mean (standard error)	-14.9 (± 8.18)	-9.4 (± 10.67)		

Statistical analyses

Statistical analysis title	Erythema Scores - AUC comperison (FAS)

Statistical analysis description:

The superiority of Soventol 1% vs. Placebo with respect to the AUC of baseline corrected erythema scores was assessed by testing the Hypothesis H0 against the alternative H1 applying the two-sided paired t-test with a type I error of 5 %.

Comparison groups	Placebo v Soventol HydroCort 1% Cream
Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	superiority[1]
P-value	= 0.0002
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Point estimate	-5.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.2
upper limit	-2.8

Notes:

[1] - If the obtained p-value was less than 0.05 and the mean AUC for IMP was less than the mean AUC for the vehicle to IMP, then the superiority of the IMP vs. vehicle was established.

Primary: Erythema Scores - AUC comparison (Valid case set)

End point title	Erythema Scores - AUC comparison (Valid case set)

End point description:

End point type	Primary

End point timeframe:

The severity of the lesions was clinically assessed by the investigator on Days 1, 4, 8 and 15

End point values	Soventol HydroCort 1% Cream	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	49	49		
Units: AUC				
geometric mean (standard error)	-14.7 (± 8.17)	-9.1 (± 10.58)		

Statistical analyses

Statistical analysis title	Erythema Scores - AUC comparison (VCS)
Comparison groups	Soventol HydroCort 1% Cream v Placebo

Number of subjects included in analysis	98
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0002
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Point estimate	-5.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.4
upper limit	-2.9

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
AEs were recorded throughout the entire trial	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	16.1

Reporting groups	
Reporting group title	all subjects
Reporting group description:	
Non-serious TEAEs were reported in 4 patients which were not corresponding to a specific test field.	

Serious adverse events	all subjects		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 50 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

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

Non-serious adverse events	all subjects		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 50 (8.00%)		
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 50 (2.00%)		
occurrences (all)	1		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 50 (2.00%)		
occurrences (all)	1		
Nausea			
subjects affected / exposed	2 / 50 (4.00%)		
occurrences (all)	2		
Musculoskeletal and connective tissue disorders			

Back pain subjects affected / exposed occurrences (all)	1 / 50 (2.00%) 1		
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all)	1 / 50 (2.00%) 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

None reported