Clinical trial results:
Double-blind, randomized clinical trial to compare the efficacy and safety of fusidic acid 2% betamethasone 0,1% cream vs. Fucicort cream vs. vehicle for patients with bacterial infected eczema

These results have been removed from public view whilst they are reviewed and may need to be corrected before being returned to public view

Summary

EudraCT number	2011-004370-28
Trial protocol	DE
Global end of trial date	26 June 2014

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	11-03/FusBet-C

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	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	13 November 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	26 June 2014
Global end of trial reached?	Yes
Global end of trial date	26 June 2014
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 fusidic acid 2% betamethasone 0.1% cream vs. the originator Fucicort cream (licensed) vs. vehicle in patients with bacterial infected eczema

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	21 August 2012
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: 400
Worldwide total number of subjects	400
EEA total number of subjects	400

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)	317
From 65 to 84 years	78
85 years and over	5

Subject disposition

Recruitment

Recruitment details:

all study centers in Germany; first patient first visit: 07 September 2012; last patient last visit: 26 June 2014

Pre-assignment

Screening details:

Main criteria for inclusion:
women and men ≥ 18 years of age; diagnosis of "bacterial super-infected eczema" based on clinical symptoms in a treatment area between 5 and 25 cm²; at least moderately severe clinical picture with presence of the clinical parameter "exudate/pus"

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 tubes of identical appearance.

Arms

Are arms mutually exclusive?	Yes
Arm title	FusBet Cream

Arm description:

Test product

Arm type	Experimental
Investigational medicinal product name	Fusidic acid 2%_betamethasone 0.1% cream
Investigational medicinal product code	D07CC01
Other name	
Pharmaceutical forms	Cream
Routes of administration	Cutaneous use

Dosage and administration details:

Twice daily on the affected area of the skin.

Arm title	Fucicort Cream

Arm description:

Reference product

Arm type	Active comparator
Investigational medicinal product name	Fucicort
Investigational medicinal product code	D07CC01
Other name	
Pharmaceutical forms	Cream
Routes of administration	Cutaneous use

Dosage and administration details:

Twice daily on the affected area of the skin.

Arm title	Vehicle

Arm description: -

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:

Twice daily on the affected area of the skin.

Number of subjects in period 1	FusBet Cream	Fucicort Cream	Vehicle
Started	161	158	81
Completed	150	149	72
Not completed	11	9	9
Consent withdrawn by subject	-	1	-
Adverse event, non-fatal	1	-	-
Lost to follow-up	6	4	1
Lack of efficacy	4	4	8

Period 2

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

Blinding implementation details:

No treatment in the follow-up period.

Arms

Are arms mutually exclusive?	Yes
Arm title	FusBet Cream

Arm description:

Test product

Arm type	Experimental
Investigational medicinal product name	Fusidic acid 2%_betamethasone 0.1% cream
Investigational medicinal product code	D07CC01
Other name	
Pharmaceutical forms	Cream
Routes of administration	Cutaneous use

Dosage and administration details:

Application twice daily at the affected area of the skin.

Arm title	Fucicort Cream

Arm description:

Reference product

Arm type	Active comparator
Investigational medicinal product name	Fucicort
Investigational medicinal product code	D07CC01
Other name	
Pharmaceutical forms	Cream
Routes of administration	Cutaneous use

Dosage and administration details:

Twice daily on the affected area of the skin.

Arm title	Vehicle

Arm description: -

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:

Twice daily on the affected area of the skin.

Number of subjects in period 2	FusBet Cream	Fucicort Cream	Vehicle
Started	150	149	72
Completed	146	144	64
Not completed	4	5	8
Consent withdrawn by subject	-	2	1
Technical-logistic reasons	-	-	1
Lost to follow-up	2	2	-
Lack of efficacy	2	1	6

Baseline characteristics

Reporting groups

Reporting group title	Treatment Period

Reporting group description: -

Reporting group values	Treatment Period	Total	
Number of subjects	400	400	
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)	317	317	
From 65-84 years	78	78	
85 years and over	5	5	
Gender categorical Units: Subjects			
Female	173	173	
Male	227	227	

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 set 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
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
Number of subjects	392	359	394
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0

Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	309	282	311
From 65-84 years	78	72	78
85 years and over	5	5	5
Gender categorical Units: Subjects			
Female	170	154	171
Male	222	205	223

End points

End points reporting groups

Reporting group title	FusBet Cream
Reporting group description: Test product	
Reporting group title	Fucicort Cream
Reporting group description: Reference product	
Reporting group title	Vehicle
Reporting group description: -	
Reporting group title	FusBet Cream
Reporting group description: Test product	
Reporting group title	Fucicort Cream
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 set 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
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[1]
End point description: Number (percentage) of patients with "clinical treatment success" according to predefined criteria at end of treatment	
End point type	Primary
End point timeframe: start of treatment (visit 1) and end of treatment (visit 3)	

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 orimary goal of this trial was to show non-inferiority of the test to the reference product. The vehicle arm served as verification of the assay sensitivity. The three end point tests had to be done separately in order to avoid the otherwise necessary adjustment of the significance levels.

End point values	FusBet Cream	Fucicort Cream	ITT	PP
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	142	144	311	286
Units: Number	122	109	249	231

Statistical analyses

Statistical analysis title	Analysis of efficacy
Statistical analysis description:	
Non-inferiority test (one-sided test) with alpha = 0.025 and beta = 0.20, based on the PP data set. The Non-Inferiority limit was set to 0.1 (= 10%)	
Comparison groups	FusBet Cream v Fucicort Cream
Number of subjects included in analysis	286
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	Mean difference (final values)
Point estimate	0.1022
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.0048
upper limit	0.1997

Other pre-specified: Superiority of Test over Vehicle

End point title	Superiority of Test over Vehicle[2]
End point description:	
Number (percentage) of patients with "clinical treatment success" according to predefined criteria at end of treatment	
End point type	Other pre-specified
End point timeframe:	
start of treatment (visit 1) and end of treatment (visit 3)	
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	FusBet Cream	Vehicle	ITT	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	157	81	392	
Units: Number	133	46	295	

Statistical analyses

Statistical analysis title	Sensitivity analysis
Statistical analysis description:	
Superiority of Test over Vehicle for the primary efficacy variable	
Comparison groups	FusBet Cream v Vehicle
Number of subjects included in analysis	238
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Fisher exact

Other pre-specified: Superiority of Reference over Vehicle

End point title	Superiority of Reference over Vehicle[3]
End point description:	
Number (percentage) of patients with "clinical treatment success" according to predefined criteria at end of treatment	
End point type	Other pre-specified
End point timeframe:	
start of treatment (visit 1) and end of treatment (visit 3)	
Notes:	
[3] - 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	Fucicort Cream	Vehicle	ITT	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	154	81	392	
Units: Number	116	46	295	

Statistical analyses

Statistical analysis title	Sensitivity analysis
Statistical analysis description:	
Superiority of Reference over Vehicle for the primary efficacy variable	
Comparison groups	Fucicort Cream v Vehicle
Number of subjects included in analysis	235
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0047
Method	Fisher exact

Adverse events

Adverse events information	
Timeframe for reporting adverse events: from the inclusion visit (visit 1) to the final visit (visit 4)	
Assessment type	Non-systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	17.1
Reporting groups	
Reporting group title	FusBet Cream
Reporting group description: treatment arm with test product	
Reporting group title	Fucicort Cream
Reporting group description: treatment arm with reference product	
Reporting group title	Vehicle
Reporting group description: treatment arm with placebo	

Serious adverse events	FusBet Cream	Fucicort Cream	Vehicle
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 158 (0.00%)	0 / 155 (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	FusBet Cream	Fucicort Cream	Vehicle
Total subjects affected by non-serious adverse events			
subjects affected / exposed	10 / 158 (6.33%)	7 / 155 (4.52%)	4 / 81 (4.94%)
Injury, poisoning and procedural complications			
Burns second degree			
subjects affected / exposed	0 / 158 (0.00%)	0 / 155 (0.00%)	1 / 81 (1.23%)
occurrences (all)	0	0	1
Fall			
subjects affected / exposed	1 / 158 (0.63%)	0 / 155 (0.00%)	0 / 81 (0.00%)
occurrences (all)	1	0	0
Rib fracture			

subjects affected / exposed	1 / 158 (0.63%)	0 / 155 (0.00%)	0 / 81 (0.00%)
occurrences (all)	1	0	0
Surgical and medical procedures			
Skin neoplasm excision			
subjects affected / exposed	1 / 158 (0.63%)	0 / 155 (0.00%)	0 / 81 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 158 (0.63%)	0 / 155 (0.00%)	0 / 81 (0.00%)
occurrences (all)	1	0	0
Toothache			
subjects affected / exposed	0 / 158 (0.00%)	1 / 155 (0.65%)	0 / 81 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 158 (0.00%)	1 / 155 (0.65%)	0 / 81 (0.00%)
occurrences (all)	0	1	0
Skin and subcutaneous tissue disorders			
Dermatitis			
subjects affected / exposed	0 / 158 (0.00%)	1 / 155 (0.65%)	1 / 81 (1.23%)
occurrences (all)	0	1	1
Dermatitis atopic			
subjects affected / exposed	1 / 158 (0.63%)	0 / 155 (0.00%)	0 / 81 (0.00%)
occurrences (all)	1	0	0
Eczema			
subjects affected / exposed	0 / 158 (0.00%)	2 / 155 (1.29%)	0 / 81 (0.00%)
occurrences (all)	0	2	0
Solar dermatitis			
subjects affected / exposed	1 / 158 (0.63%)	0 / 155 (0.00%)	0 / 81 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal and connective tissue disorders			
Osteitis			
subjects affected / exposed	1 / 158 (0.63%)	0 / 155 (0.00%)	0 / 81 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			

Abscess limb			
subjects affected / exposed	1 / 158 (0.63%)	0 / 155 (0.00%)	0 / 81 (0.00%)
occurrences (all)	1	0	0
Cystitis			
subjects affected / exposed	0 / 158 (0.00%)	1 / 155 (0.65%)	0 / 81 (0.00%)
occurrences (all)	0	1	0
Folliculitis			
subjects affected / exposed	1 / 158 (0.63%)	0 / 155 (0.00%)	0 / 81 (0.00%)
occurrences (all)	1	0	0
Gingival abscess			
subjects affected / exposed	0 / 158 (0.00%)	0 / 155 (0.00%)	1 / 81 (1.23%)
occurrences (all)	0	0	1
Nasopharyngitis			
subjects affected / exposed	2 / 158 (1.27%)	1 / 155 (0.65%)	1 / 81 (1.23%)
occurrences (all)	2	1	1
Superinfection			
subjects affected / exposed	1 / 158 (0.63%)	0 / 155 (0.00%)	0 / 81 (0.00%)
occurrences (all)	1	0	0
Tinea pedis			
subjects affected / exposed	1 / 158 (0.63%)	0 / 155 (0.00%)	0 / 81 (0.00%)
occurrences (all)	1	0	0
Viral rash			
subjects affected / exposed	0 / 158 (0.00%)	1 / 155 (0.65%)	0 / 81 (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