Clinical trial results:
Double-blind, randomised clinical study comparing efficacy and safety of Gentamicin 0.1%_Betamethasone 0.05% Cream (Test) vs. Diprogenta (R) Cream (Reference) vs. Vehicle in patients with bacterial infected eczema

Summary

EudraCT number	2014-005518-44
Trial protocol	DE
Global end of trial date	11 January 2017

Results information

Result version number	v1 (current)
This version publication date	11 January 2022
First version publication date	11 January 2022

Trial information

Trial identification

Sponsor protocol code	15-01/GentaBet-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, Grünwald, Germany, 82031
Public contact	Clinical Research Department, Dermapharm AG, +49 089641860, Clinicaltrials.Dermapharm@dermapharm.com
Scientific contact	Clinical Research Department, Dermapharm AG, +49 089641860, 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	09 November 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	11 January 2017
Global end of trial reached?	Yes
Global end of trial date	11 January 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Assessment of efficacy and safety of a new cream with gentamicin 0.1% and betamethasone dipropionate 0.05% in comparison with the approved preparation Diprogenta(R) Cream and the underlying 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 comparable efficacy and safety to the comparator in order to obtain a generic marketing authorization for the test product.

Actual start date of recruitment	04 November 2015
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: 401
Worldwide total number of subjects	401
EEA total number of subjects	401

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)	343

From 65 to 84 years	51
85 years and over	7

Subject disposition

Recruitment

Recruitment details:

12 study centers in Germany; first patient first visit: 17 November 2015; last patient last visit: 11 January 2017

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 cm^2; 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	GentaBet Cream

Arm description:

Test product

Arm type	Experimental
Investigational medicinal product name	Gentamicin 0.1%_Betamethasone 0.05% Cream
Investigational medicinal product code	D07CC01
Other name	
Pharmaceutical forms	Cream
Routes of administration	Cutaneous use

Dosage and administration details:

twice daily (in the morning and in the evening) at the affected area of the skin

Arm title	Diprogenta

Arm description:

Reference Product

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

Dosage and administration details:

twice daily (in the morning and the evening) 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 (in the morning and the evening) on the affected area of the skin

Number of subjects in period 1	GentaBet Cream	Diprogenta	Vehicle
Started	159	159	83
Completed	148	149	76
Not completed	11	10	7
Consent withdrawn by subject	3	3	-
Adverse event, non-fatal	1	3	-
Lost to follow-up	4	2	3
Lack of efficacy	2	1	2
Protocol deviation	1	1	2

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	GentaBet Cream

Arm description:

Test product

Arm type	Experimental
Investigational medicinal product name	Gentamicin 0.1%_Betamethasone 0.05% Cream
Investigational medicinal product code	D07CC01
Other name	
Pharmaceutical forms	Cream
Routes of administration	Cutaneous use

Dosage and administration details:

twice daily (in the morning and in the evening) at the affected area of the skin

Arm title	Diprogenta

Arm description:	
Reference Product	
Arm type	Active comparator
Investigational medicinal product name	Diprogenta Cream
Investigational medicinal product code	D07CC01
Other name	
Pharmaceutical forms	Cream
Routes of administration	Cutaneous use
Dosage and administration details:	
twice daily (in the morning and the evening) 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 (in the morning and the evening) on the affected area of the skin	

Number of subjects in period 2	GentaBet Cream	Diprogenta	Vehicle
Started	148	149	76
Completed	142	142	74
Not completed	6	7	2
Consent withdrawn by subject	2	2	-
Complete healing at day 7	2	2	-
Lost to follow-up	2	1	-
Lack of efficacy	-	2	2

Baseline characteristics

Reporting groups	
Reporting group title	Treatment Period

Reporting group description: -

Reporting group values	Treatment Period	Total	
Number of subjects	401	401	
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)	334	334	
From 65-84 years	47	47	
85 years and over	6	6	
Not recorded	14	14	
Gender categorical Units: Subjects			
Female	198	198	
Male	203	203	

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 provide the baseline value and at least one post-baseline value of the symptom score.

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

Subject analysis set description:

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

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 violation

Reporting group values	ITT	Safety data set	PP
Number of subjects	387	387	357
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)	334	334	309
From 65-84 years	47	47	43
85 years and over	6	6	5
Not recorded	0	0	0
Gender categorical Units: Subjects			
Female	192	192	184
Male	195	195	173

End points

End points reporting groups

Reporting group title	GentaBet Cream
Reporting group description: Test product	
Reporting group title	Diprogenta
Reporting group description: Reference Product	
Reporting group title	Vehicle
Reporting group description: -	
Reporting group title	GentaBet Cream
Reporting group description: Test product	
Reporting group title	Diprogenta
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 provide the baseline value and at least one post-baseline value of the symptom score.	
Subject analysis set title	Safety data set
Subject analysis set type	Safety analysis
Subject analysis set description: comprises all patients who had administered the study medication at least once	
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 violation	

Primary: Treatment effect

End point title	Treatment effect
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) to end of treatment (visit 3)	

End point values	GentaBet Cream	Diprogenta	Vehicle	ITT
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	140	142	78	309
Units: Number	127	124	46	268

End point values	PP			
Subject group type	Subject analysis set			
Number of subjects analysed	282			
Units: Number	251			

Statistical analyses

Statistical analysis title	Analysis of efficacy
Statistical analysis description:	
Non-Inferiority test (one-sided) with alpha = 0.025 and beta = 0.20, based on the PP data set. The Non-Inferiority margin was set to 0.1 (= 10%)	
Comparison groups	Diprogenta v GentaBet Cream
Number of subjects included in analysis	282
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	Mean difference (final values)
Point estimate	0.0339
Confidence interval	
level	95 %
sides	1-sided
lower limit	-0.046

Other pre-specified: Superiority of Test over Vehicle

End point title	Superiority of Test over Vehicle[1]
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) to 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 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	GentaBet Cream	Vehicle	ITT	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	154	78	232	
Units: Number	135	46	181	

Statistical analyses

Statistical analysis title	Sensitivity analysis

Statistical analysis description:

Superiority of the efficacy of Test over Vehicle for the primary variable

Comparison groups	GentaBet Cream v Vehicle
Number of subjects included in analysis	232
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[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) to 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	Diprogenta	Vehicle	ITT	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	155	78	233	
Units: Number	133	46	179	

Statistical analyses

Statistical analysis title	Sensitivity analysis

Statistical analysis description:

Superiority of the efficacy of Reference over Vehicle for the primary variable

Comparison groups	Vehicle v Diprogenta

Number of subjects included in analysis	233
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
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	20.1

Reporting groups	
Reporting group title	GentaBet Cream
Reporting group description: Test product	
Reporting group title	Diprogenta
Reporting group description: Reference Product	
Reporting group title	Vehicle
Reporting group description: -	

Serious adverse events	GentaBet Cream	Diprogenta	Vehicle
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 154 (0.00%)	2 / 155 (1.29%)	0 / 78 (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			
Fall			
subjects affected / exposed	0 / 154 (0.00%)	1 / 155 (0.65%)	0 / 78 (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
Surgical and medical procedures			
Hospitalisation			
subjects affected / exposed	0 / 154 (0.00%)	1 / 155 (0.65%)	0 / 78 (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
Nervous system disorders			
Syncope			
subjects affected / exposed	0 / 154 (0.00%)	1 / 155 (0.65%)	0 / 78 (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	GentaBet Cream	Diprogenta	Vehicle
Total subjects affected by non-serious adverse events			
subjects affected / exposed	11 / 154 (7.14%)	11 / 155 (7.10%)	3 / 78 (3.85%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Seborrhoeic keratosis			
subjects affected / exposed	1 / 154 (0.65%)	0 / 155 (0.00%)	0 / 78 (0.00%)
occurrences (all)	1	0	0
Squamous cell carcinoma			
subjects affected / exposed	1 / 154 (0.65%)	0 / 155 (0.00%)	0 / 78 (0.00%)
occurrences (all)	1	0	0
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 154 (0.00%)	1 / 155 (0.65%)	0 / 78 (0.00%)
occurrences (all)	0	1	0
Skin abrasion			
subjects affected / exposed	1 / 154 (0.65%)	0 / 155 (0.00%)	0 / 78 (0.00%)
occurrences (all)	1	0	0
Wound			
subjects affected / exposed	0 / 154 (0.00%)	1 / 155 (0.65%)	0 / 78 (0.00%)
occurrences (all)	0	1	0
Surgical and medical procedures			
Varicose vein operation			
subjects affected / exposed	0 / 154 (0.00%)	1 / 155 (0.65%)	0 / 78 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 154 (0.65%)	0 / 155 (0.00%)	0 / 78 (0.00%)
occurrences (all)	1	0	0
Sciatica			

subjects affected / exposed	0 / 154 (0.00%)	1 / 155 (0.65%)	0 / 78 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions			
Application site pain			
subjects affected / exposed	0 / 154 (0.00%)	2 / 155 (1.29%)	0 / 78 (0.00%)
occurrences (all)	0	2	0
Pyrexia			
subjects affected / exposed	1 / 154 (0.65%)	0 / 155 (0.00%)	0 / 78 (0.00%)
occurrences (all)	1	0	0
Eye disorders			
Visual impairment			
subjects affected / exposed	1 / 154 (0.65%)	0 / 155 (0.00%)	0 / 78 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
Toothache			
subjects affected / exposed	1 / 154 (0.65%)	0 / 155 (0.00%)	0 / 78 (0.00%)
occurrences (all)	1	0	0
Reproductive system and breast disorders			
Prostatitis			
subjects affected / exposed	0 / 154 (0.00%)	1 / 155 (0.65%)	0 / 78 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
Dysphonia			
subjects affected / exposed	1 / 154 (0.65%)	0 / 155 (0.00%)	0 / 78 (0.00%)
occurrences (all)	1	0	0
Skin and subcutaneous tissue disorders			
Eczema			
subjects affected / exposed	1 / 154 (0.65%)	0 / 155 (0.00%)	0 / 78 (0.00%)
occurrences (all)	1	0	0
Nail bed inflammation			
subjects affected / exposed	0 / 154 (0.00%)	1 / 155 (0.65%)	0 / 78 (0.00%)
occurrences (all)	0	1	0
Seborrhoeic dermatitis			
subjects affected / exposed	0 / 154 (0.00%)	1 / 155 (0.65%)	0 / 78 (0.00%)
occurrences (all)	0	1	0
Skin ulcer			

subjects affected / exposed	0 / 154 (0.00%)	1 / 155 (0.65%)	0 / 78 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 154 (0.65%)	0 / 155 (0.00%)	0 / 78 (0.00%)
occurrences (all)	1	0	0
Pain in extremity			
subjects affected / exposed	0 / 154 (0.00%)	0 / 155 (0.00%)	1 / 78 (1.28%)
occurrences (all)	0	0	1
Infections and infestations			
Cellulitis			
subjects affected / exposed	1 / 154 (0.65%)	0 / 155 (0.00%)	0 / 78 (0.00%)
occurrences (all)	1	0	0
Impetigo			
subjects affected / exposed	1 / 154 (0.65%)	0 / 155 (0.00%)	0 / 78 (0.00%)
occurrences (all)	1	0	0
Oral herpes			
subjects affected / exposed	1 / 154 (0.65%)	0 / 155 (0.00%)	0 / 78 (0.00%)
occurrences (all)	1	0	0
Respiratory tract infection			
subjects affected / exposed	0 / 154 (0.00%)	1 / 155 (0.65%)	2 / 78 (2.56%)
occurrences (all)	0	1	2
Tinea pedis			
subjects affected / exposed	1 / 154 (0.65%)	0 / 155 (0.00%)	0 / 78 (0.00%)
occurrences (all)	1	0	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

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

None reported

Notes: