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

Summary

EudraCT number	2014-005519-18
Trial protocol	DE
Global end of trial date	09 June 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	15-02/GentaBet-S

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, +49 08964180, 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	02 January 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	09 June 2017
Global end of trial reached?	Yes
Global end of trial date	09 June 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 ointment with gentamicin 0.1% and betamethasone dipropionate 0.05% in comparison with the approved preparation Diprogenta® Ointment 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	27 January 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: 416
Worldwide total number of subjects	416
EEA total number of subjects	416

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)	309
From 65 to 84 years	104

85 years and over	3

Subject disposition

Recruitment

Recruitment details:

15 study centers in Germany; first patient first visit: 29 January 2016; last patient last visit: 09 June 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 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	GentaBet Ointment

Arm description:

Test product

Arm type	Experimental
Investigational medicinal product name	Gentamicin 0.1%_Betamethasone 0.05% Ointment
Investigational medicinal product code	D07CC01
Other name	
Pharmaceutical forms	Ointment
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 Ointment
Investigational medicinal product code	D07CC01
Other name	
Pharmaceutical forms	Ointment
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	Ointment
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 Ointment	Diprogenta	Vehicle
Started	166	167	83
Completed	153	154	71
Not completed	13	13	12
Consent withdrawn by subject	2	-	2
Adverse event, non-fatal	1	1	1
Technical-logistic reasons	3	2	2
Lost to follow-up	6	4	2
Lack of efficacy	1	5	4
Protocol deviation	-	1	1

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 Ointment

Arm description:
Test product

Arm type	Experimental
Investigational medicinal product name	Gentamicin 0.1%_Betamethasone 0.05% Ointment
Investigational medicinal product code	D07CC01
Other name	
Pharmaceutical forms	Ointment
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 Ointment
Investigational medicinal product code	D07CC01
Other name	
Pharmaceutical forms	Ointment
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	Ointment
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 Ointment	Diprogenta	Vehicle
Started	153	154	71
Completed	136	139	66
Not completed	17	15	5
Complete healing at day 7	10	9	2
Consent withdrawn by subject	-	-	1
Technical-logistic reasons	3	1	-
Lost to follow-up	-	1	-
Lack of efficacy	2	2	1
Protocol deviation	2	2	1

Baseline characteristics

Reporting groups	
Reporting group title	Treatment Period

Reporting group description: -

Reporting group values	Treatment Period	Total	
Number of subjects	416	416	
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)	298	298	
From 65-84 years	104	104	
85 years and over	3	3	
Not recorded	11	11	
Gender categorical Units: Subjects			
Female	221	221	
Male	195	195	

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	405	405	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)	298	298	258
From 65-84 years	104	104	96
85 years and over	3	3	3
Not recorded	0	0	0
Gender categorical Units: Subjects			
Female	215	215	
Male	190	190	

End points

End points reporting groups

Reporting group title	GentaBet Ointment
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 Ointment
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 Ointment	Diprogenta	Vehicle	ITT
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	144	143	81	324
Units: Number	123	115	48	267

End point values	PP			
Subject group type	Subject analysis set			
Number of subjects analysed	287			
Units: Number	238			

Statistical analyses

Statistical analysis title	Analysis of efficacy
Statistical analysis description:	
Non-Inferiority test (one-sided) with alpha = 0.025 and beta = 0.02, based on the PP data set. The Non-Inferiority margin was set to 0.1 (= 10%)	
Comparison groups	GentaBet Ointment v Diprogenta
Number of subjects included in analysis	287
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	Mean difference (final values)
Point estimate	0.05
Confidence interval	
level	95 %
sides	1-sided
lower limit	-0.0439

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 Ointment	Vehicle	ITT	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	161	81	242	
Units: Number	135	48	183	

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 Ointment v Vehicle
Number of subjects included in analysis	242
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	163	81	244	
Units: Number	132	48	180	

Statistical analyses

Statistical analysis title	Sensitivity analysis

Statistical analysis description:

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

Comparison groups	Diprogenta v Vehicle

Number of subjects included in analysis	244
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0006
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 Ointment
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 Ointment	Diprogenta	Vehicle
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	1 / 81 (1.23%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Reproductive system and breast disorders			
Haemorrhagic ovarian cyst			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	0 / 81 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Herpes zoster			
subjects affected / exposed	0 / 161 (0.00%)	0 / 163 (0.00%)	1 / 81 (1.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
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 Ointment	Diprogenta	Vehicle
Total subjects affected by non-serious adverse events			
subjects affected / exposed	12 / 161 (7.45%)	11 / 163 (6.75%)	9 / 81 (11.11%)
Investigations			
Herpes simplex test positive			
subjects affected / exposed	0 / 161 (0.00%)	1 / 163 (0.61%)	0 / 81 (0.00%)
occurrences (all)	0	1	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	0 / 161 (0.00%)	1 / 163 (0.61%)	0 / 81 (0.00%)
occurrences (all)	0	1	0
Vascular disorders			
Circulatory collapse			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	0 / 81 (0.00%)
occurrences (all)	1	0	0
Phlebitis			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	0 / 81 (0.00%)
occurrences (all)	1	0	0
Vascular pain			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	0 / 81 (0.00%)
occurrences (all)	1	0	0
Surgical and medical procedures			
Pterygium operation			
subjects affected / exposed	0 / 161 (0.00%)	0 / 163 (0.00%)	1 / 81 (1.23%)
occurrences (all)	0	0	1
Nervous system disorders			
Headache			
subjects affected / exposed	2 / 161 (1.24%)	1 / 163 (0.61%)	0 / 81 (0.00%)
occurrences (all)	2	1	0
Migraine			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	0 / 81 (0.00%)
occurrences (all)	1	0	0
General disorders and administration site conditions			
Application site pruritus			
subjects affected / exposed	0 / 161 (0.00%)	1 / 163 (0.61%)	0 / 81 (0.00%)
occurrences (all)	0	1	0
Mass			

subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	0 / 81 (0.00%)
occurrences (all)	1	0	0
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	0 / 81 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
Lip blister			
subjects affected / exposed	0 / 161 (0.00%)	1 / 163 (0.61%)	0 / 81 (0.00%)
occurrences (all)	0	1	0
Reproductive system and breast disorders			
Balanoposthitis			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	0 / 81 (0.00%)
occurrences (all)	1	0	0
Dysmenorrhoea			
subjects affected / exposed	0 / 161 (0.00%)	1 / 163 (0.61%)	0 / 81 (0.00%)
occurrences (all)	0	1	0
Skin and subcutaneous tissue disorders			
Eczema			
subjects affected / exposed	1 / 161 (0.62%)	1 / 163 (0.61%)	0 / 81 (0.00%)
occurrences (all)	1	1	0
Eosinophilic cellulitis			
subjects affected / exposed	0 / 161 (0.00%)	0 / 163 (0.00%)	1 / 81 (1.23%)
occurrences (all)	0	0	1
Urticaria			
subjects affected / exposed	1 / 161 (0.62%)	0 / 163 (0.00%)	1 / 81 (1.23%)
occurrences (all)	1	0	1
Infections and infestations			
Acarodermatitis			
subjects affected / exposed	0 / 161 (0.00%)	0 / 163 (0.00%)	1 / 81 (1.23%)
occurrences (all)	0	0	1
Nasopharyngitis			
subjects affected / exposed	4 / 161 (2.48%)	2 / 163 (1.23%)	3 / 81 (3.70%)
occurrences (all)	4	2	3
Pharyngitis			

subjects affected / exposed	0 / 161 (0.00%)	1 / 163 (0.61%)	0 / 81 (0.00%)
occurrences (all)	0	1	0
Pulpitis dental			
subjects affected / exposed	0 / 161 (0.00%)	0 / 163 (0.00%)	1 / 81 (1.23%)
occurrences (all)	0	0	1
Tinea pedis			
subjects affected / exposed	0 / 161 (0.00%)	1 / 163 (0.61%)	1 / 81 (1.23%)
occurrences (all)	0	1	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 reported

Notes: