Clinical trial results:
Double-blind, randomised clinical study comparing efficacy and safety of Miconazole 2% Fluprednidene 0.1% Cream (Test) vs. Vobaderm® Cream (Reference) vs. Vehicle in patients with moderate to severely inflamed candidiasis of the skin.

Summary

EudraCT number	2015-005707-92
Trial protocol	DE
Global end of trial date	10 August 2018

Results information

Result version number	v1 (current)
This version publication date	06 April 2022
First version publication date	06 April 2022

Trial information

Trial identification

Sponsor protocol code	16-03/MicoFlu-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	Clinical Research Department, Dermapharm AG, +49 89641860, Clinicaltrials.Dermapharm@dermapharm.com
Scientific contact	Clinical Research Department, Dermapharm AG, +49 89641860, 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	23 April 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	10 August 2018
Global end of trial reached?	Yes
Global end of trial date	10 August 2018
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 miconazole 2 % and fluprednidene 0.1 % in comparison with the approved preparation Vobaderm® Cream and the underlying vehicle in patients with moderate to severely inflamed candidiasis of the skin.

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	06 January 2017
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: 340
Worldwide total number of subjects	340
EEA total number of subjects	340

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)	187
From 65 to 84 years	140

85 years and over	13

Subject disposition

Recruitment

Recruitment details:

21 study centers in Germany; first patient first visit: 19 January 2017; last patient last visit: 10 August 2018

Pre-assignment

Screening details:

Main criteria for inclusion:
Women and men ≥ 18 years of age; Diagnosis of candidiasis of the skin based on clinical symptoms; Positive mycological result of a swab revealing at least a moderate number of fungi, microscopically proven; Sum score of all clinical parameters ≥ 7; At least moderate severity of parameters erythema and exudation

Period 1

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

Blinding implementation details:

The tubes containing the study medications were neutral white. The attached labels were identical for all preparations, but they differed in terms of the specified week of treatment (i.e. "week 1" or "week 2"). This applied to all three treatment arms. All study medications were indistinguishable in terms of appearance. The random code was transferred to the data base not before the following actions were completed: data base closure, finalisation of the SAP, and a Blind Data Review Report.

Arms

Are arms mutually exclusive?	Yes
Arm title	MicoFlu-C

Arm description:

Test product

Arm type	Experimental
Investigational medicinal product name	Miconazole 2%_Fluprednidene 0.1% Cream
Investigational medicinal product code	D07XB03
Other name	
Pharmaceutical forms	Cream
Routes of administration	Cutaneous use

Dosage and administration details:

In the treatment period: Application twice daily as a thin film on the affected area.

Arm title	Vobaderm

Arm description:

Reference Product

Arm type	Active comparator
Investigational medicinal product name	Vobaderm Cream
Investigational medicinal product code	D07XB03
Other name	
Pharmaceutical forms	Cream
Routes of administration	Cutaneous use

Dosage and administration details:

In the treatment period: Application twice daily as a thin film on the affected area.

Arm title	Vehicle

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

Dosage and administration details:

In the treatment period: Application twice daily as a thin film on the affected area.

Number of subjects in period 1	MicoFlu-C	Vobaderm	Vehicle
Started	116	118	106
Completed	105	108	96
Not completed	11	10	10
Consent withdrawn by subject	3	3	2
Adverse event, non-fatal	1	1	1
Technical-logistic reasons	1	1	2
Lost to follow-up	1	-	-
Strong worsening of symptoms in FU	3	4	1
Lack of efficacy	1	1	4
Protocol deviation	1	-	-

Baseline characteristics

Reporting groups

Reporting group title	Treatment Period

Reporting group description: -

Reporting group values	Treatment Period	Total	
Number of subjects	340	340	
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)	187	187	
From 65-84 years	140	140	
85 years and over	13	13	
Gender categorical Units: Subjects			
Female	173	173	
Male	167	167	

Subject analysis sets

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

Subject analysis set description:

Includes all randomised patients who had administered the study medication at least once and who provided at least one safety related outcome.

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 complied with the study diagnosis (according to the associated inclusion criteria) and provided at least one post-baseline value to ensure the evaluation of the primary efficacy variable.

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	Safety data set	ITT	PP
Number of subjects	340	337	302
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)	187	186	168
From 65-84 years	140	138	123
85 years and over	13	13	11
Gender categorical			
Units: Subjects			
Female	173	171	153
Male	167	166	149

End points

End points reporting groups

Reporting group title	MicoFlu-C
Reporting group description: Test product	
Reporting group title	Vobaderm
Reporting group description: Reference Product	
Reporting group title	Vehicle
Reporting group description: Vehicle of Test product	
Subject analysis set title	Safety data set
Subject analysis set type	Safety analysis
Subject analysis set description: Includes all randomised patients who had administered the study medication at least once and who provided at least one safety related outcome.	
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 complied with the study diagnosis (according to the associated inclusion criteria) and provided at least one post-baseline value to ensure the evaluation of the primary efficacy variable.	
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: The primary efficacy variable is treatment success (yes, no) at Visit 4 (LOCF) (i.e. the final examination visit; “test-of-cure”). Treatment success is defined as fulfilment of clinical success (defined as fulfilment of both, sum score of clinical parameters ≤ 2 and all individual clinical scores ≤ 1) and mycological success (defined as negative microscopical testing, i.e. a score value of 0 = no fungi to be seen).	
End point type	Primary
End point timeframe: Start of treatment (visit 1) to "test of cure" (visit 4); with 2 weeks treatment (1 week with the trial medication + 1 week follow-up treatment) + 1 week follow-up without treatment.	

End point values	MicoFlu-C	Vobaderm	Vehicle	ITT
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	101	106	106	337
Units: Percentage				
number (not applicable)	65	65	50	190

End point values	PP			
Subject group type	Subject analysis set			
Number of subjects analysed	302			
Units: Percentage				
number (not applicable)	179			

Statistical analyses

Statistical analysis title	Analysis of efficacy

Statistical analysis description:

The primary objective of this study was to show non-inferiority of MicoFlu-C in comparison to Vobaderm with respect to the primary efficacy variable. The non-inferiority margin was set to Δ = 0.2 (20%).

Comparison groups	MicoFlu-C v Vobaderm v PP
Number of subjects included in analysis	509
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	Mean difference (final values)
Point estimate	-3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.09
upper limit	17.16

Statistical analysis title	Superiority of Test over Vehicle

Statistical analysis description:

In order to verify assay sensitivity of the study, superiority of the two active preparations over the vehicle was tested by means of two-sided significance tests with α = 0.05. The primary test of superiority was carried out for the ITT data set.

Comparison groups	MicoFlu-C v Vehicle v ITT
Number of subjects included in analysis	544
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0601
Method	Fisher exact

Statistical analysis title	Superiority of Reference over Vehicle

Statistical analysis description:

In order to verify assay sensitivity of the study, superiority of the two active preparations over the vehicle was tested by means of two-sided significance tests with α = 0.05. The primary test of superiority was carried out for the ITT data set.

Comparison groups	Vobaderm v Vehicle v ITT

Number of subjects included in analysis	549
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0431
Method	Fisher exact

Adverse events

Adverse events information	
Timeframe for reporting adverse events: From the inclusion visit (V1, day 0) to the final visit (V4, day 21, "test of cure").	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	21.1

Reporting groups	
Reporting group title	MicoFlu-C
Reporting group description: Test product	
Reporting group title	Vobaderm
Reporting group description: Reference Product	
Reporting group title	Vehicle
Reporting group description: Vehicle of Test product	

Serious adverse events	MicoFlu-C	Vobaderm	Vehicle
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 116 (0.86%)	0 / 118 (0.00%)	1 / 106 (0.94%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 116 (0.00%)	0 / 118 (0.00%)	1 / 106 (0.94%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Anaphylactoid reaction			
subjects affected / exposed	1 / 116 (0.86%)	0 / 118 (0.00%)	0 / 106 (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			
Peritonitis			
subjects affected / exposed	0 / 116 (0.00%)	0 / 118 (0.00%)	1 / 106 (0.94%)
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	MicoFlu-C	Vobaderm	Vehicle
Total subjects affected by non-serious adverse events			
subjects affected / exposed	11 / 116 (9.48%)	10 / 118 (8.47%)	7 / 106 (6.60%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	0 / 116 (0.00%)	1 / 118 (0.85%)	0 / 106 (0.00%)
occurrences (all)	0	1	0
Fibroma			
subjects affected / exposed	1 / 116 (0.86%)	0 / 118 (0.00%)	0 / 106 (0.00%)
occurrences (all)	1	0	0
Rectal adenoma			
subjects affected / exposed	0 / 116 (0.00%)	0 / 118 (0.00%)	1 / 106 (0.94%)
occurrences (all)	0	0	1
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 116 (0.00%)	1 / 118 (0.85%)	0 / 106 (0.00%)
occurrences (all)	0	1	0
Skin laceration			
subjects affected / exposed	0 / 116 (0.00%)	1 / 118 (0.85%)	0 / 106 (0.00%)
occurrences (all)	0	1	0
Traumatic haematoma			
subjects affected / exposed	1 / 116 (0.86%)	0 / 118 (0.00%)	0 / 106 (0.00%)
occurrences (all)	1	0	0
Vascular disorders			
Flushing			
subjects affected / exposed	0 / 116 (0.00%)	0 / 118 (0.00%)	1 / 106 (0.94%)
occurrences (all)	0	0	1
Surgical and medical procedures			
Tooth extraction			

subjects affected / exposed	1 / 116 (0.86%)	0 / 118 (0.00%)	0 / 106 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 116 (0.86%)	1 / 118 (0.85%)	2 / 106 (1.89%)
occurrences (all)	1	1	2
Neuralgia			
subjects affected / exposed	1 / 116 (0.86%)	0 / 118 (0.00%)	0 / 106 (0.00%)
occurrences (all)	1	0	0
General disorders and administration site conditions			
Application site eczema			
subjects affected / exposed	1 / 116 (0.86%)	0 / 118 (0.00%)	0 / 106 (0.00%)
occurrences (all)	1	0	0
Chills			
subjects affected / exposed	0 / 116 (0.00%)	0 / 118 (0.00%)	1 / 106 (0.94%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Duodenitis			
subjects affected / exposed	0 / 116 (0.00%)	0 / 118 (0.00%)	1 / 106 (0.94%)
occurrences (all)	0	0	1
Nausea			
subjects affected / exposed	0 / 116 (0.00%)	1 / 118 (0.85%)	0 / 106 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
Epistaxis			
subjects affected / exposed	0 / 116 (0.00%)	1 / 118 (0.85%)	0 / 106 (0.00%)
occurrences (all)	0	1	0
Pleural effusion			
subjects affected / exposed	0 / 116 (0.00%)	0 / 118 (0.00%)	1 / 106 (0.94%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
Dermatitis contact			
subjects affected / exposed	0 / 116 (0.00%)	1 / 118 (0.85%)	0 / 106 (0.00%)
occurrences (all)	0	1	0
Eczema			

subjects affected / exposed	0 / 116 (0.00%)	1 / 118 (0.85%)	0 / 106 (0.00%)
occurrences (all)	0	1	0
Hyperhidrosis			
subjects affected / exposed	0 / 116 (0.00%)	1 / 118 (0.85%)	0 / 106 (0.00%)
occurrences (all)	0	1	0
Lichen planus			
subjects affected / exposed	1 / 116 (0.86%)	0 / 118 (0.00%)	0 / 106 (0.00%)
occurrences (all)	1	0	0
Papule			
subjects affected / exposed	0 / 116 (0.00%)	0 / 118 (0.00%)	1 / 106 (0.94%)
occurrences (all)	0	0	1
Infections and infestations			
Abscess			
subjects affected / exposed	0 / 116 (0.00%)	0 / 118 (0.00%)	1 / 106 (0.94%)
occurrences (all)	0	0	1
Hordeolum			
subjects affected / exposed	1 / 116 (0.86%)	0 / 118 (0.00%)	0 / 106 (0.00%)
occurrences (all)	1	0	0
Infected bite			
subjects affected / exposed	0 / 116 (0.00%)	1 / 118 (0.85%)	0 / 106 (0.00%)
occurrences (all)	0	1	0
Nasopharyngitis			
subjects affected / exposed	5 / 116 (4.31%)	0 / 118 (0.00%)	1 / 106 (0.94%)
occurrences (all)	5	0	1
Oral herpes			
subjects affected / exposed	0 / 116 (0.00%)	1 / 118 (0.85%)	0 / 106 (0.00%)
occurrences (all)	0	1	0
Pulpitis dental			
subjects affected / exposed	1 / 116 (0.86%)	0 / 118 (0.00%)	0 / 106 (0.00%)
occurrences (all)	1	0	0
Urinary tract infection			
subjects affected / exposed	0 / 116 (0.00%)	1 / 118 (0.85%)	0 / 106 (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

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

None reported.

Notes: