



## Clinical trial results:

**Randomised, double-blind, vehicle controlled trial comparing Amphotericin B 100.000 I.E./g oral gel vs. Ampho-Moronal® suspension vs. modified vehicle to suspension in adult patients with oropharyngeal candidiasis**

### Summary

EudraCT number	2013-000371-32
Trial protocol	DE
Global end of trial date	11 April 2019

### Results information

Result version number	v1 (current)
This version publication date	14 May 2020
First version publication date	14 May 2020

### Trial information

#### Trial identification

Sponsor protocol code	13-02/AM-MG
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#### 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, Clinicaltrials.Dermapharm@dermapharm.com
Scientific contact	Clinical Research Department, Dermapharm AG, 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	08 April 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	11 April 2019
Global end of trial reached?	Yes
Global end of trial date	11 April 2019
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

Evaluation of the safety and efficacy of a new dosage form containing Amphotericin B on an oral gel base in comparison to the approved Ampho-Moronal® suspension. The study aimed to show therapeutic non-inferiority of the test preparation compared to the reference preparation and superiority of both active medications over the vehicle.

Protection of trial subjects:

The study was conducted in accordance with the principles of ICH GCP, the declaration of Helsinki, as well as all other applicable ethical and legal requirements. The reference product Ampho Moronal suspension is already registered for the application in the study indication and commercially available for years in Germany. For the purpose of approval the efficacy and safety of this medicinal product has already been shown in clinical trials. Any patient with lack of efficacy and/or deterioration of symptoms could stop treatment at any moment based on the clinical judgment of the investigator or on his/ her own request and without giving reasons. The planned procedures within the trial represented no special risks to the patients as, apart from usual medicinal practice procedures, no additional invasive procedures were planned.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 October 2014
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: 391
Worldwide total number of subjects	391
EEA total number of subjects	391

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)	214
From 65 to 84 years	172
85 years and over	5

## Subject disposition

### Recruitment

Recruitment details:

Multi-centric study in Germany; first volunteer enrolled: 11-Nov-2014; date of last completion: 11-Apr-2019

### Pre-assignment

Screening details:

Diagnosis and main criteria for inclusion:

Men and women aged  $\geq 18$  years; clinical signs and symptoms of oropharyngeal candidiasis (OPC) with a sum score of  $\geq 4$  of

the parameters erythematous areas, removable white patches, soreness/burning and extent of oral lesions (single scores between 0 and 3); existence of predisposing risk factors for OPC

### 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, Data analyst

Blinding implementation details:

The preparations were filled in brown glass bottles and labelled indistinguishably. All study preparations were coloured and contained flavouring substances. So the investigator and patients could not draw any conclusion from colour and flavour about the preparation with which they were treated.

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	Test product

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Amphotericin B oral gel
Investigational medicinal product code	A07AA07
Other name	
Pharmaceutical forms	Oromucosal gel
Routes of administration	Buccal use

Dosage and administration details:

1 g four times a day into the oral cavity

<b>Arm title</b>	Reference product
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Arm description: -

Arm type	Active comparator
Investigational medicinal product name	Ampho-Moronal Suspension
Investigational medicinal product code	A07AA07
Other name	
Pharmaceutical forms	Oromucosal suspension
Routes of administration	Buccal use

Dosage and administration details:

1 ml four times a day into the oral cavity

<b>Arm title</b>	Vehicle
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Arm description: -

Arm type	Placebo
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Investigational medicinal product name	Modified vehicle to reference product
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oromucosal suspension
Routes of administration	Buccal use

Dosage and administration details:

1 g four times a day into the oral cavity

Number of subjects in period 1	Test product	Reference product	Vehicle
Started	126	133	132
Completed	113	118	114
Not completed	13	15	18
Physician decision	1	4	1
Consent withdrawn by subject	3	5	4
Adverse event, non-fatal	6	5	6
Lost to follow-up	1	-	4
Healing	1	-	1
Lack of efficacy	1	1	2

## Period 2

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

## Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	Test - Follow up
Arm description: -	
Arm type	No intervention
No investigational medicinal product assigned in this arm	
<b>Arm title</b>	Reference Follow up
Arm description: -	
Arm type	No intervention
No investigational medicinal product assigned in this arm	
<b>Arm title</b>	Vehicle Follow up
Arm description: -	
Arm type	No intervention
No investigational medicinal product assigned in this arm	

<b>Number of subjects in period 2</b>	Test - Follow up	Reference Follow up	Vehicle Follow up
Started	113	118	114
Completed	110	111	110
Not completed	3	7	4
Consent withdrawn by subject	3	7	4

## Baseline characteristics

## End points

### End points reporting groups

Reporting group title	Test product
Reporting group description: -	
Reporting group title	Reference product
Reporting group description: -	
Reporting group title	Vehicle
Reporting group description: -	
Reporting group title	Test - Follow up
Reporting group description: -	
Reporting group title	Reference Follow up
Reporting group description: -	
Reporting group title	Vehicle Follow up
Reporting group description: -	

### Primary: Primary endpoint

End point title	Primary endpoint
End point description: The primary endpoint of the study was the clinical success rate at the end of treatment (Day 14). The success rate was defined as clinical and mycological cure. Clinical cure is gained when the total score of the 4 clinical parameters is $\leq 1$ on Day 14 and no further treatment is necessary. Mycological cure is specified as a fungal culture score of $\leq 1$ (only single forms of <i>Candida albicans</i> ).	
End point type	Primary
End point timeframe: Initial examination to main examination (EOT, day 14)	

End point values	Test product	Reference product	Vehicle	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	105	114	106	
Units: percentage	26	49	28	

### Statistical analyses

Statistical analysis title	Non-Inferiority
Statistical analysis description: The primary objective of this study was to show non-inferiority of the test product in comparison to the reference product. Non-inferiority was statistically proven if the lower limit of the two-sided 95% confidence interval (CI) was $> -D$ , where $\Delta = 0.20$ was the non-inferiority limit.	
Comparison groups	Test product v Reference product



Number of subjects included in analysis	219
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	Median difference (final values)
Point estimate	-18.22
Confidence interval	
level	95 %
sides	2-sided
lower limit	-31.41
upper limit	-5.03

<b>Statistical analysis title</b>	Superiority of test product to vehicle
Statistical analysis description: The analysis was intended to provide supportive evidence with regard to assay sensitivity.	
Comparison groups	Test product v Vehicle
Number of subjects included in analysis	211
Analysis specification	Pre-specified
Analysis type	superiority <sup>[1]</sup>
P-value	= 1
Method	Fisher exact
Notes: [1] - Difference between success rates	

<b>Statistical analysis title</b>	Superiority of reference product to vehicle
Statistical analysis description: This analysis was intended to provide supportive evidence with regard to assay sensitivity.	
Comparison groups	Reference product v Vehicle
Number of subjects included in analysis	220
Analysis specification	Pre-specified
Analysis type	superiority <sup>[2]</sup>
P-value	< 0.05
Method	Fisher exact
Notes: [2] - Difference between success rates	

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

From baseline to the end of follow-up.

Assessment type	Non-systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	22
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### Reporting groups

Reporting group title	Test product
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Reporting group description: -

Reporting group title	Reference product
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Reporting group description: -

Reporting group title	Vehicle
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Reporting group description: -

Serious adverse events	Test product	Reference product	Vehicle
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 125 (0.80%)	0 / 130 (0.00%)	2 / 127 (1.57%)
number of deaths (all causes)	0	0	1
number of deaths resulting from adverse events	0	0	1
Cardiac disorders			
Cardiac failure			
subjects affected / exposed	0 / 125 (0.00%)	0 / 130 (0.00%)	1 / 127 (0.79%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	0 / 125 (0.00%)	0 / 130 (0.00%)	1 / 127 (0.79%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	0 / 125 (0.00%)	0 / 130 (0.00%)	1 / 127 (0.79%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			

subjects affected / exposed	0 / 125 (0.00%)	0 / 130 (0.00%)	1 / 127 (0.79%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>Infections and infestations</b>			
Urosepsis			
subjects affected / exposed	0 / 125 (0.00%)	0 / 130 (0.00%)	1 / 127 (0.79%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
<b>Metabolism and nutrition disorders</b>			
Diabetes mellitus inadequate control			
subjects affected / exposed	1 / 125 (0.80%)	0 / 130 (0.00%)	0 / 127 (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

Frequency threshold for reporting non-serious adverse events: 0.05 %

<b>Non-serious adverse events</b>	Test product	Reference product	Vehicle
<b>Total subjects affected by non-serious adverse events</b>			
subjects affected / exposed	18 / 125 (14.40%)	26 / 130 (20.00%)	25 / 127 (19.69%)
<b>General disorders and administration site conditions</b>			
Influenza like illness			
subjects affected / exposed	0 / 125 (0.00%)	2 / 130 (1.54%)	4 / 127 (3.15%)
occurrences (all)	0	2	4
Pyrexia			
subjects affected / exposed	0 / 125 (0.00%)	0 / 130 (0.00%)	1 / 127 (0.79%)
occurrences (all)	0	0	1
<b>Immune system disorders</b>			
Seasonal allergy			
subjects affected / exposed	0 / 125 (0.00%)	0 / 130 (0.00%)	1 / 127 (0.79%)
occurrences (all)	0	0	1
<b>Respiratory, thoracic and mediastinal disorders</b>			
Dysphonia			
subjects affected / exposed	1 / 125 (0.80%)	0 / 130 (0.00%)	0 / 127 (0.00%)
occurrences (all)	1	0	0
Dyspnoea			

subjects affected / exposed occurrences (all)	1 / 125 (0.80%) 1	0 / 130 (0.00%) 0	0 / 127 (0.00%) 0
Oropharyngeal discomfort subjects affected / exposed occurrences (all)	1 / 125 (0.80%) 1	0 / 130 (0.00%) 0	0 / 127 (0.00%) 0
Oropharyngeal pain subjects affected / exposed occurrences (all)	0 / 125 (0.00%) 0	0 / 130 (0.00%) 0	1 / 127 (0.79%) 1
Throat tightness subjects affected / exposed occurrences (all)	1 / 125 (0.80%) 1	0 / 130 (0.00%) 0	0 / 127 (0.00%) 0
Investigations			
Blood lactic acid increased subjects affected / exposed occurrences (all)	0 / 125 (0.00%) 0	0 / 130 (0.00%) 0	1 / 127 (0.79%) 1
Body temperature increased subjects affected / exposed occurrences (all)	0 / 125 (0.00%) 0	1 / 130 (0.77%) 1	0 / 127 (0.00%) 0
Injury, poisoning and procedural complications			
Ligament rupture subjects affected / exposed occurrences (all)	0 / 125 (0.00%) 0	0 / 130 (0.00%) 0	1 / 127 (0.79%) 1
Ligament sprain subjects affected / exposed occurrences (all)	0 / 125 (0.00%) 0	1 / 130 (0.77%) 1	0 / 127 (0.00%) 0
Thermal burn subjects affected / exposed occurrences (all)	0 / 125 (0.00%) 0	1 / 130 (0.77%) 1	0 / 127 (0.00%) 0
Cardiac disorders			
Palpitations subjects affected / exposed occurrences (all)	0 / 125 (0.00%) 0	1 / 130 (0.77%) 1	0 / 127 (0.00%) 0
Nervous system disorders			
Dizziness subjects affected / exposed occurrences (all)	0 / 125 (0.00%) 0	0 / 130 (0.00%) 0	1 / 127 (0.79%) 1

Headache			
subjects affected / exposed	2 / 125 (1.60%)	3 / 130 (2.31%)	1 / 127 (0.79%)
occurrences (all)	2	3	1
Migraine			
subjects affected / exposed	1 / 125 (0.80%)	2 / 130 (1.54%)	0 / 127 (0.00%)
occurrences (all)	1	2	0
Sciatica			
subjects affected / exposed	1 / 125 (0.80%)	0 / 130 (0.00%)	0 / 127 (0.00%)
occurrences (all)	1	0	0
Ear and labyrinth disorders			
Tinnitus			
subjects affected / exposed	0 / 125 (0.00%)	0 / 130 (0.00%)	1 / 127 (0.79%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 125 (0.00%)	1 / 130 (0.77%)	0 / 127 (0.00%)
occurrences (all)	0	1	0
Abdominal pain			
subjects affected / exposed	1 / 125 (0.80%)	2 / 130 (1.54%)	1 / 127 (0.79%)
occurrences (all)	1	2	1
Abdominal pain upper			
subjects affected / exposed	1 / 125 (0.80%)	1 / 130 (0.77%)	0 / 127 (0.00%)
occurrences (all)	1	1	0
Aphthous ulcer			
subjects affected / exposed	0 / 125 (0.00%)	1 / 130 (0.77%)	1 / 127 (0.79%)
occurrences (all)	0	1	1
Constipation			
subjects affected / exposed	0 / 125 (0.00%)	1 / 130 (0.77%)	0 / 127 (0.00%)
occurrences (all)	0	1	0
Diarrhoea			
subjects affected / exposed	1 / 125 (0.80%)	2 / 130 (1.54%)	0 / 127 (0.00%)
occurrences (all)	1	2	0
Dry mouth			
subjects affected / exposed	0 / 125 (0.00%)	1 / 130 (0.77%)	0 / 127 (0.00%)
occurrences (all)	0	1	0
Dyspepsia			

subjects affected / exposed	0 / 125 (0.00%)	1 / 130 (0.77%)	0 / 127 (0.00%)
occurrences (all)	0	1	0
Faeces hard			
subjects affected / exposed	0 / 125 (0.00%)	0 / 130 (0.00%)	1 / 127 (0.79%)
occurrences (all)	0	0	1
Flatulence			
subjects affected / exposed	0 / 125 (0.00%)	1 / 130 (0.77%)	0 / 127 (0.00%)
occurrences (all)	0	1	0
Gingival bleeding			
subjects affected / exposed	0 / 125 (0.00%)	1 / 130 (0.77%)	0 / 127 (0.00%)
occurrences (all)	0	1	0
Glossodynia			
subjects affected / exposed	0 / 125 (0.00%)	0 / 130 (0.00%)	1 / 127 (0.79%)
occurrences (all)	0	0	1
Nausea			
subjects affected / exposed	3 / 125 (2.40%)	1 / 130 (0.77%)	0 / 127 (0.00%)
occurrences (all)	3	1	0
Oesophageal pain			
subjects affected / exposed	1 / 125 (0.80%)	0 / 130 (0.00%)	0 / 127 (0.00%)
occurrences (all)	1	0	0
Oral discomfort			
subjects affected / exposed	2 / 125 (1.60%)	0 / 130 (0.00%)	0 / 127 (0.00%)
occurrences (all)	2	0	0
Paraesthesia oral			
subjects affected / exposed	0 / 125 (0.00%)	1 / 130 (0.77%)	0 / 127 (0.00%)
occurrences (all)	0	1	0
Stomatitis			
subjects affected / exposed	1 / 125 (0.80%)	0 / 130 (0.00%)	0 / 127 (0.00%)
occurrences (all)	1	0	0
Swollen tongue			
subjects affected / exposed	0 / 125 (0.00%)	1 / 130 (0.77%)	0 / 127 (0.00%)
occurrences (all)	0	1	0
Vomiting			
subjects affected / exposed	2 / 125 (1.60%)	2 / 130 (1.54%)	0 / 127 (0.00%)
occurrences (all)	2	2	0
Skin and subcutaneous tissue disorders			

Dermatitis			
subjects affected / exposed	0 / 125 (0.00%)	0 / 130 (0.00%)	1 / 127 (0.79%)
occurrences (all)	0	0	1
Dermatitis allergic			
subjects affected / exposed	0 / 125 (0.00%)	0 / 130 (0.00%)	1 / 127 (0.79%)
occurrences (all)	0	0	1
Dermatitis contact			
subjects affected / exposed	1 / 125 (0.80%)	0 / 130 (0.00%)	0 / 127 (0.00%)
occurrences (all)	1	0	0
Eczema			
subjects affected / exposed	0 / 125 (0.00%)	1 / 130 (0.77%)	0 / 127 (0.00%)
occurrences (all)	0	1	0
Lichen sclerosus			
subjects affected / exposed	0 / 125 (0.00%)	0 / 130 (0.00%)	1 / 127 (0.79%)
occurrences (all)	0	0	1
rash			
subjects affected / exposed	1 / 125 (0.80%)	0 / 130 (0.00%)	1 / 127 (0.79%)
occurrences (all)	1	0	1
Rosacea			
subjects affected / exposed	0 / 125 (0.00%)	1 / 130 (0.77%)	0 / 127 (0.00%)
occurrences (all)	0	1	0
Stasis dermatitis			
subjects affected / exposed	0 / 125 (0.00%)	0 / 130 (0.00%)	1 / 127 (0.79%)
occurrences (all)	0	0	1
Renal and urinary disorders			
Urinary hesitation			
subjects affected / exposed	0 / 125 (0.00%)	0 / 130 (0.00%)	1 / 127 (0.79%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 125 (0.00%)	1 / 130 (0.77%)	1 / 127 (0.79%)
occurrences (all)	0	1	1
Rheumatoid arthritis			
subjects affected / exposed	0 / 125 (0.00%)	0 / 130 (0.00%)	1 / 127 (0.79%)
occurrences (all)	0	0	1
Infections and infestations			

Bronchitis			
subjects affected / exposed	1 / 125 (0.80%)	0 / 130 (0.00%)	1 / 127 (0.79%)
occurrences (all)	1	0	1
Conjunctivitis			
subjects affected / exposed	1 / 125 (0.80%)	0 / 130 (0.00%)	0 / 127 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal candidiasis			
subjects affected / exposed	0 / 125 (0.00%)	0 / 130 (0.00%)	1 / 127 (0.79%)
occurrences (all)	0	0	1
Gastrointestinal infection			
subjects affected / exposed	0 / 125 (0.00%)	0 / 130 (0.00%)	1 / 127 (0.79%)
occurrences (all)	0	0	1
Gonococcal infection			
subjects affected / exposed	0 / 125 (0.00%)	1 / 130 (0.77%)	0 / 127 (0.00%)
occurrences (all)	0	1	0
Laryngitis			
subjects affected / exposed	1 / 125 (0.80%)	0 / 130 (0.00%)	0 / 127 (0.00%)
occurrences (all)	1	0	0
Paronychia			
subjects affected / exposed	0 / 125 (0.00%)	1 / 130 (0.77%)	0 / 127 (0.00%)
occurrences (all)	0	1	0
Rhinitis			
subjects affected / exposed	0 / 125 (0.00%)	0 / 130 (0.00%)	1 / 127 (0.79%)
occurrences (all)	0	0	1
Sinusitis			
subjects affected / exposed	0 / 125 (0.00%)	0 / 130 (0.00%)	1 / 127 (0.79%)
occurrences (all)	0	0	1
Tonsillitis			
subjects affected / exposed	0 / 125 (0.00%)	0 / 130 (0.00%)	1 / 127 (0.79%)
occurrences (all)	0	0	1
Upper respiratory tract infection			
subjects affected / exposed	0 / 125 (0.00%)	0 / 130 (0.00%)	1 / 127 (0.79%)
occurrences (all)	0	0	1
Urethritis			
subjects affected / exposed	0 / 125 (0.00%)	1 / 130 (0.77%)	0 / 127 (0.00%)
occurrences (all)	0	1	0



Viral infection			
subjects affected / exposed	1 / 125 (0.80%)	0 / 130 (0.00%)	0 / 127 (0.00%)
occurrences (all)	1	0	0

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

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### 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
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Notes: