Clinical trial results:
Subject adherence and satisfaction for treatment of Onychomycosis with Loceryl® Nail Lacquer 5% versus Ciclopoli® Nail Lacquer.

Summary

EudraCT number	2015-001237-24
Trial protocol	DE
Global end of trial date	16 June 2016

Results information

Result version number	v1 (current)
This version publication date	31 May 2020
First version publication date	31 May 2020

Trial information

Trial identification

Sponsor protocol code	RD.03.SPR.105082

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02679911
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	GALDERMA R&D
Sponsor organisation address	Les Templiers, 2400, Route des Colles, Biot, France, 06410
Public contact	Farzaneh Sidou, Galderma R&D, 0033 493957051, Farzaneh.sidou@galderma.com
Scientific contact	Farzaneh Sidou, Galderma R&D, 0033 493957051, Farzaneh.sidou@galderma.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	16 June 2016
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	16 June 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of this study was to compare subject-reported adherence and satisfaction for two modes of treatment of Distal and Lateral Subungual Onychomycosis (DLSO) in toenail treatment with Loceryl nail lacquer (Amorolfine) and Ciclopoli nail lacquer (Ciclopirox).

Protection of trial subjects:

This study protocol was reviewed and approved by the appropriate independent ethics committee/institutional review board prior to study initiation. This study was conducted in accordance with the protocol, the HELSINKI declaration (1964) and subsequent amendments, and the International Conference on Harmonization Good Clinical Practice, and in compliance with applicable regulatory requirements. All subjects who participated in this trial were fully informed about the study in accordance with the applicable regulations and guidelines and in accordance with local legal requirements. All subjects signed the informed consent form which was written in the local language and a copy of the same was given to the subject. In any medical emergency, the investigator unblinded the treatment only for the subject involved.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	18 September 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: 20
Worldwide total number of subjects	20
EEA total number of subjects	20

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)	18
From 65 to 84 years	2
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted at a single center in Germany between 18 September 2015 (first subject screened) to 16 June 2016 (last subject completed). A total of subjects completed the study.

Pre-assignment

Screening details:

A total of 20 subjects with a clinical diagnosis of DLSO on at least one toenail of each foot confirmed by positive direct microscopic examination for dermatophytes and/or yeast (including Candida) and positive culture results without matrix involvement were randomised and treated in the study. A total of 20 subjects completed the study.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Single blind
Roles blinded	Investigator[1]

Blinding implementation details:

The study was considered to be an investigator-blinded study design.

Arms

Arm title	All Subjects

Arm description:

Each subject received 2 topical treatments with Loceryl in one foot and Ciclopoli in the other foot.
Loceryl (amorolfine hydrochloride 5 percent [%]) nail lacquer was applied once weekly for 12 weeks over the entire toenail plate of all affected toenails in the evening (at bed time) after filing down the affected toenails.
Ciclopoli nail lacquer was applied once daily for 12 weeks over the entire toenail plate of all affected toenails and surrounding skin in the evening (at bed time) after removing the free toenail edge and diseased toenails, if needed.

Arm type	Experimental
Investigational medicinal product name	Loceryl
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Medicated nail lacquer
Routes of administration	Topical use

Dosage and administration details:

Loceryl nail lacquer was applied once weekly, topically over the entire toenail plate of all affected toenails in the evening (at bed time) for 12 weeks.

Investigational medicinal product name	Ciclopoli
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Medicated nail lacquer
Routes of administration	Topical use

Dosage and administration details:

Ciclopoli nail lacquer was applied once daily, topically over the entire toenail plate of all affected toenails and surrounding skin in the evening (at bed time) for 12 weeks.

Notes:

[1] - The roles blinded appear inconsistent with a simple blinded trial.

Justification: The study was considered to be an investigator-blinded study design.

Number of subjects in period 1	All Subjects
Started	20
Completed	20

Baseline characteristics

Reporting groups	
Reporting group title	All Subjects

Reporting group description:

Each subject received 2 topical treatments with Loceryl in one foot and Ciclopoli in the other foot.
Loceryl (amorolfine hydrochloride 5 percent [%]) nail lacquer was applied once weekly for 12 weeks over the entire toenail plate of all affected toenails in the evening (at bed time) after filing down the affected toenails.
Ciclopoli nail lacquer was applied once daily for 12 weeks over the entire toenail plate of all affected toenails and surrounding skin in the evening (at bed time) after removing the free toenail edge and diseased toenails, if needed.

Reporting group values	All Subjects	Total	
Number of subjects	20	20	
Age categorical Units: Subjects			
Age continuous Units: years arithmetic mean standard deviation	 54.5 ± 8.7	 -	
Gender categorical Units: Subjects			
Female	10	10	
Male	10	10	
Race Units: Subjects			
White	20	20	

End points

End points reporting groups

Reporting group title	All Subjects

Reporting group description:

Each subject received 2 topical treatments with Loceryl in one foot and Ciclopoli in the other foot.
Loceryl (amorolfine hydrochloride 5 percent [%]) nail lacquer was applied once weekly for 12 weeks over the entire toenail plate of all affected toenails in the evening (at bed time) after filing down the affected toenails.
Ciclopoli nail lacquer was applied once daily for 12 weeks over the entire toenail plate of all affected toenails and surrounding skin in the evening (at bed time) after removing the free toenail edge and diseased toenails, if needed.

Subject analysis set title	Loceryl
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Loceryl nail lacquer was applied once weekly for 12 weeks over the entire toenail plate of all affected toenails in the evening (at bed time) after filing down the affected toenails.

Subject analysis set title	Ciclopoli
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Ciclopoli nail lacquer was applied once daily for 12 weeks over the entire toenail plate of all affected toenails and surrounding skin in the evening (at bed time) after removing the free toenail edge and diseased toenails, if needed.

Primary: Adherence rate as per label

End point title	Adherence rate as per label

End point description:

Adherence to medications is defined as the process by which subjects take their medications as prescribed. Subject’s adherence as per summary of product characteristics (SmPC) was defined as Loceryl nail lacquer application once weekly and Ciclopoli nail lacquer application once daily. At Baseline visit, subjects were provided with a subject diary to record on a daily/weekly basis the frequency of applications of study products (Loceryl nail lacquer and Ciclopoli nail lacquer) on the affected toenails of each foot. Adherence rate is defined as the percentage of subjects “in and off label. The analysis was performed on the intent-to-treat (ITT) population which included all subjects who were enrolled and randomised.

End point type	Primary

End point timeframe:

Up to Week 12

End point values	Loceryl	Ciclopoli		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	20	20		
Units: percentage of subjects				
number (not applicable)				
Yes (as per label)	85.0	60.0		
No (off label)	15.0	40.0		

Statistical analyses

Statistical analysis title	Loceryl Versus Ciclopoli
Statistical analysis description:	
For ‘number of subjects included in the analysis’ field: total number of subjects analysed were 20 instead of 40.	
Comparison groups	Loceryl v Ciclopoli
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.025
Method	Wilcoxon signed-rank test

Primary: Non-adherence Count as Per Label

End point title	Non-adherence Count as Per Label
End point description:	
Study treatment non-adherence was defined as the number of "off label" episodes. The analysis was performed on the ITT population which included all subjects who were enrolled and randomised. Here 'N' number of subjects anlaysed signifies number of subjects evaluable for this end point. Here '99999' signifies that standard deviation data for loceryl group was not calculated due to single subject availability for the analysis .	
End point type	Primary
End point timeframe:	
Up to Week 12	

End point values	Loceryl	Ciclopoli		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	1	8		
Units: off label episodes count				
arithmetic mean (standard deviation)	2.0 (± 99999)	3.0 (± 1.7)		

Statistical analyses

Statistical analysis title	Loceryl Versus Ciclopoli
Comparison groups	Loceryl v Ciclopoli

Number of subjects included in analysis	9
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.008
Method	Wilcoxon signed-rank test

Primary: Non-adherence Duration as Per Label

End point title	Non-adherence Duration as Per Label

End point description:

Non-adherence duration as per label is defined as the total duration of "off label" episodes assessed in days. The analysis was performed on the ITT population which included all subjects who were enrolled and randomised. Here 'N' number of subjects anlaysed signifies number of subjects evaluable for this end point. Here '99999' signifies that standard deviation data for loceryl group was not calculated due to single subject availability for the analysis .

End point type	Primary

End point timeframe:

Up to Week 12

End point values	Loceryl	Ciclopoli		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	1	8		
Units: days				
arithmetic mean (standard deviation)	20.0 (± 99999)	3.5 (± 1.8)		

Statistical analyses

Statistical analysis title	Loceryl Versus Ciclopoli
Comparison groups	Ciclopoli v Loceryl
Number of subjects included in analysis	9
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.195
Method	Wilcoxon signed-rank test

Primary: Adherence Rate as Per Effective Exposure

End point title	Adherence Rate as Per Effective Exposure

End point description:

Adherence to medications is defined as the process by which subjects take their medications as prescribed. Subject's adherence as per effective nail exposure was defined as Loceryl nail lacquer application at least once every other week on all affected toenails of one foot and Ciclopoli nail lacquer application at least once every other day on all affected toenails of the opposite foot. Adherence rate as per effective exposure is defined as the percentage of subjects with "in" and "off" effective exposure. The analysis was performed on the ITT population which included all subjects who were enrolled and randomised.

End point type	Primary
End point timeframe:	
Up to Week 12	

End point values	Loceryl	Ciclopoli		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	20	20		
Units: percentage of subjects				
number (not applicable)				
Yes (in effective exposure)	95.0	85.0		
No (off effective exposure)	5.0	15.0		

Statistical analyses

Statistical analysis title	Loceryl Versus Ciclopoli
Comparison groups	Ciclopoli v Loceryl
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.157
Method	Wilcoxon signed-rank test

Primary: Non-adherence Count as Per Effective Exposure

End point title	Non-adherence Count as Per Effective Exposure
End point description:	
Study treatment non-adherence was defined as the number of "off exposure" episodes. The analysis was performed on the ITT population which included all subjects who were enrolled and randomised. Here 'N' number of subjects anlaysed signifies number of subjects evaluable for this end point. Here '99999' signifies that standard deviation data for loceryl group was not calculated due to single subject availability for the analysis.	
End point type	Primary
End point timeframe:	
Up to Week 12	

End point values	Loceryl	Ciclopoli		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	1	3		
Units: off exposure episodes count				
arithmetic mean (standard deviation)	2.0 (± 99999)	1.0 (± 0.0)		

Statistical analyses

Statistical analysis title	Loceryl Versus Ciclopoli
Comparison groups	Ciclopoli v Loceryl
Number of subjects included in analysis	4
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.999
Method	Wilcoxon signed-rank test

Primary: Non-adherence Duration as Per Effective Exposure

End point title	Non-adherence Duration as Per Effective Exposure

End point description:

Non-adherence duration as per effective exposure was defined as the total duration of "off exposure" episodes assessed in days. The analysis was performed on the ITT population which included all subjects who were enrolled and randomised. Here 'N' number of subjects anlaysed signifies number of subjects evaluable for this end point. Here '99999' signifies that standard deviation data for loceryl group was not calculated due to single subject availability for the analysis.

End point type	Primary

End point timeframe:

Up to Week 12

End point values	Loceryl	Ciclopoli		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	1	3		
Units: days				
arithmetic mean (standard deviation)	4.0 (± 99999)	1.3 (± 0.6)		

Statistical analyses

Statistical analysis title	Loceryl Versus Ciclopoli
Comparison groups	Loceryl v Ciclopoli

Number of subjects included in analysis	4
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.999
Method	Wilcoxon signed-rank test

Primary: Overall Preference for Loceryl or Ciclopoli

End point title	Overall Preference for Loceryl or Ciclopoli[1]

End point description:

Subject's overall preference for study treatments was assessed according to a 3-grade preference scale (-1: left better than right, 0: no preference, 1: right better than left) based on subject judgment of criteria such as ease of use, smell and drying rate, where the right and left refers to the foot on which the subject applied Loceryl or Ciclopoli. The analysis was performed on the ITT population which included all subjects who were enrolled and randomised.

End point type	Primary

End point timeframe:

At Week 4, Week 8 and Week 12/early discontinuation

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The data presented for this primary endpoint is not analysed by the reporting arms. So, the statistical comparisons could not be presented.

End point values	All Subjects			
Subject group type	Reporting group			
Number of subjects analysed	20			
Units: subjects				
number (not applicable)				
Week 4: Ciclopoli better than Loceryl	9			
Week 4: No preference	2			
Week 4: Loceryl better than Ciclopoli	9			
Week 8: Ciclopoli better than Loceryl	9			
Week 8: No preference	2			
Week 8: Loceryl better than Ciclopoli	9			
Week 12: Ciclopoli better than Loceryl	9			
Week 12: No preference	1			
Week 12: Loceryl better than Ciclopoli	10			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Satisfied with Each Study Treatment as Assessed by Subject's Questionnaire

End point title	Percentage of Subjects Satisfied with Each Study Treatment as Assessed by Subject's Questionnaire

End point description:

Subject's questionnaire aimed to collect information on what subject think about the prescribed Loceryl/Ciclopoli naillacquer treatments. There was no "right" or "wrong" answer. It consisted of 9-

questions as followed: 1) where did you apply the products? 2) how much time did it take you to apply the study treatments on your nails? 3) how easy was it to spread the treatment on your nails using the package contents? 4) were you satisfied with the frequency of application of the treatments? 5) overall during the whole treatment period how easy to use did you find the treatments? 6) if you did not apply the study products as often as required, what were the reasons? 7) overall, how satisfied are you with the treatments? 8) would you consider continuing to use the treatment after the study end? 9) would you recommend the use of either of the study treatments to family or friends? Analysis was performed on the ITT population which included all subjects who were enrolled and randomized.

End point type	Secondary

End point timeframe:

At Week 12

End point values	Loceryl	Ciclopoli		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	20	20		
Units: percentage of subjects				
number (not applicable)	95	100		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From signing of the informed consent up to last visit (Week 12) or early termination	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	18.0

Reporting groups	
Reporting group title	All Subjects

Reporting group description:

Each subject received 2 topical treatments with Loceryl in one foot and Ciclopoli in the other foot.
Loceryl (amorolfine hydrochloride 5 percent [%]) nail lacquer was applied once weekly for 12 weeks over the entire toenail plate of all affected toenails in the evening (at bed time) after filing down the affected toenails.
Ciclopoli nail lacquer was applied once daily for 12 weeks over the entire toenail plate of all affected toenails and surrounding skin in the evening (at bed time) after removing the free toenail edge and diseased toenails, if needed.

Serious adverse events	All Subjects		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 20 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	All Subjects		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 20 (15.00%)		
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Infections and infestations			

Bronchiolitis subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1		
Nasopharyngitis subjects affected / exposed occurrences (all)	2 / 20 (10.00%) 2		

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