Clinical trial results:
Determination of antifungal activity of Loceryl® Nail Lacquer 5% when used concomitantly with a cosmetic nail varnish compared to a Loceryl® Nail Lacquer 5% alone in treatment of toenail Distal Subungual Onychomycosis

Summary

EudraCT number	2013-000544-26
Trial protocol	IS
Global end of trial date	21 January 2016

Results information

Result version number	v1 (current)
This version publication date	24 May 2020
First version publication date	24 May 2020

Trial information

Trial identification

Sponsor protocol code	RD.03.SPR.29106

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02321098
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Galderma R&D
Sponsor organisation address	2400 Route des colles - Les templiers, Biot, France, 06410
Public contact	Clinical Project manager, Galderma R&D, 33 493957051, farzaneh.sidou@galderma.com
Scientific contact	Clinical Project manager, Galderma R&D, 33 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	21 January 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	31 October 2015
Global end of trial reached?	Yes
Global end of trial date	21 January 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective was to compare the efficacy, in terms of antifungal activity of Loceryl Nail Lacquer (amorolfine) associated with a Cosmetic Varnish and Loceryl Nail Lacquer alone, in the treatment of mild to moderate toenail Distal Subungual Onychomycosis

Protection of trial subjects:

This study was conducted in compliance with the ethical principles of the International Conference of Harmonization (ICH) Good Clinical Practice (GCP), the Declaration of Helsinki (1964 and subsequent amendments) and applicable regulatory requirements.

Background therapy:

All subjects used test product Loceryl Nail Lacquer (NL) during the whole study period. During the first 12 weeks of the study half of subjects applied a cosmetic varnish 24 hours after that of Loceryl NL. No other product was used during the study. At week 12 visit eligible subjects entered to the second period of the study to apply Loceryl NL additional 15 months.

Evidence for comparator:

Onychomycosis can have a marked effect on a subject's social life. Several studies clearly documented that Onychomycosis had a substantial negative effect on the quality of life (QoL) of subjects.
Subjects' embarrassment has generated a strong demand for allowing the concomitant use of a cosmetic Nail Lacquer to mask the diseased nail until clinical improvement with their treatment.
Unfortunately, data are lacking with regard to possible interactions between cosmetic Nail Lacquers and Loceryl Nail Lacquer.
The present study was to evaluate if antifungal activity of Loceryl Nail Lacquer was modified when a cosmetic varnish was applied on the affected toenails at least 24 hours after application of Loceryl Nail Lacquer.

Actual start date of recruitment	11 February 2014
Long term follow-up planned	Yes
Long term follow-up rationale	Scientific research
Long term follow-up duration	15 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Iceland: 50
Worldwide total number of subjects	50
EEA total number of subjects	50

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)	36
From 65 to 84 years	14
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted at a single center in Iceland between 11 February 2014 (first subject screened) to 21 January 2016 (last subject completed follow-up period).

Pre-assignment

Screening details:

A total of 98 subjects were screened to have a mycological sampling of the Target nail (big toenail). Among them 50 subjects were randomized and 48 completed the study.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Loceryl + Cosmetic Varnish

Arm description:

Subjects applied Loceryl Nail Lacquer once a week in the morning for 12 weeks and cosmetic varnish was applied once a week in the morning (24 hours after application of Loceryl Nail Lacquer).

Arm type	Experimental
Investigational medicinal product name	Loceryl Nail Lacquer
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 a week in the morning.

Investigational medicinal product name	Cosmetic Varnish
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cutaneous suspension
Routes of administration	Topical use

Dosage and administration details:

Cosmetic varnish was applied once a week in the morning (24 hours after application of Loceryl Nail Lacquer).

Arm title	Loceryl Nail Lacquer Alone

Arm description:

Subjects applied Loceryl Nail Lacquer alone once a week in the morning for 12 weeks after filing down the affected toenails.

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

Dosage and administration details:

Loceryl Nail Lacquer alone was applied once weekly in the morning for 12 weeks after filing down the

affected toenails.

Notes:

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

Justification: This was an investigator blinded study.

Number of subjects in period 1	Loceryl + Cosmetic Varnish	Loceryl Nail Lacquer Alone
Started	26	24
Completed	25	23
Not completed	1	1
Lost to follow-up	1	1

Period 2

Period 2 title	Follow Up Period
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Single blind
Roles blinded	Investigator[2]

Arms

Arm title	Loceryl Nail Lacquer up to Additional 15 months

Arm description:

Subjects without clinical signs of aggravation of onychomycosis at Week 12 in both the reporting arms of treatment period continued to apply Loceryl Nail Lacquer once a week in the morning for additional 15 months.

Arm type	Experimental
Investigational medicinal product name	Loceryl Nail Lacquer
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 a week in the morning.

Notes:

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

Justification: This was an investigator blinded study.

Number of subjects in period 2[3]	Loceryl Nail Lacquer up to Additional 15 months
Started	29
Completed	21
Not completed	8
Consent withdrawn by subject	1
Lost to follow-up	1
Lack of efficacy	6

Notes:

[3] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: This was an additional follow up period after the treatment period.

Baseline characteristics

Reporting groups	
Reporting group title	Loceryl + Cosmetic Varnish
Reporting group description:	
Subjects applied Loceryl Nail Lacquer once a week in the morning for 12 weeks and cosmetic varnish was applied once a week in the morning (24 hours after application of Loceryl Nail Lacquer).	
Reporting group title	Loceryl Nail Lacquer Alone
Reporting group description:	
Subjects applied Loceryl Nail Lacquer alone once a week in the morning for 12 weeks after filing down the affected toenails.	

Reporting group values	Loceryl + Cosmetic Varnish	Loceryl Nail Lacquer Alone	Total
Number of subjects	26	24	50
Age categorical			
Units: Subjects			
Age continuous			
Units: years			
arithmetic mean	55.1	53.7	
standard deviation	± 12	± 12.5	-
Gender categorical			
Units: Subjects			
Female	7	4	11
Male	19	20	39
Race			
Units: Subjects			
White	26	24	50

End points

End points reporting groups

Reporting group title	Loceryl + Cosmetic Varnish
Reporting group description:	
Subjects applied Loceryl Nail Lacquer once a week in the morning for 12 weeks and cosmetic varnish was applied once a week in the morning (24 hours after application of Loceryl Nail Lacquer).	
Reporting group title	Loceryl Nail Lacquer Alone
Reporting group description:	
Subjects applied Loceryl Nail Lacquer alone once a week in the morning for 12 weeks after filing down the affected toenails.	
Reporting group title	Loceryl Nail Lacquer up to Additional 15 months
Reporting group description:	
Subjects without clinical signs of aggravation of onychomycosis at Week 12 in both the reporting arms of treatment period continued to apply Loceryl Nail Lacquer once a week in the morning for additional 15 months.	

Primary: Antifungal Activity of Loceryl Nail Lacquer

End point title	Antifungal Activity of Loceryl Nail Lacquer
End point description:	
Antifungal activity was measured by the diameter of zones of inhibition in toenail clippings from the target nail and all affected treated toenails. The Intent-to-Treat (ITT) population consisted of the subjects enrolled and randomized in the study. Here, the number of subjects analyzed refer to the subjects evaluable for this outcome at specified time point.	
End point type	Primary
End point timeframe:	
Week 12/early termination (ET) visit	

End point values	Loceryl + Cosmetic Varnish	Loceryl Nail Lacquer Alone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	23		
Units: Milimeter				
arithmetic mean (standard deviation)	53.6 (± 9.1)	53.5 (± 6.2)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Loceryl + Cosmetic Varnish v Loceryl Nail Lacquer Alone

Number of subjects included in analysis	48
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.942 [1]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Mean difference (final values)

Notes:

[1] - P-value for between treatment difference, by CMH test based on ridit scores.

Secondary: Number of Subjects with Negative Mycological Culture Results

End point title	Number of Subjects with Negative Mycological Culture Results

End point description:

Number of subjects with negative (absence) mycological culture results were reported. ITT population population consisted of the subjects enrolled and randomized in the study. Here, the number of subjects analyzed refer to the subjects evaluable for this outcome at specified time point.

End point type	Secondary

End point timeframe:

Week 12/early termination (ET) visit

End point values	Loceryl + Cosmetic Varnish	Loceryl Nail Lacquer Alone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	23		
Units: Number of subjects	25	23		

Statistical analyses

No statistical analyses for this end point

Secondary: Investigator-Assessed Disease Improvement

End point title	Investigator-Assessed Disease Improvement

End point description:

Disease improvement by Investigator was assessed on a 3-point scale where 1=Improved, 2=Stable, 3=Worse. Investigator-Assessed disease improvement was reported. ITT population consisted of the subjects enrolled and randomized in the study. Here, the number of subjects analyzed refer to the subjects evaluable for this outcome at specified time point.

End point type	Secondary

End point timeframe:

Week 12/early termination (ET) visit

End point values	Loceryl + Cosmetic Varnish	Loceryl Nail Lacquer Alone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	23		
Units: Units on scale				
log mean (standard deviation)	2.12 (± 0.60)	2.09 (± 0.51)		

Statistical analyses

No statistical analyses for this end point

Secondary: Subject-Assessed Disease Improvement

End point title	Subject-Assessed Disease Improvement

End point description:

Subject-assessed disease improvement assessment was assessed on across a 3-point scale where 1=Improved, 2=Stable, 3=Worse. Subject-assessed disease improvement was reported. ITT population consisted of the subjects enrolled and randomized in the study. Here, the number of subjects analyzed refer to the subjects evaluable for this outcome at specified time point.

End point type	Secondary

End point timeframe:

Week 12/early termination (ET) visit

End point values	Loceryl + Cosmetic Varnish	Loceryl Nail Lacquer Alone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	23		
Units: Units on scale				
log mean (standard deviation)	1.44 (± 0.65)	1.22 (± 0.42)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with Adverse Events (AEs)

End point title	Number of subjects with Adverse Events (AEs)

End point description:

An adverse event (AE) was any unfavorable and/or unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal/investigational product, whether or not related to the medicinal/investigational
products or to the study procedures. Thus any new sign, symptom or disease, or clinically significant increase in the intensity of an existing sign, symptom or disease was considered as an AE. Number of subjects with AEs was reported.

End point type	Secondary

End point timeframe:

From start of the study to end of Follow up period (up to Month 18)

End point values	Loceryl + Cosmetic Varnish	Loceryl Nail Lacquer Alone	Loceryl Nail Lacquer up to Additional 15 months	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	26	24	29	
Units: Subjects	13	11	20	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From start of the study to end of Follow up period (up to Month 18)	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	16.0

Reporting groups	
Reporting group title	Loceryl + Cosmetic Varnish
Reporting group description:	
Subjects applied Loceryl Nail Lacquer once a week in the morning for 12 weeks and cosmetic varnish was applied once a week in the morning (24 hours after application of Loceryl Nail Lacquer).	
Reporting group title	Loceryl Nail Lacquer Alone
Reporting group description:	
Subjects applied Loceryl Nail Lacquer alone once a week in the morning for 12 weeks after filing down the affected toenails.	
Reporting group title	Loceryl Nail Lacquer up to Additional 15 months
Reporting group description:	
Subjects without clinical signs of aggravation of onychomycosis at Week 12 in both the reporting arms of treatment period continued to apply Loceryl Nail Lacquer once a week in the morning for additional 15 months.	

Serious adverse events	Loceryl + Cosmetic Varnish	Loceryl Nail Lacquer Alone	Loceryl Nail Lacquer up to Additional 15 months
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 26 (0.00%)	0 / 24 (0.00%)	2 / 29 (6.90%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tonsil cancer			
subjects affected / exposed	0 / 26 (0.00%)	0 / 24 (0.00%)	1 / 29 (3.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Coronary artery disease			
subjects affected / exposed	0 / 26 (0.00%)	0 / 24 (0.00%)	1 / 29 (3.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Loceryl + Cosmetic Varnish	Loceryl Nail Lacquer Alone	Loceryl Nail Lacquer up to Additional 15 months
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 26 (11.54%)	4 / 24 (16.67%)	10 / 29 (34.48%)
General disorders and administration site conditions			
Influenza like illness			
subjects affected / exposed	0 / 26 (0.00%)	4 / 24 (16.67%)	5 / 29 (17.24%)
occurrences (all)	0	4	5
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	1 / 26 (3.85%)	2 / 24 (8.33%)	3 / 29 (10.34%)
occurrences (all)	1	2	3
Sinusitis			
subjects affected / exposed	2 / 26 (7.69%)	0 / 24 (0.00%)	0 / 29 (0.00%)
occurrences (all)	2	0	0
Tonsillitis			
subjects affected / exposed	2 / 26 (7.69%)	0 / 24 (0.00%)	2 / 29 (6.90%)
occurrences (all)	2	0	2

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
29 July 2014	Amendment 1: Addition of a 15-month Follow-up period with photographic assessment every 3 months.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported