Clinical trial results:
Multicentre, open label study to assess the tolerability of P-3058 nail solution in paediatric patients affected by mild-to-moderate onychomycosis

Summary

EudraCT number	2013-005595-17
Trial protocol	IT DE BE LV ES
Global end of trial date	02 August 2017

Results information

Result version number	v1 (current)
This version publication date	07 February 2018
First version publication date	07 February 2018

Trial information

Trial identification

Sponsor protocol code	PM Ped-004

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02547701
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Polichem S.A.
Sponsor organisation address	Via Senago 42 D, Lugano, Switzerland, 6912
Public contact	Director, Clinical Development, Polichem S.A., +41 0919864024, maurizio.caserini@polichem.com
Scientific contact	Director, Clinical Development, Polichem S.A., +41 0919864024, maurizio.caserini@polichem.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-001259-PIP02-13
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 September 2017
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	02 August 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objectives of the study was to evaluate the tolerability and safety of topical treatment with P-3058 10% once a week in pediatric subjects with onychomycosis.

Protection of trial subjects:

The clinical trial was conducted in compliance with globally accepted standards of good clinical practice (as defined in the ICH E6 guideline for good clinical practice, January 1997), in agreement with the Declaration of Helsinki (Seoul, October 2008).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	26 August 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	Spain: 3
Country: Number of subjects enrolled	Belgium: 7
Country: Number of subjects enrolled	Germany: 3
Country: Number of subjects enrolled	Italy: 4
Country: Number of subjects enrolled	Latvia: 3
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)	16
Adolescents (12-17 years)	4
Adults (18-64 years)	0

From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted in Italy, Belgium, Germany, Latvia and Spain between 26 August 2014 (first subject first visit) and 02 August 2017 (last subject last visit).

Pre-assignment

Screening details:

A total of 46 subjects were screened, 20 entered the study and received treatment while 26 subjects were screening failures.

Period 1

Period 1 title	Overall Trial (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Age group 2-11 years

Arm description:

Pediatrics subjects with mild to moderate distal subungual onychomycosis (DSO) or White Superficial Onychomycosis (WSO) were planned for enrolment. However, only subjects with mild to moderate toenails DSO were included in the study. They applied P-3058 10% to all toenails according to the appropriate treatment schedule.

Arm type	Experimental
Investigational medicinal product name	P-3058
Investigational medicinal product code	P-3058
Other name	
Pharmaceutical forms	Cutaneous solution
Routes of administration	Topical use

Dosage and administration details:

Nails affected by mild to moderate DSO or WSO were applied with P-3058 10% nail solution preferably at bedtime, over the nail plate, hyponychium and in the surrounding skin once a day for the first 4 weeks and then once a week according to the different dosage schedule per age group.

Arm title	Age group 12-17 years

Arm description:

Pediatrics subjects with mild to moderate DSO or WSO were planned for enrollment. However, only subjects with mild to moderate toenails DSO were included in the study. They applied P-3058 10% to all toenails according to the appropriate treatment schedule.

Arm type	Experimental
Investigational medicinal product name	P 3058
Investigational medicinal product code	P 3058
Other name	
Pharmaceutical forms	Cutaneous solution
Routes of administration	Topical use

Dosage and administration details:

Nails affected by mild to moderate DSO or WSO were applied with P-3058 10% nail solution preferably at bedtime, over the nail plate, hyponychium and in the surrounding skin once a day application for the first 4 weeks and then once a week according to the different dosage schedule per age group.

Number of subjects in period 1	Age group 2-11 years	Age group 12-17 years
Started	16	4
Completed	15	4
Not completed	1	0
Lost to follow-up	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Age group 2-11 years
Reporting group description:	
Pediatrics subjects with mild to moderate distal subungual onychomycosis (DSO) or White Superficial Onychomycosis (WSO) were planned for enrolment. However, only subjects with mild to moderate toenails DSO were included in the study. They applied P-3058 10% to all toenails according to the appropriate treatment schedule.	
Reporting group title	Age group 12-17 years
Reporting group description:	
Pediatrics subjects with mild to moderate DSO or WSO were planned for enrollment. However, only subjects with mild to moderate toenails DSO were included in the study. They applied P-3058 10% to all toenails according to the appropriate treatment schedule.	

Reporting group values	Age group 2-11 years	Age group 12-17 years	Total
Number of subjects	16	4	20
Age categorical			
Units: Subjects			
Age continuous			
Units: years			
arithmetic mean	7.19	14.00	
standard deviation	± 3.12	± 1.83	-
Gender categorical			
Units: Subjects			
Female	8	1	9
Male	8	3	11
Race			
Units: Subjects			
Black or African American	1	0	1
White	14	4	18
Other	1	0	1

End points

End points reporting groups

Reporting group title	Age group 2-11 years

Reporting group description:

Pediatrics subjects with mild to moderate distal subungual onychomycosis (DSO) or White Superficial Onychomycosis (WSO) were planned for enrolment. However, only subjects with mild to moderate toenails DSO were included in the study. They applied P-3058 10% to all toenails according to the appropriate treatment schedule.

Reporting group title	Age group 12-17 years

Reporting group description:

Pediatrics subjects with mild to moderate DSO or WSO were planned for enrollment. However, only subjects with mild to moderate toenails DSO were included in the study. They applied P-3058 10% to all toenails according to the appropriate treatment schedule.

Subject analysis set title	Safety population (SAF)
Subject analysis set type	Safety analysis

Subject analysis set description:

SAF included all enrolled subjects with signed informed consent who have at least one documented application of the investigational drug and one post-baseline safety assessment.

Primary: Local tolerability at the application site

End point title	Local tolerability at the application site[1]

End point description:

Local tolerability at the application site (all treated nails) was assessed during the study by means of the Severity Score for Skin Irritation. Incidence rate was calculated. Incidence Rate was calculated dividing the number of skin irritation events by the 10 toenails*time * 1000.

End point type	Primary

End point timeframe:

From start of study drug administration until 12 weeks after the last dose of study treatment

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: Descriptive statistics were done, no inferential statistical analyses were performed.

End point values	Age group 2-11 years	Age group 12-17 years		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16[2]	4[3]		
Units: Events per 1,000 toenails-time				
number (not applicable)	0.015	0.000		

Notes:

[2] - SAF

[3] - SAF

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Treatment-emergent Adverse Events (TEAEs)

End point title	Number of Subjects With Treatment-emergent Adverse Events (TEAEs)

End point description:

An adverse event (AE) was any untoward medical occurrence in a clinical study subject (regardless of the administration of the study treatment and its causal relationship to it). A treatment emergent AE

was defined as an AE with an onset date after treatment initiation.

End point type	Secondary

End point timeframe:

From start of study drug administration until 12 weeks after the last dose of study treatment

End point values	Age group 2-11 years	Age group 12-17 years		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16[4]	4[5]		
Units: Subject	12	3		

Notes:

[4] - SAF

[5] - SAF

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From start of study drug administration until 12 weeks after the last dose of study treatment

Adverse event reporting additional description:

Adverse event data provided below was for treatment emergent AEs. A treatment emergent AE was defined as an AE with an onset date after treatment initiation.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.0

Reporting groups

Reporting group title	Age group 12-17 years

Reporting group description:

Pediatrics subjects with mild to moderate DSO or WSO were planned for enrolment. However, only subjects with mild to moderate toenails DSO were included in the study. They applied P-3058 10% to all toenails according to the appropriate treatment schedule.

Reporting group title	Age group 2-11 years

Reporting group description:

Pediatrics subjects with mild to moderate DSO or WSO were planned for enrolment. However, only subjects with mild to moderate toenails DSO were included in the study. They applied P-3058 10% to all toenails according to the appropriate treatment schedule.

Serious adverse events	Age group 12-17 years	Age group 2-11 years	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 4 (0.00%)	1 / 16 (6.25%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Infections and infestations			
Erysipelas			
subjects affected / exposed	0 / 4 (0.00%)	1 / 16 (6.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Age group 12-17 years	Age group 2-11 years	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 4 (75.00%)	12 / 16 (75.00%)	
Injury, poisoning and procedural complications			

Fall			
subjects affected / exposed	0 / 4 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 4 (0.00%)	2 / 16 (12.50%)	
occurrences (all)	0	2	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	1 / 4 (25.00%)	2 / 16 (12.50%)	
occurrences (all)	1	2	
Nausea			
subjects affected / exposed	0 / 4 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Reproductive system and breast disorders			
Adnexa uteri pain			
subjects affected / exposed	0 / 4 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	0 / 4 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			
Onychoclasis			
subjects affected / exposed	1 / 4 (25.00%)	1 / 16 (6.25%)	
occurrences (all)	1	1	
Skin irritation			
subjects affected / exposed	0 / 4 (0.00%)	3 / 16 (18.75%)	
occurrences (all)	0	3	
Rash pruritic			
subjects affected / exposed	0 / 4 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	

Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 4 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 4 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Cystitis			
subjects affected / exposed	0 / 4 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Ear infection			
subjects affected / exposed	0 / 4 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Gastroenteritis viral			
subjects affected / exposed	0 / 4 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Influenza			
subjects affected / exposed	1 / 4 (25.00%)	1 / 16 (6.25%)	
occurrences (all)	1	1	
Gastrointestinal infection			
subjects affected / exposed	0 / 4 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Gastroenteritis			
subjects affected / exposed	1 / 4 (25.00%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Varicella			
subjects affected / exposed	0 / 4 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Viral upper respiratory tract infection			
subjects affected / exposed	2 / 4 (50.00%)	3 / 16 (18.75%)	
occurrences (all)	2	5	
Viral infection			
subjects affected / exposed	0 / 4 (0.00%)	2 / 16 (12.50%)	
occurrences (all)	0	2	
Tonsillitis			

subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 1	0 / 16 (0.00%) 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

None reported