Clinical trial results:
Assessment of the efficacy of POLYGYNAX® in the empirical treatment of infectious vaginitis
International, multicentre, randomised, double-blind, parallel group study, comparative versus miconazole

Summary

EudraCT number	2014-001759-22
Trial protocol	FR CZ SK
Global end of trial date	25 August 2016

Results information

Result version number	v1 (current)
This version publication date	15 July 2018
First version publication date	15 July 2018

Trial information

Trial identification

Sponsor protocol code	PGX401-11

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02515656
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Laboratoire Innotech International
Sponsor organisation address	22 avenue Aristide Briand, ARCUEIL, France, 94111 Cedex
Public contact	Medical Affairs Department, Laboratoire Innotech International, 0033 146152800,
Scientific contact	Medical Affairs Department, Laboratoire Innotech International, 0033 146152800,

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	25 August 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	25 August 2016
Global end of trial reached?	Yes
Global end of trial date	25 August 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study is to demonstrate the superior clinical efficacy of POLYGYNAX® at the End of Treatment Visit (Visit 2 / D15 or Premature Discontinuation Visit if any) compared to miconazole in the empirical treatment of infectious vaginitis

Protection of trial subjects:

Not applicable

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	07 September 2015
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Slovakia: 131
Country: Number of subjects enrolled	Czech Republic: 318
Country: Number of subjects enrolled	France: 148
Country: Number of subjects enrolled	Serbia: 61
Worldwide total number of subjects	658
EEA total number of subjects	597

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)	658
From 65 to 84 years	0

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Recruitment period: 07 Sep 2015 to 03 Aug 2016.
Countries involved: France - Czech Republic - Slovakia - Serbia

Pre-assignment

Screening details: -

Pre-assignment period milestones

Number of subjects started	658
Number of subjects completed	658

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Polygynax

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Polygynax
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Vaginal capsule, soft
Routes of administration	Vaginal use

Dosage and administration details:

Nystatin (100 000 IU) + Neomycin sulphate (35 000 IU) + Polymyxin B sulphate (35 000 IU).
One vaginal capsule once daily for 12 consecutive days.

Arm title	Miconazole+Placebo

Arm description: -

Arm type	Active comparator
Investigational medicinal product name	Miconazole+Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Vaginal capsule, soft
Routes of administration	Vaginal use

Dosage and administration details:

Miconazole nitrate (400mg) + Placebo
One Miconazole capsule once daily for 3 consecutive days then one placebo capsule once daily for 9 consecutive days.

Number of subjects in period 1	Polygynax	Miconazole+Placebo
Started	326	332
Completed	270	261
Not completed	56	71
Consent withdrawn by subject	1	5
Screening failure	1	-
Adverse event, non-fatal	1	3
Use of treatment not allowed	-	1
Lost to follow-up	-	2
Lack of efficacy	25	39
STI detected from the first vaginal sample	24	19
Final visit not done	4	2

Baseline characteristics

Reporting groups	
Reporting group title	Polygynax
Reporting group description: -	
Reporting group title	Miconazole+Placebo
Reporting group description: -	

Reporting group values	Polygynax	Miconazole+Placebo	Total
Number of subjects	326	332	658
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)	326	332	658
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	34.26	33.51	
standard deviation	± 10.18	± 9.97	-
Gender categorical Units: Subjects			
Female	326	332	658
Male	0	0	0

Subject analysis sets	
Subject analysis set title	FAS population
Subject analysis set type	Full analysis

Subject analysis set description:

The FAS population is defined as all randomised patients excluding (as allowed by ICH E9):
• Patients who did not take at least one dose of the study medication
• Patients who present an STI (trichomoniasis; gonococcal and chlamydial infections) detected from the vaginal sample taken before randomisation at the Baseline Visit (Visit 1 / D1).
• Patients without post-randomisation data.

Subject analysis set title	PPS population
Subject analysis set type	Per protocol

Subject analysis set description:

The PPS population consists of all patients of the FAS without any major protocol deviation. This is the set of patients who participated in the study as intended. Before locking the data base, the precise reasons for excluding patients from the PP data set were fully defined and documented during a blind review meeting.

Subject analysis set title	mPPS Population
Subject analysis set type	Sub-group analysis

Subject analysis set description:

The mPPS population consists of all patients of the FAS without any major protocol deviation except deviations about randomization process. This population was used for an additional sensitivity analysis on the PPS to document the influence of including or excluding these patients with deviations from the randomisation schedule.

Subject analysis set title	Safety Population
Subject analysis set type	Safety analysis

Subject analysis set description:

The SS population comprises all enrolled patients in the study, who have been administered at least one capsule of study drug.

Reporting group values	FAS population	PPS population	mPPS Population
Number of subjects	611	552	585
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)	611	552	585
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	34.21	34.33	34.16
standard deviation	± 10.11	± 10.14	± 10.03
Gender categorical Units: Subjects			
Female	611	552	585
Male	0	0	0

Reporting group values	Safety Population		
Number of subjects	653		
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	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)	653		
From 65-84 years	0		
85 years and over	0		
Age continuous Units: years			
arithmetic mean	33.94		
standard deviation	± 10.09		

Gender categorical Units: Subjects			
Female	653		
Male	0		

End points

End points reporting groups

Reporting group title	Polygynax
Reporting group description: -	
Reporting group title	Miconazole+Placebo
Reporting group description: -	
Subject analysis set title	FAS population
Subject analysis set type	Full analysis

Subject analysis set description:

The FAS population is defined as all randomised patients excluding (as allowed by ICH E9):
• Patients who did not take at least one dose of the study medication
• Patients who present an STI (trichomoniasis; gonococcal and chlamydial infections) detected from the vaginal sample taken before randomisation at the Baseline Visit (Visit 1 / D1).
• Patients without post-randomisation data.

Subject analysis set title	PPS population
Subject analysis set type	Per protocol

Subject analysis set description:

The PPS population consists of all patients of the FAS without any major protocol deviation. This is the set of patients who participated in the study as intended. Before locking the data base, the precise reasons for excluding patients from the PP data set were fully defined and documented during a blind review meeting.

Subject analysis set title	mPPS Population
Subject analysis set type	Sub-group analysis

Subject analysis set description:

The mPPS population consists of all patients of the FAS without any major protocol deviation except deviations about randomization process. This population was used for an additional sensitivity analysis on the PPS to document the influence of including or excluding these patients with deviations from the randomisation schedule.

Subject analysis set title	Safety Population
Subject analysis set type	Safety analysis

Subject analysis set description:

The SS population comprises all enrolled patients in the study, who have been administered at least one capsule of study drug.

Primary: Clinical treatment efficacy assessed by the investigator

End point title	Clinical treatment efficacy assessed by the investigator[1]

End point description:

End point type	Primary

End point timeframe:

Visit 2 / Day 15

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 procedure for the primary endpoint statistical analysis at the final analysis is: the proportion of patients with a success according to investigator clinical assessment was computed and compared between treatment groups using a test for the difference between two binomial proportions in SAS SEQTEST procedure.

End point values	Polygynax	Miconazole+Placebo	FAS population	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	302	309	611	
Units: % Success				
number (not applicable)	91.1	86.7	88.9	

Statistical analyses

No statistical analyses for this end point

Secondary: Change in vaginal discharge and in each associated clinical symptoms reported by the patient in the diary

End point title	Change in vaginal discharge and in each associated clinical symptoms reported by the patient in the diary

End point description:

End point type	Secondary

End point timeframe:

From visit 1 / D1 to visit 2 / D14

End point values	Polygynax	Miconazole+Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	302	309		
Units: mm				
least squares mean (confidence interval 95%)				
Vaginal Discharge	31.43 (29.94 to 32.91)	29.54 (28.07 to 31.01)		
Vaginal Burning	27.89 (26.66 to 29.12)	27.03 (25.81 to 28.25)		
Vaginal Pain	16.93 (15.86 to 18.01)	17.17 (16.1 to 18.24)		
Vaginal Irritation	29.37 (28.06 to 30.67)	28.79 (27.51 to 30.08)		
Combined clinical symptoms	28.96 (26.79 to 31.14)	28.2 (26.04 to 30.35)		

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical treatment efficacy at end of study

End point title	Clinical treatment efficacy at end of study

End point description:

End point type	Secondary

End point timeframe:
Visit 3 / Day 22

End point values	Polygynax	Miconazole+Placebo	FAS population	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	302	309	611	
Units: % Success				
number (not applicable)	84.8	82.5	83.7	

Statistical analyses

No statistical analyses for this end point

Secondary: Investigator's global satisfaction

End point title	Investigator's global satisfaction

End point description:

End point type	Secondary

End point timeframe:
Visit 2 / Day 15

End point values	Polygynax	Miconazole+Placebo	FAS population	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	302	309	611	
Units: % satisfaction				
number (not applicable)				
Very Good - Good	88.3	82.1	85.2	
Somewhat Good - Somewhat Bad	8.3	13	10.7	
Bad - Very Bad	3.3	4.9	4.1	

Statistical analyses

No statistical analyses for this end point

Secondary: Patient's global satisfaction

End point title	Patient's global satisfaction

End point description:

End point type	Secondary

End point timeframe:
Visit 2 / Day 15

End point values	Polygynax	Miconazole+Placebo	FAS population	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	302	309	611	
Units: % Satisfaction				
number (not applicable)				
Very Good - Good	81.8	78.2	80	
Somewhat Good - Somewhat Bad	17.1	21.1	19.2	
Bad - Very Bad	1	0.7	0.8	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: 22 days	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	19
Reporting groups	
Reporting group title	Polygynax
Reporting group description: -	
Reporting group title	Miconazole + Placebo
Reporting group description: -	

Serious adverse events	Polygynax	Miconazole + Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 325 (0.31%)	0 / 328 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Patient pregnant exposed to study medication			
subjects affected / exposed	1 / 325 (0.31%)	0 / 328 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 2 %

Non-serious adverse events	Polygynax	Miconazole + Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	18 / 325 (5.54%)	5 / 328 (1.52%)	
Nervous system disorders			
Headache			
subjects affected / exposed	18 / 325 (5.54%)	5 / 328 (1.52%)	
occurrences (all)	24	6	

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