Clinical trial results:
A prospective, multicentre, uncontrolled study of Geonistin vaginal tablets effectiveness with pharmacokinetic evaluation for unspecific and mixed vulvovaginal infections characterized by vaginal discharge

Summary

EudraCT number	2016-000078-39
Trial protocol	HR
Global end of trial date	13 December 2016

Results information

Result version number	v1 (current)
This version publication date	28 February 2020
First version publication date	28 February 2020

Trial information

Trial identification

Sponsor protocol code	GEO-2014/01-HR

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	PLIVA Croatia Ltd.
Sponsor organisation address	Prilaz baruna Filipovića 25, Zagreb, Croatia, 10000
Public contact	Mirjana Matrapazovski Kukuruzović, MD, PLIVA Croatia Ltd., 385 13724962, Mirjana.Matrapazovski-Kukuruzovic@pliva.com
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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	31 March 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	13 December 2016
Global end of trial reached?	Yes
Global end of trial date	13 December 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study was to evaluate the clinical effectiveness of Geonistin vaginal tablets administered in empirical treatment of female adult patients with unspecific and mixed vulvovaginal infections characterized by vaginal discharge.
The secondary objectives of the study were to evaluate the: (1) systemic exposure to oxytetracycline in local treatment of vulvovaginal infections with Geonistin vaginal tablets; (2) cure rate according to the Nugent score (where applicable); (3) microbiology and microscopy results (outcome); and (4) safety of Geonistin vaginal tablets.

Protection of trial subjects:

The study was conducted according to Helsinki Declaration, in compliance with local regulations and in accordance with PLIVA Croatia Ltd. standard procedures.
This study was conducted in full accordance with the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) Consolidated Guideline (E6) and any applicable national and local laws and regulations, European Union [EU] Directive 2001/20/EC on the approximation of the laws, regulations and administrative provisions of the Member States relating to the implementation of GCP in the conduct of clinical trials on medicinal products for human use).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 September 2016
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	Croatia: 192
Worldwide total number of subjects	192
EEA total number of subjects	192

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)	192
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Physicians were asked to recruit patients that require Geonistin vaginal tablets treatment from their everyday practice during regular office visit, according to predefined inclusion and exclusion criteria. In total 194 patients were assessed for eligibility, 192 patients were enrolled and 189 completed the study.

Pre-assignment

Screening details:

2 subjects were assessed for eligibility but they were excluded per exclusion criteria.

Period 1

Period 1 title	Geonistin (Baseline)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Period 1
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	Geonistin vaginal tablets
Investigational medicinal product code	
Other name	Geonistin
Pharmaceutical forms	Tablet
Routes of administration	Vaginal use

Dosage and administration details:

One vaginal tablet containing 100 mg oxytetracycline and 100,000 IU nystatin was self-administered by a patient once daily over 6 consecutive days.

Number of subjects in period 1	Period 1
Started	192
Completed	189
Not completed	3
Lost to follow-up	3

Period 2

Period 2 title	Geonistin End of Study
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Period 1
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	Geonistin vaginal tablets
Investigational medicinal product code	
Other name	Geonistin
Pharmaceutical forms	Tablet
Routes of administration	Vaginal use

Dosage and administration details:

One vaginal tablet containing 100 mg oxytetracycline and 100,000 IU nystatin was self-administered by a patient once daily over 6 consecutive days.

Number of subjects in period 2	Period 1
Started	189
Completed	189

Baseline characteristics

Reporting groups	
Reporting group title	Geonistin (Baseline)
Reporting group description:	
Geonistin tablets administered for 6 day open label treatment period. One tablet containing 100 mg oxytetracycline and 100,000 IU nystatin was self-administered once daily.	

Reporting group values	Geonistin (Baseline)	Total	
Number of subjects	192	192	
Age Categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	192	192	
From 65-84 years	0	0	
85 years and over	0	0	
Age Continuous Units: years			
arithmetic mean	32.6		
standard deviation	± 8.1	-	
Gender Categorical Units: Subjects			
Female	192	192	
Male	0	0	

End points

End points reporting groups

Reporting group title	Period 1
Reporting group description: -	
Reporting group title	Period 1
Reporting group description: -	

Primary: Clinical cure rate after 6 days of treatment

End point title	Clinical cure rate after 6 days of treatment
End point description:	
Clinical effectiveness was evaluated on Day 13 (Visit 2) after 6 days of treatment. Signs and symptoms such as vaginal discharge, odor, itching, were rated as present or absent. Clinical cure was defined as signs or symptoms identified on Day 1 that were absent on Day 13. Signs and symptoms were also rated by severity. Severity was rated as mild, moderate, or severe. Cure rate was defined as absent or improved from severe to mild.	
End point type	Primary
End point timeframe:	
Day 13	

End point values	Period 1	Period 1		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	189[1]	189[2]		
Units: Participants	0	154		

Notes:

[1] - All participants were assessed at end of the study.

[2] - Of 189 participants counted, 154 were considered cured.

Statistical analyses

Statistical analysis title	Confidence interval of a binomial proportion
Statistical analysis description:	
95% two-sided Clopper-Pearson confidence interval for clinical cure rate	
Comparison groups	Period 1 v Period 1
Number of subjects included in analysis	378
Analysis specification	Pre-specified
Analysis type	other[3]
P-value	< 0.025 [4]
Method	Clopper-Pearson
Parameter estimate	Percentage
Point estimate	81.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	75.2
upper limit	86.7

Notes:

[3] - Single arm assessed at end of the study (189 participants, not 378 as shown below). 154 out of 189 participants counted were considered cured (154 out of 189 = 81.5%).
[4] - Statistically significant clinical effect implied by lower limit of 95% confidence interval for cure rate above 60%

Secondary: Steady-state serum concentrations of oxytetracycline

End point title	Steady-state serum concentrations of oxytetracycline

End point description:

Steady-state serum concentrations were calculated from pharmacokinetic measurements on Day 7.

End point type	Secondary

End point timeframe:

Day 7

End point values	Period 1			
Subject group type	Reporting group			
Number of subjects analysed	11[5]			
Units: ng/ml				
arithmetic mean (standard deviation)				
oxytetracycline level	20.16 (± 4.99)			

Notes:

[5] - Number of subjects analyzed equals number of participants with quantifiable data available

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants clinically cured based on Nugent score

End point title	Number of participants clinically cured based on Nugent score

End point description:

Effectiveness was assessed based on improvement in Nugent scores from Day 1 to Day 13. Nugent scores of 4-6 (intermediate flora) and greater than or equal to 7 (bacterial vaginosis) were included in the analysis. Cured was defined as a Nugent score of 0-3 on Day 13.

End point type	Secondary

End point timeframe:

Day 13 after 6 days of treatment

End point values	Period 1			
Subject group type	Reporting group			
Number of subjects analysed	138[6]			
Units: Number of participants	67			

Notes:

[6] - 138 participants had countable data. 67 out of 138 were considered cured.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants cured according to microbiological results

End point title	Number of participants cured according to microbiological results

End point description:

Microbiological cure rate was assessed for participants with microorganisms identified at Day 1 visit. Cure was defined as a negative culture (no growth) for baseline pathogens or 1+ if the baseline value was greater than 1+.

End point type	Secondary

End point timeframe:

Day 13 after 6 days of treatment

End point values	Period 1			
Subject group type	Reporting group			
Number of subjects analysed	151[7]			
Units: Number of participants	119			

Notes:

[7] - Of 151 participants assessed, 119 were considered cured.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants who reported at least one adverse event

End point title	Number of participants who reported at least one adverse event

End point description:

Adverse events were collected from signing the informed consent form through Day 13 (Visit 2) and were self-reported until the end of the follow up period (Day 30).

End point type	Secondary

End point timeframe:

Up to Day 30

End point values	Period 1			
Subject group type	Reporting group			
Number of subjects analysed	192[8]			
Units: Number of participants	13			

Notes:

[8] - 13 participants experienced at least one adverse event.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events (AEs) were collected from the signature of the informed consent form through Day 13 (Visit 2) and were self-reported until the follow up period, Day 30.

Adverse event reporting additional description:

Reported adverse events (AEs) are adverse events that are treatment emergent. Treatment emergent adverse events were AEs reported between the first dose of Geonistin up until the follow up period, Day 30.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.1

Reporting groups

Reporting group title	Geonistin

Reporting group description:

Received at least one dose of Geonistin

Serious adverse events	Geonistin		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 192 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

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

Non-serious adverse events	Geonistin		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	13 / 192 (6.77%)		
Cardiac disorders			
Tachycardia			
subjects affected / exposed	1 / 192 (0.52%)		
occurrences (all)	1		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	1 / 192 (0.52%)		
occurrences (all)	1		
Ear and labyrinth disorders			

Vertigo subjects affected / exposed occurrences (all)	1 / 192 (0.52%) 1		
Reproductive system and breast disorders Breast pain subjects affected / exposed occurrences (all) Vulvovaginal discomfort subjects affected / exposed occurrences (all) Vaginitis gardnerella subjects affected / exposed occurrences (all)	 1 / 192 (0.52%) 1 1 / 192 (0.52%) 1 1 / 192 (0.52%) 1		
Gastrointestinal disorders Anal pruritis subjects affected / exposed occurrences (all)	 1 / 192 (0.52%) 1		
Renal and urinary disorders Cystitis subjects affected / exposed occurrences (all)	 1 / 192 (0.52%) 1		
Psychiatric disorders Insomnia subjects affected / exposed occurrences (all)	 1 / 192 (0.52%) 1		
Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all)	 1 / 192 (0.52%) 1		
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all) Enterovirus subjects affected / exposed occurrences (all) Urinary tract infection	 1 / 192 (0.52%) 1 1 / 192 (0.52%) 1		

subjects affected / exposed	2 / 192 (1.04%)		
occurrences (all)	2		
Tooth abscess			
subjects affected / exposed	1 / 192 (0.52%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
07 November 2016	Protocol amendment 1 was prepared to clarify exclusion criteria 13 (ongoing use of vaginal probiotics)

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported