Clinical trial results:
A Phase 2b, Double-blind, Randomized, Parallel, Placebo-Controlled Study to Evaluate the 12-week Efficacy of Vagitocin in Postmenopausal Women with Symptoms of Vulvovaginal Atrophy

Summary

EudraCT number	2016-000158-36
Trial protocol	SE
Global end of trial date	03 May 2017

Results information

Result version number	v1 (current)
This version publication date	08 November 2020
First version publication date	08 November 2020
Summary attachment (see zip file)	2016-000158-36, OXYPEP202, Study Report Summary (2016-000158-36, OXYPEP202, Study Report Summary.pdf)

Trial information

Trial identification

Sponsor protocol code	OXYPEP202

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	PEPTONIC medical AB
Sponsor organisation address	Gustavslundsvägen 143, Bromma, Sweden, 16751
Public contact	Dan Markusson, PEPTONIC medical AB, 46 853020110, dan.markusson@peptonicmedical.se
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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	22 June 2017
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	03 May 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of Vagitocin in reducing the severity of the most bothersome symptom of vulvovaginal atrophy (VVA) associated with menopause after 12 weeks of treatment.

Protection of trial subjects:

The study was performed in accordance with the ethical principles that have their origin in the Declaration of Helsinki that are consistent with International Conference on Harmonisation (ICH)/Good Clinical Practice (GCP) and applicable regulatory requirements.

Background therapy:

Prior and concomitant medications was collected at Screening and throughout the study. Any hormonal therapy taken within 1 year prior to the Screening visit was recorded as a prior medication with the corresponding indication. Any other medication and dietary supplements taken within 12 weeks prior to the initial administration of the Screening visit were also recorded as prior medications. Concomitant medications included any medication including OTC products and herbal or nutritional supplements/medications taken during the active study period. The investigator or designee assessed changes in concomitant medications throughout the study by asking the subject at each visit and, when appropriate, during

Evidence for comparator: -

Actual start date of recruitment	02 May 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	Sweden: 202
Worldwide total number of subjects	202
EEA total number of subjects	202

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	0

months)	
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	193
From 65 to 84 years	9
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

First subject was screened on 2016-04-19. A total of 211 women were screened. 161 were randomised in the main part of the study, which was conducted at 3 centres in Sweden. Last subject last visit was 2017-02-15

Pre-assignment

Screening details:

Patients fulfilling all of the inclusion criteria and none of the exclusion criteria were to be asked to participate in the trial. A total of 211 women were screened and 161 were randomised in the main part of the study. Forty-one subjects were screen failures.

Period 1

Period 1 title	Main part
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Blinding implementation details:

This was a double-blind study, and therefore, subjects, the investigator, study site personnel, and Sponsor personnel involved with data review and analysis, remained blinded to study treatment throughout the study.
The packaging of Vagitocin and placebo was identical in appearance to maintain adequate blinding of study subjects and investigators. Neither the subject nor the investigator could identify the treatment from the packaging or label of the IMP..

Arms

Are arms mutually exclusive?	Yes
Arm title	Vagitocin 400 IU

Arm description:

Vagitocin 400 IU vaginal gel

Arm type	Experimental
Investigational medicinal product name	Vagitocin 400 IU vaginal gel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Vaginal gel
Routes of administration	Vaginal use

Dosage and administration details:

Vagitocin 400 IU/g vaginal gel, 1 mL administered once daily for 12 weeks.

Arm title	Placebo

Arm description:

Placebo vaginal gel

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Vaginal gel
Routes of administration	Vaginal use

Dosage and administration details:

Vaginal gel (placebo), 1 mL administered once daily for 12 weeks.

Number of subjects in period 1[1]	Vagitocin 400 IU	Placebo
Started	81	80
Completed	78	79
Not completed	3	1
Consent withdrawn by subject	-	1
Adverse event, non-fatal	3	-

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: The study includes 2 parts, the main part and the exploratory part. Subjects were included in either the main part or the exploratory part, not in both parts. Thus, the exploratory part is not a continuation of the main part but a separate part. The total number of subjects in the study (202) includes subjects from both parts of the study (main part 161 subjects and 41 subjects).

Period 2

Period 2 title	Exploratory part
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Investigator, Monitor, Data analyst, Carer, Assessor, Subject

Blinding implementation details:

This was a double-blind study, and therefore, subjects, the investigator, study site personnel, and Sponsor personnel involved with data review and analysis, remained blinded to study treatment throughout the study.
The packaging of Vagitocin and placebo was identical in appearance to maintain adequate blinding of study subjects and investigators. Neither the subject nor the investigator could identify the treatment from the packaging or label of the IMP.

Arms

Are arms mutually exclusive?	Yes
Arm title	Vagitocin 400 IU

Arm description:

Vagitocin 400 IU vaginal gel

Arm type	Experimental
Investigational medicinal product name	Vagitocin 400 IU vaginal gel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Vaginal gel
Routes of administration	Vaginal use

Dosage and administration details:

Vagitocin 400 IU/g vaginal gel, 1 mL administered once daily for 12 weeks.

Arm title	Placebo

Arm description:

Placebo vaginal gel

Arm type	Placebo

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Vaginal gel
Routes of administration	Vaginal use

Dosage and administration details:

Vaginal gel (placebo), 1 mL administered once daily for 12 weeks.

Number of subjects in period 2[2]	Vagitocin 400 IU	Placebo
Started	31	10
Completed	30	9
Not completed	1	1
Adverse event, non-fatal	1	1

Notes:

[2] - 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: The study includes 2 parts, the main part and the exploratory part. Subjects were included in either the main part or the exploratory part, not in both parts. Thus, the exploratory part is not a continuation of the main part but a separate part. The total number of subjects in the study (202) includes subjects from both parts of the study (main part 161 subjects and 41 subjects).

Baseline characteristics

Reporting groups	
Reporting group title	Main part
Reporting group description:	
Females aged 40-65 years who were either postmenopausal or had undergone surgical bilateral oophorectomy, with ≤5% superficial cells in vaginal smear cytology, a vaginal pH >5.0, a body mass index (BMI) ≤32 kg/m2, an endometrial thickness of <4 mm and one moderate to severe VVA symptom but who were otherwise in good health and had provided signed informed consent were considered eligible to participate in the study.	

Reporting group values	Main part	Total	
Number of subjects	161	161	
Age categorical			
Females aged 40-65 years who were either postmenopausal or had undergone surgical bilateral oophorectomy, with ≤5% superficial cells in vaginal smear cytology, a vaginal pH >5.0, a body mass index (BMI) ≤32 kg/m2, an endometrial thickness of <4 mm and one moderate to severe VVA symptom but who were otherwise in good health and had provided signed informed consent were considered eligible to participate in the study.			
Units: Subjects			
Adults (18-64 years)	150	150	
From 65-84 years	11	11	
Age continuous			
Females aged 40-65 years who were either postmenopausal or had undergone surgical bilateral oophorectomy, with ≤5% superficial cells in vaginal smear cytology, a vaginal pH >5.0, a body mass index (BMI) ≤32 kg/m2, an endometrial thickness of <4 mm and one moderate to severe VVA symptom but who were otherwise in good health and had provided signed informed consent were considered eligible to participate in the study.			
Units: years			
arithmetic mean	58.3		
standard deviation	± 3.5	-	
Gender categorical			
Females aged 40-65 years			
Units: Subjects			
Female	161	161	
Race Units: Subjects			
Caucasian	159	159	
Other	2	2	
Use of tobacco Units: Subjects			
Never	93	93	
Current	7	7	
Former	60	60	
Missing	1	1	
Alcohol consumption Units: Subjects			
Never	17	17	
Current	144	144	
Height Units: cm			
arithmetic mean	165.9		

standard deviation	± 5.8	-	
Weight			
Units: kg			
arithmetic mean	69.68		
standard deviation	± 9.88	-	
BMI			
Units: kg/m2			
arithmetic mean	25.31		
standard deviation	± 3.28	-	

End points

End points reporting groups

Reporting group title	Vagitocin 400 IU
Reporting group description: Vagitocin 400 IU vaginal gel	
Reporting group title	Placebo
Reporting group description: Placebo vaginal gel	
Reporting group title	Vagitocin 400 IU
Reporting group description: Vagitocin 400 IU vaginal gel	
Reporting group title	Placebo
Reporting group description: Placebo vaginal gel	
Subject analysis set title	Vagitocin 40 IU, baseline 2 (Moderate)
Subject analysis set type	Modified intention-to-treat
Subject analysis set description: VVA symptoms that has been self-identified by the subject as being the most bothersome to her at baseline, shift from baseline (mITT population. Main part)	
Subject analysis set title	Vagitocin 40 IU, baseline 3 (Severe)
Subject analysis set type	Modified intention-to-treat
Subject analysis set description: VVA symptoms that has been self-identified by the subject as being the most bothersome to her at baseline, shift from baseline (mITT population. Main part)	
Subject analysis set title	Placebo , baseline 2 (Moderate)
Subject analysis set type	Modified intention-to-treat
Subject analysis set description: VVA symptoms that has been self-identified by the subject as being the most bothersome to her at baseline, shift from baseline (mITT population. Main part)	
Subject analysis set title	Placebo , baseline 3 (Severe)
Subject analysis set type	Modified intention-to-treat
Subject analysis set description: VVA symptoms that has been self-identified by the subject as being the most bothersome to her at baseline, shift from baseline (mITT population. Main part)	

Primary: Change from baseline to Week 12 in severity of the VVA symptom that has been self-identified by the subject as being the MBS to her at baseline.

End point title	Change from baseline to Week 12 in severity of the VVA symptom that has been self-identified by the subject as being the MBS to her at baseline.
End point description: Change from baseline to Week 12 in severity of the VVA symptom that has been self-identified by the subject as being the MBS to her at baseline. Severity was defined as; 0=None, 1 = Mild, 2 = Moderate, 3=Severe	
End point type	Primary
End point timeframe: Change from baseline to Week 12	

End point values	Vagitocin 400 IU	Placebo	Vagitocin 40 IU, baseline 2 (Moderate)	Vagitocin 40 IU, baseline 3 (Severe)
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	0[1]	0[2]	31	48
Units: percentage				
number (not applicable)				
0=None			14	9
1=Mild			8	6
2=Moderate			6	20
3=Severe			3	13
Missing			0	0

Notes:

[1] - Endpoint reported on other reporting groups

[2] - Endpoint reported on other reporting groups

End point values	Placebo , baseline 2 (Moderate)	Placebo , baseline 3 (Severe)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	43	35		
Units: percentage				
number (not applicable)				
0=None	19	6		
1=Mild	17	12		
2=Moderate	4	6		
3=Severe	3	11		
Missing	0	0		

Statistical analyses

Statistical analysis title	Statistical analysis, Main part

Statistical analysis description:

A Cochran-Mantel-Haenszel test using modified ridit scores (Wilcoxon rank sum test) adjusted for the baseline value was performed.

Comparison groups	Vagitocin 40 IU, baseline 2 (Moderate) v Vagitocin 40 IU, baseline 3 (Severe) v Placebo , baseline 2 (Moderate) v Placebo , baseline 3 (Severe)
Number of subjects included in analysis	157
Analysis specification	Pre-specified
Analysis type	superiority[3]
P-value	< 0.05
Method	Cochran-Mantel-Haenszel

Notes:

[3] - The study was to be considered successful if the two-sided p-value in the statistical analysis of the primary endpoint for the main study was less than 0.0500 and in favour of the active treatment.

Adverse events

Adverse events information	
Timeframe for reporting adverse events: AE reporting from signed informed consent to study completion (Approximately 14 weeks)	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	19.1

Reporting groups	
Reporting group title	Vagitocin 400 IU, main part
Reporting group description: Vagitocin 400 IU vaginal gel,	
Reporting group title	Placebo, main part
Reporting group description: Placebo vaginal gel	
Reporting group title	Vagitocin 400 IU, exploratory part
Reporting group description: -	
Reporting group title	Placebo, exploratory part
Reporting group description: -	

Serious adverse events	Vagitocin 400 IU, main part	Placebo, main part	Vagitocin 400 IU, exploratory part
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 81 (1.23%)	1 / 80 (1.25%)	0 / 31 (0.00%)
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)			
Breast cancer			
subjects affected / exposed	1 / 81 (1.23%)	0 / 80 (0.00%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 81 (0.00%)	1 / 80 (1.25%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Rib fracture			

subjects affected / exposed	0 / 81 (0.00%)	1 / 80 (1.25%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Placebo, exploratory part		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 10 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Rib fracture			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Vagitocin 400 IU, main part	Placebo, main part	Vagitocin 400 IU, exploratory part
Total subjects affected by non-serious adverse events			
subjects affected / exposed	20 / 81 (24.69%)	9 / 80 (11.25%)	7 / 31 (22.58%)
Investigations			
Biopsy endometrium normal			
subjects affected / exposed	0 / 81 (0.00%)	0 / 80 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			

Vaginal discharge			
subjects affected / exposed	8 / 81 (9.88%)	4 / 80 (5.00%)	2 / 31 (6.45%)
occurrences (all)	8	4	2
Vaginal odour			
subjects affected / exposed	2 / 81 (2.47%)	2 / 80 (2.50%)	2 / 31 (6.45%)
occurrences (all)	5	2	2
Vaginal haemorrhage			
subjects affected / exposed	0 / 81 (0.00%)	0 / 80 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	1 / 81 (1.23%)	0 / 80 (0.00%)	0 / 31 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	5 / 81 (6.17%)	2 / 80 (2.50%)	1 / 31 (3.23%)
occurrences (all)	6	2	1
Influenza			
subjects affected / exposed	4 / 81 (4.94%)	1 / 80 (1.25%)	1 / 31 (3.23%)
occurrences (all)	4	1	1
Nasopharyngitis			
subjects affected / exposed	0 / 81 (0.00%)	0 / 80 (0.00%)	1 / 31 (3.23%)
occurrences (all)	0	0	1

Non-serious adverse events	Placebo, exploratory part		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 10 (60.00%)		
Investigations			
Biopsy endometrium normal			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Reproductive system and breast disorders			
Vaginal discharge			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Vaginal odour			

subjects affected / exposed	2 / 10 (20.00%)		
occurrences (all)	2		
Vaginal haemorrhage			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Influenza			
subjects affected / exposed	2 / 10 (20.00%)		
occurrences (all)	2		
Nasopharyngitis			
subjects affected / exposed	2 / 10 (20.00%)		
occurrences (all)	2		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
22 August 2016	There was one substantial amendment to the clinical study protocol during the study, which resulted in the removal of an inclusion criterion and in the update of the vulvovaginal atrophy (VVA) symptoms self-assessment questionnaire.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported