Clinical trial results:
A double-blind, placebo controlled single centre trial to evaluate the dose-relationship of the effects of vaginally administered oxytocin on the vaginal mucosal membrane in postmenopausal women

Summary

EudraCT number	2011-005465-20
Trial protocol	SE
Global end of trial date	08 February 2013

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)	2011-005465-20, OXYPEP002 Clinical Trial Report, Summary (2011-005465-20, OXYPEP002 Clinical Trial Report, Summary.pdf)

Trial information

Trial identification

Sponsor protocol code	OXYPEP002

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01987804
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Peptonic Medical
Sponsor organisation address	Gustavslundsvägen 143, Bromma, Sweden, 16751
Public contact	Dan Markusson, PeP-Tonic Medical AB, +46 0768550200, dan.markusson@peptonicmedical.se
Scientific contact	Dan Markusson, PeP-Tonic Medical AB, +46 0768550200, dan.markusson@peptonicmedical.se

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 August 2012
Is this the analysis of the primary completion data?	Yes
Primary completion date	27 July 2012
Global end of trial reached?	Yes
Global end of trial date	08 February 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective is to investigate the dose-relationship of topical Vagitocin on the vaginal mucosal membrane.

Protection of trial subjects:

The trial was carried out in accordance with:
- The Guidelines of the World Medical Association (WMA) Declaration of Helsinki (as amended by the 59th WMA General Assembly, Seoul, October 2008)
- The Guidelines of Good Clinical Practice (GCP) (CPMP/ICH/135/95)
- Explanatory Note and Comments to the above, issued as CPMP/768/9.
- EU Directive (2005/28/EG, April 2005)
- LVFS 2003:6 (Lakemedelsverkets Forfattningssamling, 2003-06-26); replaced by LVFS 2011:19, 2012-02-01
- Demands of national drug and data protection laws and other applicable regulatory requirements

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

Informed consent was obtained from all patients, at the Baseline visit, prior to initiation of the trial.

Background therapy:

Relevant medication history (prior medications), as judged by the investigator, for a month prior to trial start, was to be recorded in the e-CRF. Prescription medications, over-the-counter (OTC) medications, and herbal products were to be asked for.
The investigator or designee was to assess changes in concomitant medications throughout the trial by asking the patient at each visit. Any changes reported by the patient were to be recorded in the e- CRF.
Usage of any sex steroids, including phytoestrogens, hormonal intra-uterine device or herbal medicinal products with known estrogenic effects was not permitted during the trial.
Usage of any lubricant and/or pharmaceutical agents for symptomatic treatment of vaginal atrophy, including herbal drugs, was not permitted during the trial.

Evidence for comparator:

Not applicable.

Actual start date of recruitment	17 January 2012
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: 64
Worldwide total number of subjects	64
EEA total number of subjects	64

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)	47
From 65 to 84 years	17
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Start of recruitment period: 2012-02-15
End of recrutiment period: 2012-04-27
Territory: Sweden

Pre-assignment

Screening details:

67 patients were screened at the investigational centre and of these, 64 patients (24 each in Vagitocin 100 IU and Vagitocin 400 IU treatment groups and 16 in the placebo group) were randomised.

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, Data analyst, Carer, Assessor

Blinding implementation details:

This was a double-blind trial, and therefore, the allocation of the treatment groups was not known to the patient, the staff at the centre or any other trial personnel (e.g. the sponsor’s or CRO’s representatives), until after the database was locked.
Blinding was accomplished by ensuring that the active substance and placebo were of identical appearance (clear gel), packaging and labelling, with the only difference being the patient identification number/randomisation number on the label.

Arms

Are arms mutually exclusive?	Yes
Arm title	Vagitocin 100 IU

Arm description:

The gel formulation containing 100 IU of oxytocin/ml.

Arm type	Experimental
Investigational medicinal product name	Vagitocin 100 IU
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Gel
Routes of administration	Vaginal use

Dosage and administration details:

The IMP was to be topically administered on the vaginal mucosa, once daily during seven weeks.

Arm title	Vagitocin 400 IU

Arm description:

The gel formulation containing 400 IU of oxytocin/ml.

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

Dosage and administration details:

The IMP was to be topically administered on the vaginal mucosa, once daily during seven weeks.

Arm title	Placebo

Arm description:

The gel formulation containing no active substance.

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

Dosage and administration details:

The IMP was to be topically administered on the vaginal mucosa, once daily during seven weeks.

Number of subjects in period 1	Vagitocin 100 IU	Vagitocin 400 IU	Placebo
Started	24	24	16
Completed	18	23	14
Not completed	6	1	2
Adenocarcinoma	1	-	-
Physician decision	3	-	1
Consent withdrawn by subject	1	1	-
Adverse event, non-fatal	1	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Vagitocin 100 IU
Reporting group description:	
The gel formulation containing 100 IU of oxytocin/ml.	
Reporting group title	Vagitocin 400 IU
Reporting group description:	
The gel formulation containing 400 IU of oxytocin/ml.	
Reporting group title	Placebo
Reporting group description:	
The gel formulation containing no active substance.	

Reporting group values	Vagitocin 100 IU	Vagitocin 400 IU	Placebo
Number of subjects	24	24	16
Age categorical			
Units: Subjects			
Age continuous			
=> 40 years of age			
Units: years			
arithmetic mean	62.0	61.1	63.2
standard deviation	± 5.7	± 5.3	± 5.8
Gender categorical			
Women aged 40 and above			
Units: Subjects			
Female	24	24	16
Ethnicity			
Ethnic group			
Units: Subjects			
African Descent	0	0	0
Asian or Pacific Islanders	0	0	0
Caucasian	24	24	16
Mixed / Multi-racial	0	0	0
Other	0	0	0
Height			
Height (cm)			
Units: Centimeter			
arithmetic mean	166.0	165.5	164.4
standard deviation	± 6.3	± 7.4	± 5.3
Weight			
Weight (kg)			
Units: kilogram(s)			
arithmetic mean	62.94	66.58	64.68
standard deviation	± 6.60	± 12.02	± 7.84

Reporting group values	Total		
Number of subjects	64		

Age categorical Units: Subjects			

Age continuous			
=> 40 years of age			
Units: years arithmetic mean standard deviation	- -		
Gender categorical			
Women aged 40 and above			
Units: Subjects			
Female	64		
Ethnicity			
Ethnic group			
Units: Subjects			
African Descent Asian or Pacific Islanders Caucasian Mixed / Multi-racial Other	0 0 64 0 0		
Height			
Height (cm)			
Units: Centimeter arithmetic mean standard deviation	- -		
Weight			
Weight (kg)			
Units: kilogram(s) arithmetic mean standard deviation	- -		

End points

End points reporting groups

Reporting group title	Vagitocin 100 IU
Reporting group description:	
The gel formulation containing 100 IU of oxytocin/ml.	
Reporting group title	Vagitocin 400 IU
Reporting group description:	
The gel formulation containing 400 IU of oxytocin/ml.	
Reporting group title	Placebo
Reporting group description:	
The gel formulation containing no active substance.	

Primary: Change in percentage points of superficial cells from Baseline visit to 7 weeks of treatment.

End point title	Change in percentage points of superficial cells from Baseline visit to 7 weeks of treatment.
End point description:	
The primary endpoint was the change in percentage points of superficial cells from Baseline visit (Visit 1) to 7 weeks of treatment (Visit 3).	
End point type	Primary
End point timeframe:	
From baseline to 7 weeks of treatment	

End point values	Vagitocin 100 IU	Vagitocin 400 IU	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	24[1]	24[2]	16[3]	
Units: percentage points				
median (full range (min-max))	0.55 (-1.0 to 26.7)	0.20 (-3.5 to 74.1)	0.30 (-4.4 to 8.1)	

Notes:

[1] - Full analysis set

[2] - Full analysis set

[3] - Full analysis set

Statistical analyses

Statistical analysis title	Statistical analysis 1
Statistical analysis description:	
Each active treatment group was separately compared to placebo for superiority in a hierarchical manner. First the superiority of the Vagitocin 400 IU group was tested versus the placebo group and only if the superiority was established, the superiority of the Vagitocin 100 IU group against the placebo group was tested.	
Comparison groups	Vagitocin 100 IU v Placebo

Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	superiority[4]
P-value	< 0.05 [5]
Method	ANCOVA

Notes:

[4] - No adjustment to the type-1 error was made as it was protected by the hierarchical structure of analysis.
The primary efficacy endpoint was to be analysed using ANCOVA with treatment as factor and baseline value as covariate. However, the assumption of normality was not met when tested using the Anderson-Darling test. As a result ANCOVA model on the ranked data was fitted in order to compare the treatment effects.
[5] - All tests were to be two-sided and performed at the 5% significance level if not otherwise specified. When reporting the results of significance tests p-values were to be reported.

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

Each active treatment group was separately compared to placebo for superiority in a hierarchical manner. First the superiority of the Vagitocin 400 IU group was tested versus the placebo group and only if the superiority was
established, the superiority of the Vagitocin 100 IU group against the placebo group was tested.

Comparison groups	Vagitocin 400 IU v Placebo
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	superiority[6]
P-value	< 0.05 [7]
Method	ANCOVA

Notes:

[6] - No adjustment to the type-1 error was made as it was protected by the hierarchical structure of analysis.
The primary efficacy endpoint was to be analysed using ANCOVA with treatment as factor and baseline value as covariate. However, the assumption of normality was not met when tested using the Anderson-Darling test. As a result ANCOVA model on the ranked data was fitted in order to compare the treatment effects.
[7] - All tests were to be two-sided and performed at the 5% significance level if not otherwise specified. When reporting the results of significance tests p-values were to be reported.

Statistical analysis title	Statistical analysis 3

Statistical analysis description:

Each active treatment group was separately compared to placebo for superiority in a hierarchical manner. First the superiority of the Vagitocin 400 IU group was tested versus the placebo group and only if the superiority was
established, the superiority of the Vagitocin 100 IU group against the placebo group was tested.

Comparison groups	Vagitocin 400 IU v Vagitocin 100 IU
Number of subjects included in analysis	48
Analysis specification	Pre-specified
Analysis type	superiority[8]
P-value	< 0.05 [9]
Method	ANCOVA

Notes:

[8] - No adjustment to the type-1 error was made as it was protected by the hierarchical structure of analysis.
The primary efficacy endpoint was to be analysed using ANCOVA with treatment as factor and baseline value as covariate. However, the assumption of normality was not met when tested using the Anderson-Darling test. As a result ANCOVA model on the ranked data was fitted in order to compare the treatment effects.
[9] - All tests were to be two-sided and performed at the 5% significance level if not otherwise specified. When reporting the results of significance tests p-values were to be reported.

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Any apparent side effects experienced by the patient were to be assessed from the time of the first administration of IMP and throughout the course of the entire trial.

Adverse event reporting additional description:

The occurrence of an AE may come to the attention of trial personnel during trial visits and interviews of a trial recipient presenting for medical care, or upon review by a trial monitor who was scrutinising relevant source data.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	15.0

Reporting groups

Reporting group title	Vagitocin 100 IU

Reporting group description:

The gel formulation containing 100 IU of oxytocin/ml.

Reporting group title	Vagitocin 400 IU

Reporting group description:

The gel formulation containing 400 IU of oxytocin/ml.

Reporting group title	Placebo

Reporting group description:

The gel formulation containing no active substance.

Serious adverse events	Vagitocin 100 IU	Vagitocin 400 IU	Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 24 (0.00%)	0 / 24 (0.00%)	0 / 16 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

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

Non-serious adverse events	Vagitocin 100 IU	Vagitocin 400 IU	Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	8 / 24 (33.33%)	9 / 24 (37.50%)	8 / 16 (50.00%)
Cardiac disorders			
Palpitations			
subjects affected / exposed	0 / 24 (0.00%)	1 / 24 (4.17%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Reproductive system and breast disorders			

Vaginal discharge			
subjects affected / exposed	2 / 24 (8.33%)	2 / 24 (8.33%)	2 / 16 (12.50%)
occurrences (all)	2	2	2
Pelvic pain			
subjects affected / exposed	1 / 24 (4.17%)	1 / 24 (4.17%)	1 / 16 (6.25%)
occurrences (all)	1	1	1
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	0 / 24 (0.00%)	0 / 24 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	2 / 24 (8.33%)	3 / 24 (12.50%)	0 / 16 (0.00%)
occurrences (all)	2	4	0
Influenza			
subjects affected / exposed	2 / 24 (8.33%)	1 / 24 (4.17%)	1 / 16 (6.25%)
occurrences (all)	2	1	1
Vaginal infection			
subjects affected / exposed	0 / 24 (0.00%)	0 / 24 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Nasopharyngitis			
subjects affected / exposed	1 / 24 (4.17%)	1 / 24 (4.17%)	1 / 16 (6.25%)
occurrences (all)	1	1	1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
28 February 2012	The percentage of superficial cells, the levels of FSH plasma levels and 17β-estradiol levels at the Baseline visit were the critical criteria to determine whether the patients were suitable for the trial or not. Exclusion criteria number 4 was judged to be redundant. Exclusion criteria number 4 (Vaginal pH ≤ 5.0.) removed.
17 April 2012	The vaginal biopsy from Visit 2 was removed, since it was believed to be inconvenient for both the site staff and the patients. After discussions with the sponsor and the site staff it was concluded that biopsies collected at Baseline and Visit 3 would be sufficient to obtain the desired efficacy results. The variable had no impact on the safety of the patients. Vaginal biopsy at Visit 2 removed. Vaginal biopsies to be collected from 32 patients at the Baseline visit and at Visit 3.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported