



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 recruitment 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 | - | - |
| Consent withdrawn by subject | 1 | 1 | - |
| Physician decision | 3 | - | 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 | 0 | | |
| Asian or Pacific Islanders | 0 | | |
| Caucasian | 64 | | |
| Mixed / Multi-racial | 0 | | |
| Other | 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 occurrences (all) | 2 / 24 (8.33%) 2 | 2 / 24 (8.33%) 2 | 2 / 16 (12.50%) 2 |
| Pelvic pain subjects affected / exposed occurrences (all) | 1 / 24 (4.17%) 1 | 1 / 24 (4.17%) 1 | 1 / 16 (6.25%) 1 |
| Gastrointestinal disorders | | | |
| Nausea subjects affected / exposed occurrences (all) | 0 / 24 (0.00%) 0 | 0 / 24 (0.00%) 0 | 1 / 16 (6.25%) 1 |
| Infections and infestations | | | |
| Urinary tract infection subjects affected / exposed occurrences (all) | 2 / 24 (8.33%) 2 | 3 / 24 (12.50%) 4 | 0 / 16 (0.00%) 0 |
| Influenza subjects affected / exposed occurrences (all) | 2 / 24 (8.33%) 2 | 1 / 24 (4.17%) 1 | 1 / 16 (6.25%) 1 |
| Vaginal infection subjects affected / exposed occurrences (all) | 0 / 24 (0.00%) 0 | 0 / 24 (0.00%) 0 | 1 / 16 (6.25%) 1 |
| Nasopharyngitis subjects affected / exposed occurrences (all) | 1 / 24 (4.17%) 1 | 1 / 24 (4.17%) 1 | 1 / 16 (6.25%) 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 17 β -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 \leq 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