



Clinical trial results:

A phase II, randomised, double-blind, placebo-controlled, parallel-group, multi-centre study investigating efficacy and safety of Sepranolone (UC1010) in patients with PMDD

Summary

| | |
|--------------------------|------------------|
| EudraCT number | 2017-000822-37 |
| Trial protocol | GB DE SE PL |
| Global end of trial date | 25 February 2020 |

Results information

| | |
|-----------------------------------|--|
| Result version number | v1 (current) |
| This version publication date | 06 January 2021 |
| First version publication date | 06 January 2021 |
| Summary attachment (see zip file) | UM203 Asarina CSR Synopsis (Asarina_UM203_CSR Synopsis_final v1.0_23OCT2020.pdf) |

Trial information

Trial identification

| | |
|-----------------------|-------|
| Sponsor protocol code | UM203 |
|-----------------------|-------|

Additional study identifiers

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

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | Asarina Pharma |
| Sponsor organisation address | c/o COBIS, Ole Maaloes Vej 3, Copenhagen, Denmark, 2200 |
| Public contact | Karin Ekberg, Asarina Pharma , +45 707029 80 , karin.ekberg@asarinapharma.com |
| Scientific contact | Karin Ekberg, Asarina Pharma , +45 707029 80 , karin.ekberg@asarinapharma.com |

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 | 17 April 2020 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 25 February 2020 |
| Global end of trial reached? | Yes |
| Global end of trial date | 25 February 2020 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study is to evaluate the effect of two doses of UC1010 on premenstrual symptoms in women with PMDD in comparison to placebo.

The effect of UC1010 given repeatedly to women with PMDD as subcutaneous injections during the luteal phase of three consecutive menstrual cycles will be compared with a corresponding placebo administration. Effect will be assessed by comparison of symptoms recorded daily by the patients using a validated rating scale also used for the diagnosis of PMDD.

Protection of trial subjects:

The clinical safety of the patient was followed throughout their participation in the study with physical examinations (including vital signs and inspection of injection sites), safety blood sampling and AE and concomitant medication reporting. The reporting of AEs started when the first dose of IMP was taken and continued until visit 9, i.e. the close-out visit.

Background therapy: -

Evidence for comparator: -

| | |
|---|---------------|
| Actual start date of recruitment | 20 April 2018 |
| 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 | Poland: 28 |
| Country: Number of subjects enrolled | Sweden: 46 |
| Country: Number of subjects enrolled | United Kingdom: 54 |
| Country: Number of subjects enrolled | Germany: 78 |
| Worldwide total number of subjects | 206 |
| EEA total number of subjects | 206 |

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) | 206 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

The recruitment started on 20 April 2018 and was completed in November 2019. Subjects from Germany, Sweden, Poland, and UK were recruited into the study

Pre-assignment

Screening details:

475 patients enrolled, 206 randomised. 4 randomised patients never started treatment. Patients underwent a qualification period for PMDD diagnosis of at least 2 menstrual cycles.

Screening criteria included: previous participation, height, weight, menstrual cycle details/symptoms, other medications/condition

Pre-assignment period milestones

| | |
|------------------------------|--------------------|
| Number of subjects started | 475 ^[1] |
| Number of subjects completed | 202 |

Pre-assignment subject non-completion reasons

| | |
|----------------------------|-------------------------------------|
| Reason: Number of subjects | screen failure: 269 |
| Reason: Number of subjects | subjects never started treatment: 4 |

Notes:

[1] - The number of subjects reported to have started the pre-assignment 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 number of subjects enrolled is counted as the number randomised and assigned to a treatment arm. A greater number signed the ICF and underwent a 2 month qualification period, but did not meet the criteria for PMDD diagnosis and therefore did not qualify for the study.

Period 1

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

Arms

| | |
|------------------------------|-------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | Sepranolone 10 mg |

Arm description: -

| | |
|--|-------------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Sepranolone |
| Investigational medicinal product code | |
| Other name | UC1010 |
| Pharmaceutical forms | Solution for solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

10 mg per injection once every second day during the luteal phase of 3 consecutive menstrual cycles to women with a verified diagnosis of PMDD. Treatment will start 14 days prior to the next estimated menstruation start and continue until menstruation starts, but with a maximum of 7 doses per cycle. The treatment period is followed by one menstrual cycle of non-treatment as a follow-up cycle.

| | |
|--------------------|-------------------|
| Arm title | Sepranolone 16 mg |
| Arm description: - | |
| Arm type | Experimental |

| | |
|--|-------------------------------------|
| Investigational medicinal product name | Sepranolone |
| Investigational medicinal product code | |
| Other name | UC1010 |
| Pharmaceutical forms | Solution for solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

16 mg per injection once every second day during the luteal phase of 3 consecutive menstrual cycles to women with a verified diagnosis of PMDD. Treatment will start 14 days prior to the next estimated menstruation start and continue until menstruation starts, but with a maximum of 7 doses per cycle. The treatment period is followed by one menstrual cycle of non-treatment as a follow-up cycle.

| | |
|------------------|---------|
| Arm title | Placebo |
|------------------|---------|

Arm description: -

| | |
|--|-------------------------------------|
| Arm type | Placebo |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Placebo injection once every second day during the luteal phase of 3 consecutive menstrual cycles to women with a verified diagnosis of PMDD. Treatment will start 14 days prior to the next estimated menstruation start and continue until menstruation starts, but with a maximum of 7 doses per cycle. The treatment period is followed by one menstrual cycle of non-treatment as a follow-up cycle.

| Number of subjects in period 1^[2] | Sepranolone 10 mg | Sepranolone 16 mg | Placebo |
|---|-------------------|-------------------|---------|
| Started | 64 | 68 | 70 |
| Completed | 53 | 54 | 58 |
| Not completed | 11 | 14 | 12 |
| Consent withdrawn by subject | 3 | 7 | 2 |
| other reasons | - | 2 | - |
| Adverse event, non-fatal | 5 | 3 | 4 |
| Pregnancy | - | - | 1 |
| Lost to follow-up | 3 | 2 | 2 |
| other reason | - | - | 3 |

Notes:

[2] - 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: 206 subjects enrolled in the study and were randomised into a treatment arm, but only 202 started treatment and are included in the baseline period.

Baseline characteristics

Reporting groups

| | |
|--------------------------------|-------------------|
| Reporting group title | Sepranolone 10 mg |
| Reporting group description: - | |
| Reporting group title | Sepranolone 16 mg |
| Reporting group description: - | |
| Reporting group title | Placebo |
| Reporting group description: - | |

| Reporting group values | Sepranolone 10 mg | Sepranolone 16 mg | Placebo |
|--|-------------------|-------------------|--------------|
| Number of subjects | 64 | 68 | 70 |
| Age categorical | | | |
| All subjects were aged 18 to 45 years at first visit | | | |
| 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) | 0 | 0 | 0 |
| From 65-84 years | 0 | 0 | 0 |
| 85 years and over | 0 | 0 | 0 |
| 18 to 45 years | 64 | 68 | 70 |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 32.72 | 33.35 | 34.14 |
| full range (min-max) | 23 to 44.6 | 20.3 to 44.7 | 22.4 to 44.6 |
| Gender categorical | | | |
| All patients were female | | | |
| Units: Subjects | | | |
| Female | 64 | 68 | 70 |
| Male | 0 | 0 | 0 |
| Race | | | |
| Units: Subjects | | | |
| White | 61 | 64 | 67 |
| Other | 3 | 3 | 2 |
| Black or African American | 0 | 1 | 1 |
| Smoker Status | | | |
| Units: Subjects | | | |
| Non-smoker | 34 | 43 | 40 |
| Ex-smoker | 11 | 13 | 17 |
| Smoker | 19 | 12 | 13 |
| Previous PMDD treatment | | | |
| Units: Subjects | | | |
| Yes | 17 | 20 | 17 |

| | | | |
|---|------------------------|-----------------------|------------------------|
| No | 47 | 48 | 53 |
| History of psychiatric disorders Units: Subjects | | | |
| Yes | 11 | 18 | 11 |
| No | 53 | 50 | 59 |
| History of PMDD diagnosis Units: Subjects | | | |
| Yes | 11 | 10 | 16 |
| No | 53 | 58 | 54 |
| BMI Units: mg/kg2 arithmetic mean full range (min-max) | 24.13 18.5 to 34.7 | 24.22 16.6 to 34.6 | 24.79 18.4 to 34.4 |
| PMDD History Units: years arithmetic mean full range (min-max) | 10.08 2 to 27 | 9.08 2 to 24 | 9.53 1 to 30 |
| Baseline Total Symptoms | | | |
| LmaxSum21 | | | |
| Units: points arithmetic mean full range (min-max) | 82.25 56.5 to 118.7 | 87.3 52.1 to 122.4 | 85.46 53.7 to 123.3 |
| Baseline symptoms in follicular phase | | | |
| FminSum21 | | | |
| Units: points arithmetic mean full range (min-max) | 23.96 21 to 33.6 | 23.53 21 to 30.9 | 23.39 21 to 33.5 |

| | | | |
|---|-------|--|--|
| Reporting group values | Total | | |
| Number of subjects | 202 | | |
| Age categorical | | | |
| All subjects were aged 18 to 45 years at first visit | | | |
| 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) | 0 | | |
| From 65-84 years | 0 | | |
| 85 years and over | 0 | | |
| 18 to 45 years | 202 | | |
| Age continuous Units: years arithmetic mean full range (min-max) | - | | |
| Gender categorical | | | |
| All patients were female | | | |
| Units: Subjects | | | |

| | | | |
|---------------------------------------|-----|--|--|
| Female | 202 | | |
| Male | 0 | | |
| Race | | | |
| Units: Subjects | | | |
| White | 192 | | |
| Other | 8 | | |
| Black or African American | 2 | | |
| Smoker Status | | | |
| Units: Subjects | | | |
| Non-smoker | 117 | | |
| Ex-smoker | 41 | | |
| Smoker | 44 | | |
| Previous PMDD treatment | | | |
| Units: Subjects | | | |
| Yes | 54 | | |
| No | 148 | | |
| History of psychiatric disorders | | | |
| Units: Subjects | | | |
| Yes | 40 | | |
| No | 162 | | |
| History of PMDD diagnosis | | | |
| Units: Subjects | | | |
| Yes | 37 | | |
| No | 165 | | |
| BMI | | | |
| Units: mg/kg ² | | | |
| arithmetic mean | | | |
| full range (min-max) | - | | |
| PMDD History | | | |
| Units: years | | | |
| arithmetic mean | | | |
| full range (min-max) | - | | |
| Baseline Total Symptoms | | | |
| LmaxSum21 | | | |
| Units: points | | | |
| arithmetic mean | | | |
| full range (min-max) | - | | |
| Baseline symptoms in follicular phase | | | |
| FminSum21 | | | |
| Units: points | | | |
| arithmetic mean | | | |
| full range (min-max) | - | | |

Subject analysis sets

| | |
|--|--|
| Subject analysis set title | Safety Analysis Set - Sepranolone 10mg |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: | |
| The safety analysis set includes all subjects who obtained at least one dose of the investigational drug at a dose of 10mg | |

| | |
|--|--|
| Subject analysis set title | Safety Analysis Set - Sepranolone 16mg |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: | |
| The safety analysis set includes all subjects who obtained at least one dose of the investigational drug at a dose of 16mg | |
| Subject analysis set title | Safety Analysis Set - placebo |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: | |
| The safety analysis set includes all subjects who obtained at least one dose of the placebo | |
| Subject analysis set title | Intent to Treat Sepranolone 10mg |
| Subject analysis set type | Intention-to-treat |
| Subject analysis set description: | |
| All subjects with at least one confirmed ovulatory treatment cycle and had evaluable DSRP data in that cycle who received Sepranolone 10mg | |
| Subject analysis set title | Intent to Treat Sepranolone 16mg |
| Subject analysis set type | Intention-to-treat |
| Subject analysis set description: | |
| All subjects with at least one confirmed ovulatory treatment cycle and had evaluable DSRP data in that cycle who received Sepranolone 16mg | |
| Subject analysis set title | Intent to Treat Placebo |
| Subject analysis set type | Intention-to-treat |
| Subject analysis set description: | |
| All subjects with at least one confirmed ovulatory treatment cycle and had evaluable DSRP data in that cycle who received Placebo | |
| Subject analysis set title | Intent to Treat Active |
| Subject analysis set type | Intention-to-treat |
| Subject analysis set description: | |
| All subjects with at least one confirmed ovulatory treatment cycle and had evaluable DSRP data in that cycle who received Sepranolone 10mg or 16mg | |

| Reporting group values | Safety Analysis Set - Sepranolone 10mg | Safety Analysis Set - Sepranolone 16mg | Safety Analysis Set - placebo |
|--|--|--|-------------------------------|
| Number of subjects | 64 | 68 | 70 |
| Age categorical | | | |
| All subjects were aged 18 to 45 years at first visit | | | |
| 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) | 0 | 0 | 0 |
| From 65-84 years | 0 | 0 | 0 |
| 85 years and over | 0 | 0 | 0 |
| 18 to 45 years | 64 | 68 | 70 |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 34.14 | 32.72 | 33.35 |
| full range (min-max) | 22.4 to 44.6 | 23 to 44.6 | 20.3 to 44.7 |

| | | | |
|--|-------------------------------------|-------------------------------------|----------------------------|
| Gender categorical | | | |
| All patients were female | | | |
| Units: Subjects | | | |
| Female | 64 | 68 | 70 |
| Male | 0 | 0 | 0 |
| Race | | | |
| Units: Subjects | | | |
| White | 61 | 64 | 67 |
| Other | 3 | 3 | 2 |
| Black or African American | 0 | 1 | 1 |
| Smoker Status | | | |
| Units: Subjects | | | |
| Non-smoker | 34 | 43 | 40 |
| Ex-smoker | 19 | 12 | 13 |
| Smoker | 11 | 13 | 17 |
| Previous PMDD treatment | | | |
| Units: Subjects | | | |
| Yes | 17 | 17 | 20 |
| No | 47 | 48 | 53 |
| History of psychiatric disorders | | | |
| Units: Subjects | | | |
| Yes | 11 | 18 | 11 |
| No | 53 | 50 | 59 |
| History of PMDD diagnosis | | | |
| Units: Subjects | | | |
| Yes | 11 | 10 | 16 |
| No | 53 | 58 | 54 |
| BMI | | | |
| Units: mg/kg2 | | | |
| arithmetic mean | 24.13 | 24.22 | 24.79 |
| full range (min-max) | 18.5 to 34.7 | 16.6 to 34.6 | 18.4 to 34.4 |
| PMDD History | | | |
| Units: years | | | |
| arithmetic mean | 10.08 | 9.08 | 9.53 |
| full range (min-max) | 2 to 27 | 2 to 24 | 1 to 30 |
| Baseline Total Symptoms | | | |
| LmaxSum21 | | | |
| Units: points | | | |
| arithmetic mean | 82.25 | 87.3 | 85.46 |
| full range (min-max) | 56.5 to 118.7 | 52.1 to 122.4 | 53.7 to 123.3 |
| Baseline symptoms in follicular phase | | | |
| FminSum21 | | | |
| Units: points | | | |
| arithmetic mean | 23.96 | 23.53 | 23.39 |
| full range (min-max) | 21 to 33.6 | 21 to 30.9 | 21 to 33.5 |
| Reporting group values | Intent to Treat Sepranolone 10mg | Intent to Treat Sepranolone 16mg | Intent to Treat Placebo |
| Number of subjects | 63 | 62 | 67 |
| Age categorical | | | |
| All subjects were aged 18 to 45 years at first visit | | | |
| 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) | 0 | 0 | 0 |
| From 65-84 years | 0 | 0 | 0 |
| 85 years and over | 0 | 0 | 0 |
| 18 to 45 years | 63 | 62 | 67 |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 32.7 | 33.2 | 34.35 |
| full range (min-max) | 23 to 44.6 | 20.3 to 43 | 22.4 to 44.6 |
| Gender categorical | | | |
| All patients were female | | | |
| Units: Subjects | | | |
| Female | 63 | 62 | 67 |
| Male | 0 | 0 | 0 |
| Race | | | |
| Units: Subjects | | | |
| White | 60 | 58 | 64 |
| Other | 3 | 3 | 2 |
| Black or African American | 0 | 1 | 1 |
| Smoker Status | | | |
| Units: Subjects | | | |
| Non-smoker | 34 | 40 | 38 |
| Ex-smoker | 11 | 11 | 16 |
| Smoker | 18 | 11 | 13 |
| Previous PMDD treatment | | | |
| Units: Subjects | | | |
| Yes | 17 | 19 | 16 |
| No | 46 | 43 | 51 |
| History of psychiatric disorders | | | |
| Units: Subjects | | | |
| Yes | 11 | 18 | 11 |
| No | 52 | 44 | 56 |
| History of PMDD diagnosis | | | |
| Units: Subjects | | | |
| Yes | 11 | 9 | 16 |
| No | 52 | 53 | 51 |
| BMI | | | |
| Units: mg/kg2 | | | |
| arithmetic mean | 24.19 | 24.24 | 24.82 |
| full range (min-max) | 18.5 to 34.7 | 16.6 to 34.6 | 18.4 to 34.4 |
| PMDD History | | | |
| Units: years | | | |
| arithmetic mean | 10 | 8.8 | 9.66 |
| full range (min-max) | 2 to 27 | 2 to 22 | 1 to 30 |
| Baseline Total Symptoms | | | |

| | | | |
|---------------------------------------|---------------|---------------|---------------|
| LmaxSum21 | | | |
| Units: points | | | |
| arithmetic mean | 82.35 | 87.13 | 85.05 |
| full range (min-max) | 56.5 to 118.7 | 52.1 to 122.4 | 53.7 to 123.3 |
| Baseline symptoms in follicular phase | | | |
| FminSum21 | | | |
| Units: points | | | |
| arithmetic mean | 24.01 | 23.42 | 23.36 |
| full range (min-max) | 21 to 33.6 | 21 to 30.6 | 21 to 33.5 |

| | | | |
|---|---------------------------|--|--|
| Reporting group values | Intent to Treat Active | | |
| Number of subjects | 125 | | |
| Age categorical | | | |
| All subjects were aged 18 to 45 years at first visit | | | |
| Units: Subjects | | | |
| In utero | | | |
| Preterm newborn infants (gestational age < 37 wks) | | | |
| Newborns (0-27 days) | | | |
| Infants and toddlers (28 days-23 months) | | | |
| Children (2-11 years) | | | |
| Adolescents (12-17 years) | | | |
| Adults (18-64 years) | | | |
| From 65-84 years | | | |
| 85 years and over | | | |
| 18 to 45 years | 125 | | |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 32.94 | | |
| full range (min-max) | 20.3 to 44.6 | | |
| Gender categorical | | | |
| All patients were female | | | |
| Units: Subjects | | | |
| Female | 125 | | |
| Male | 0 | | |
| Race | | | |
| Units: Subjects | | | |
| White | 118 | | |
| Other | 6 | | |
| Black or African American | 1 | | |
| Smoker Status | | | |
| Units: Subjects | | | |
| Non-smoker | 74 | | |
| Ex-smoker | 22 | | |
| Smoker | 29 | | |
| Previous PMDD treatment | | | |
| Units: Subjects | | | |
| Yes | 36 | | |
| No | 89 | | |
| History of psychiatric disorders | | | |
| Units: Subjects | | | |

| | | | |
|---|------------------------|--|--|
| Yes | 29 | | |
| No | 96 | | |
| History of PMDD diagnosis Units: Subjects | | | |
| Yes | 20 | | |
| No | 105 | | |
| BMI Units: mg/kg2 arithmetic mean full range (min-max) | 24.21 16.6 to 34.7 | | |
| PMDD History Units: years arithmetic mean full range (min-max) | 9.41 2 to 27 | | |
| Baseline Total Symptoms | | | |
| LmaxSum21 | | | |
| Units: points arithmetic mean full range (min-max) | 84.72 52.1 to 122.4 | | |
| Baseline symptoms in follicular phase | | | |
| FminSum21 | | | |
| Units: points arithmetic mean full range (min-max) | 23.72 21 to 33.6 | | |

End points

End points reporting groups

| | |
|---|--|
| Reporting group title | Sepranolone 10 mg |
| Reporting group description: - | |
| Reporting group title | Sepranolone 16 mg |
| Reporting group description: - | |
| Reporting group title | Placebo |
| Reporting group description: - | |
| Subject analysis set title | Safety Analysis Set - Sepranolone 10mg |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: The safety analysis set includes all subjects who obtained at least one dose of the investigational drug at a dose of 10mg | |
| Subject analysis set title | Safety Analysis Set - Sepranolone 16mg |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: The safety analysis set includes all subjects who obtained at least one dose of the investigational drug at a dose of 16mg | |
| Subject analysis set title | Safety Analysis Set - placebo |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: The safety analysis set includes all subjects who obtained at least one dose of the placebo | |
| Subject analysis set title | Intent to Treat Sepranolone 10mg |
| Subject analysis set type | Intention-to-treat |
| Subject analysis set description: All subjects with at least one confirmed ovulatory treatment cycle and had evaluable DSRP data in that cycle who received Sepranolone 10mg | |
| Subject analysis set title | Intent to Treat Sepranolone 16mg |
| Subject analysis set type | Intention-to-treat |
| Subject analysis set description: All subjects with at least one confirmed ovulatory treatment cycle and had evaluable DSRP data in that cycle who received Sepranolone 16mg | |
| Subject analysis set title | Intent to Treat Placebo |
| Subject analysis set type | Intention-to-treat |
| Subject analysis set description: All subjects with at least one confirmed ovulatory treatment cycle and had evaluable DSRP data in that cycle who received Placebo | |
| Subject analysis set title | Intent to Treat Active |
| Subject analysis set type | Intention-to-treat |
| Subject analysis set description: All subjects with at least one confirmed ovulatory treatment cycle and had evaluable DSRP data in that cycle who received Sepranolone 10mg or 16mg | |

Primary: Change in LmaxSum21 score before and during treatment

| | |
|--|---|
| End point title | Change in LmaxSum21 score before and during treatment |
| End point description: | |
| End point type | Primary |
| End point timeframe: Within-subject differences were calculated by taking the average LmaxSum21 from the 2nd and the 3rd treatment cycles and subtracting the average LmaxSum21 from the two menstrual cycles D1 and D2 | |

| End point values | Intent to Treat Sepranolone 10mg | Intent to Treat Sepranolone 16mg | Intent to Treat Placebo | Intent to Treat Active |
|--|--|--|----------------------------|---------------------------|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 63 | 62 | 67 | 125 |
| Units: LmaxSum21 (points) | | | | |
| arithmetic mean (full range (min-max)) | -30.53 (-90.1 to 32.2) | -30.02 (-77.7 to 9) | -27.88 (-90.7 to 11) | -30.28 (-90.1 to 32.2) |

Statistical analyses

| Statistical analysis title | Primary confirmatory efficacy analysis |
|-----------------------------------|--|
|-----------------------------------|--|

Statistical analysis description:

The primary confirmatory efficacy analysis proceeded in a hierarchical rejecting way. The null hypotheses were each tested at a two-sided type I error of $\alpha = 0.05$, but subsequent hypotheses were only tested if the previous null hypothesis had been rejected. Using this closed testing procedure, no alpha adjustment had to be applied to control the family-wise error rate of 5%.

| | |
|---|--|
| Comparison groups | Intent to Treat Placebo v Intent to Treat Active |
| Number of subjects included in analysis | 192 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.3465 |
| Method | Wilcoxon (Mann-Whitney) |

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were reported from first dose of IMP to last visit (follow-up).

| | |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|------|
| Dictionary version | 22.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|-------------------|
| Reporting group title | Sepranolone 10 mg |
|-----------------------|-------------------|

Reporting group description: -

| | |
|-----------------------|-------------------|
| Reporting group title | Sepranolone 16 mg |
|-----------------------|-------------------|

Reporting group description: -

| | |
|-----------------------|---------|
| Reporting group title | Placebo |
|-----------------------|---------|

Reporting group description: -

| Serious adverse events | Sepranolone 10 mg | Sepranolone 16 mg | Placebo |
|---|-------------------|-------------------|----------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 1 / 68 (1.47%) | 1 / 70 (1.43%) |
| 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 | 0 / 64 (0.00%) | 1 / 68 (1.47%) | 0 / 70 (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 |
| Gastrointestinal stromal tumour | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 0 / 68 (0.00%) | 1 / 70 (1.43%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

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

| Non-serious adverse events | Sepranolone 10 mg | Sepranolone 16 mg | Placebo |
|---|-------------------|-------------------|------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 17 / 64 (26.56%) | 33 / 68 (48.53%) | 18 / 70 (25.71%) |

| | | | |
|--|----------------|------------------|------------------|
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 6 / 64 (9.38%) | 4 / 68 (5.88%) | 8 / 70 (11.43%) |
| occurrences (all) | 9 | 6 | 11 |
| General disorders and administration site conditions | | | |
| Injection site erythema | | | |
| subjects affected / exposed | 3 / 64 (4.69%) | 5 / 68 (7.35%) | 1 / 70 (1.43%) |
| occurrences (all) | 15 | 16 | 3 |
| Injection site pain | | | |
| subjects affected / exposed | 2 / 64 (3.13%) | 8 / 68 (11.76%) | 3 / 70 (4.29%) |
| occurrences (all) | 3 | 59 | 27 |
| Gastrointestinal disorders | | | |
| Diarrhoea | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 1 / 68 (1.47%) | 6 / 70 (8.57%) |
| occurrences (all) | 0 | 1 | 7 |
| Nausea | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 4 / 68 (5.88%) | 0 / 70 (0.00%) |
| occurrences (all) | 0 | 4 | 0 |
| Infections and infestations | | | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 6 / 64 (9.38%) | 11 / 68 (16.18%) | 12 / 70 (17.14%) |
| occurrences (all) | 6 | 11 | 15 |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|-----------------|--|
| 17 October 2018 | Amendment in Sweden only: it became apparent that no spermicides are available, therefore inclusion criterion #4 required updating |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported