



Clinical trial results:

A randomized, double-blind, placebo-controlled, phase 2b dose-ranging study to assess the efficacy and safety of OBE2109 in subjects with endometriosis associated pain.

Summary

| | |
|--------------------------|-------------------|
| EudraCT number | 2016-001736-35 |
| Trial protocol | PL |
| Global end of trial date | 04 September 2019 |

Results information

| | |
|--------------------------------|--------------|
| Result version number | v1 (current) |
| This version publication date | 20 May 2021 |
| First version publication date | 20 May 2021 |

Trial information

Trial identification

| | |
|-----------------------|----------------|
| Sponsor protocol code | 15-OBE2109-001 |
|-----------------------|----------------|

Additional study identifiers

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

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | ObsEva SA |
| Sponsor organisation address | 12, Chemin des Aulx, Plan-les-Ouates, Geneva, Switzerland, 1228 |
| Public contact | Clinical Trials Information, ObsEva SA, clinicaltrials@obseva.ch |
| Scientific contact | Clinical Trials Information, ObsEva SA, clinicaltrials@obseva.ch |

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 | 04 November 2019 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 04 September 2019 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To assess the efficacy of a range of oral doses of linzagolix versus placebo, in reducing pelvic pain in subjects with moderate to severe endometriosis pain.

To assess the safety and tolerability of linzagolix in subjects with endometriosis.

Protection of trial subjects:

This study was performed in accordance with the protocol, the Declaration of Helsinki, the ICH Harmonised Tripartite Guideline for GCP, and all applicable local regulatory requirements.

Subjects read and understood the Informed Consent Form (ICF) and voluntarily agreed to participation in this study.

Background therapy: -

Evidence for comparator: -

| | |
|---|--------------|
| Actual start date of recruitment | 26 July 2016 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|------------------------|
| Country: Number of subjects enrolled | Poland: 67 |
| Country: Number of subjects enrolled | Ukraine: 73 |
| Country: Number of subjects enrolled | Russian Federation: 11 |
| Country: Number of subjects enrolled | United States: 177 |
| Worldwide total number of subjects | 328 |
| EEA total number of subjects | 67 |

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) | 328 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

A total of 328 females were randomized at 62 sites in 4 countries: 48 sites in USA (177 subjects), 5 sites in Poland (67 subjects), 5 sites in Ukraine (73 subjects) and 4 sites in Russia (11 subjects).

Pre-assignment

Screening details:

716 subjects were screened and 328 were randomized; 327 were included in the safety set (1 not included as didn't receive study treatment). 323 subjects were included in the FAS, 5 randomized subjects were excluded: 1 as per the safety set and 4 were prematurely discontinued at one US site due to the site's serious non-compliance to the protocol.

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, Monitor |

Arms

| | |
|------------------------------|------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | Linzagolix 50 mg |

Arm description:

50 mg linzagolix, once daily for 12 weeks.

| | |
|--|--------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Linzagolix |
| Investigational medicinal product code | OBE2109 |
| Other name | |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Study drug was taken at approximately the same time every morning (1 tablet of 50 mg). To maintain the blind, placebo tablet was also administered.

| | |
|------------------|------------------|
| Arm title | Linzagolix 75 mg |
|------------------|------------------|

Arm description:

75 mg linzagolix, once daily for 12 weeks.

| | |
|--|--------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Linzagolix |
| Investigational medicinal product code | OBE2109 |
| Other name | |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Study drug was taken at approximately the same time every morning (1 tablet of 75 mg). To maintain the blind, placebo tablet was also administered.

| | |
|------------------|-------------------|
| Arm title | Linzagolix 100 mg |
|------------------|-------------------|

Arm description:

100 mg linzagolix, once daily for 12 weeks.

| | |
|----------|--------------|
| Arm type | Experimental |
|----------|--------------|

| | |
|--|--------------------|
| Investigational medicinal product name | Linzagolix |
| Investigational medicinal product code | OBE2109 |
| Other name | |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Study drug was taken at approximately the same time every morning (1 tablet of 100 mg). To maintain the blind, placebo tablet was also administered.

| | |
|------------------|-------------------|
| Arm title | Linzagolix 200 mg |
|------------------|-------------------|

Arm description:

200 mg linzagolix, once daily for 12 weeks.

| | |
|--|--------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Linzagolix |
| Investigational medicinal product code | OBE2109 |
| Other name | |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Two tablets of 100 mg linzagolix. Study drug was taken at approximately the same time every morning.

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

Arm description:

Placebo, once daily for 12 weeks.

| | |
|--|--------------------|
| Arm type | Placebo |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | Placebo |
| Other name | |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Two placebo tablets were taken at approximately the same time every morning.

| Number of subjects in period 1^[1] | Linzagolix 50 mg | Linzagolix 75 mg | Linzagolix 100 mg |
|---|------------------|------------------|-------------------|
| Started | 49 | 114 | 51 |
| Completed | 45 | 104 | 45 |
| Not completed | 4 | 10 | 6 |
| Consent withdrawn by subject | 2 | 4 | 1 |
| Adverse event, non-fatal | 2 | 5 | 3 |
| Dosing compliance issue | - | 1 | - |
| Sponsor request | - | - | 1 |
| Lost to follow-up | - | - | - |
| Protocol deviation | - | - | 1 |

| Number of subjects in period 1^[1] | Linzagolix 200 mg | Placebo |
|---|-------------------|---------|
| Started | 56 | 53 |

| | | |
|------------------------------|----|----|
| Completed | 49 | 45 |
| Not completed | 7 | 8 |
| Consent withdrawn by subject | 3 | 5 |
| Adverse event, non-fatal | 3 | 1 |
| Dosing compliance issue | - | - |
| Sponsor request | - | - |
| Lost to follow-up | 1 | 2 |
| Protocol deviation | - | - |

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 number of subjects reported to be in the baseline period are as per the FAS.

328 subjects were randomized, 323 subjects were included in the FAS; 5 randomized subjects were excluded: 1 didn't receive study treatment and 4 subjects were prematurely discontinued at one US site due to the site's serious non-compliance to the protocol.

Baseline characteristics

Reporting groups

| | |
|------------------------------|---|
| Reporting group title | Linzagolix 50 mg |
| Reporting group description: | 50 mg linzagolix, once daily for 12 weeks. |
| Reporting group title | Linzagolix 75 mg |
| Reporting group description: | 75 mg linzagolix, once daily for 12 weeks. |
| Reporting group title | Linzagolix 100 mg |
| Reporting group description: | 100 mg linzagolix, once daily for 12 weeks. |
| Reporting group title | Linzagolix 200 mg |
| Reporting group description: | 200 mg linzagolix, once daily for 12 weeks. |
| Reporting group title | Placebo |
| Reporting group description: | Placebo, once daily for 12 weeks. |

| Reporting group values | Linzagolix 50 mg | Linzagolix 75 mg | Linzagolix 100 mg |
|--|------------------|------------------|-------------------|
| Number of subjects | 49 | 114 | 51 |
| Age categorical | | | |
| 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) | 49 | 114 | 51 |
| From 65-84 years | 0 | 0 | 0 |
| 85 years and over | 0 | 0 | 0 |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 30.9 | 31.8 | 33.0 |
| standard deviation | ± 5.98 | ± 6.17 | ± 5.78 |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 49 | 114 | 51 |
| Male | 0 | 0 | 0 |

| Reporting group values | Linzagolix 200 mg | Placebo | Total |
|--|-------------------|---------|-------|
| Number of subjects | 56 | 53 | 323 |
| Age categorical | | | |
| 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) | 56 | 53 | 323 |
| From 65-84 years | 0 | 0 | 0 |
| 85 years and over | 0 | 0 | 0 |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 30.9 | 32.4 | |
| standard deviation | ± 6.03 | ± 5.78 | - |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 56 | 53 | 323 |
| Male | 0 | 0 | 0 |

End points

End points reporting groups

| | |
|---|-------------------|
| Reporting group title | Linzagolix 50 mg |
| Reporting group description: 50 mg linzagolix, once daily for 12 weeks. | |
| Reporting group title | Linzagolix 75 mg |
| Reporting group description: 75 mg linzagolix, once daily for 12 weeks. | |
| Reporting group title | Linzagolix 100 mg |
| Reporting group description: 100 mg linzagolix, once daily for 12 weeks. | |
| Reporting group title | Linzagolix 200 mg |
| Reporting group description: 200 mg linzagolix, once daily for 12 weeks. | |
| Reporting group title | Placebo |
| Reporting group description: Placebo, once daily for 12 weeks. | |

Primary: 30% or Greater Reduction from Baseline to Week 12 in Mean Overall Pelvic Pain Score (0-3 VRS)

| | |
|---|---|
| End point title | 30% or Greater Reduction from Baseline to Week 12 in Mean Overall Pelvic Pain Score (0-3 VRS) |
| End point description: The primary efficacy endpoint of the study was a response at Week 12, with response defined as a reduction of 30% or greater from baseline in mean overall pelvic pain, recorded daily and assessed via electronic diary during the preceding 28 days (4-week period) on a VRS of 0 (no pain) to 3 (severe pain). | |
| End point type | Primary |
| End point timeframe: Week 12 of the treatment period | |

| End point values | Linzagolix 50 mg | Linzagolix 75 mg | Linzagolix 100 mg | Linzagolix 200 mg |
|-----------------------------|------------------|------------------|-------------------|-------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 48 | 114 | 51 | 55 |
| Units: responder rate | | | | |
| number (not applicable) | 49.4 | 61.5 | 56.4 | 56.3 |

| End point values | Placebo | | | |
|-----------------------------|-----------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 52 | | | |
| Units: responder rate | | | | |
| number (not applicable) | 34.5 | | | |

Statistical analyses

| | |
|---|----------------------------|
| Statistical analysis title | Statistical Analysis 50 mg |
| Statistical analysis description: | |
| Analysis of the primary endpoint was conducted via a generalized linear model for binary data with repeated (correlated) measures, using generalized estimating equations (marginal model), with the model including terms for the treatment group, 4-week period, baseline, and the interactions: treatment group x 4-week period, and baseline x 4-week period. | |
| Comparison groups | Linzagolix 50 mg v Placebo |
| Number of subjects included in analysis | 100 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.155 |
| Method | generalized linear model |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 1.85 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.791 |
| upper limit | 4.317 |

| | |
|---|----------------------------|
| Statistical analysis title | Statistical Analysis 75 mg |
| Statistical analysis description: | |
| Analysis of the primary endpoint was conducted via a generalized linear model for binary data with repeated (correlated) measures, using generalized estimating equations (marginal model), with the model including terms for the treatment group, 4-week period, baseline, and the interactions: treatment group x 4-week period, and baseline x 4-week period. | |
| Comparison groups | Linzagolix 75 mg v Placebo |
| Number of subjects included in analysis | 166 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.003 |
| Method | generalized linear model |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 3.03 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.469 |
| upper limit | 6.239 |

| | |
|-----------------------------------|-----------------------------|
| Statistical analysis title | Statistical Analysis 100 mg |
|-----------------------------------|-----------------------------|

Statistical analysis description:

Analysis of the primary endpoint was conducted via a generalized linear model for binary data with repeated (correlated) measures, using generalized estimating equations (marginal model), with the model including terms for the treatment group, 4-week period, baseline, and the interactions: treatment group x 4-week period, and baseline x 4-week period.

| | |
|---|-----------------------------|
| Comparison groups | Linzagolix 100 mg v Placebo |
| Number of subjects included in analysis | 103 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.039 |
| Method | generalized linear model |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 2.45 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.049 |
| upper limit | 5.741 |

| | |
|-----------------------------------|-----------------------------|
| Statistical analysis title | Statistical Analysis 200 mg |
|-----------------------------------|-----------------------------|

Statistical analysis description:

Analysis of the primary endpoint was conducted via a generalized linear model for binary data with repeated (correlated) measures, using generalized estimating equations (marginal model), with the model including terms for the treatment group, 4-week period, baseline, and the interactions: treatment group x 4-week period, and baseline x 4-week period.

| | |
|---|-----------------------------|
| Comparison groups | Linzagolix 200 mg v Placebo |
| Number of subjects included in analysis | 107 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.034 |
| Method | generalized linear model |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 2.45 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.069 |
| upper limit | 5.593 |

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From screening to Week 12

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 19.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|------------------|
| Reporting group title | Linzagolix 50 mg |
|-----------------------|------------------|

Reporting group description:

50 mg linzagolix, once daily for 12 weeks.

| | |
|-----------------------|------------------|
| Reporting group title | Linzagolix 75 mg |
|-----------------------|------------------|

Reporting group description:

75 mg linzagolix, once daily for 12 weeks.

| | |
|-----------------------|-------------------|
| Reporting group title | Linzagolix 100 mg |
|-----------------------|-------------------|

Reporting group description:

100 mg linzagolix, once daily for 12 weeks.

| | |
|-----------------------|-------------------|
| Reporting group title | Linzagolix 200 mg |
|-----------------------|-------------------|

Reporting group description:

200 mg linzagolix, once daily for 12 weeks.

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

Reporting group description:

Placebo, once daily for 12 weeks.

| Serious adverse events | Linzagolix 50 mg | Linzagolix 75 mg | Linzagolix 100 mg |
|---|------------------|------------------|-------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 1 / 49 (2.04%) | 0 / 114 (0.00%) | 1 / 52 (1.92%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Injury, poisoning and procedural complications | | | |
| Stab wound | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 0 / 114 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| Enterocolitis | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 0 / 114 (0.00%) | 1 / 52 (1.92%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|----------------|-----------------|----------------|
| Respiratory, thoracic and mediastinal disorders | | | |
| Pulmonary embolism | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 0 / 114 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Pyelonephritis acute | | | |
| subjects affected / exposed | 1 / 49 (2.04%) | 0 / 114 (0.00%) | 0 / 52 (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 |

| Serious adverse events | Linzagolix 200 mg | Placebo | |
|---|-------------------|----------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 1 / 57 (1.75%) | 1 / 55 (1.82%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Injury, poisoning and procedural complications | | | |
| Stab wound | | | |
| subjects affected / exposed | 0 / 57 (0.00%) | 1 / 55 (1.82%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Enterocolitis | | | |
| subjects affected / exposed | 0 / 57 (0.00%) | 0 / 55 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Pulmonary embolism | | | |
| subjects affected / exposed | 1 / 57 (1.75%) | 0 / 55 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Pyelonephritis acute | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 0 / 57 (0.00%) | 0 / 55 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| Non-serious adverse events | Linzagolix 50 mg | Linzagolix 75 mg | Linzagolix 100 mg |
|---|------------------|-------------------|-------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 28 / 49 (57.14%) | 70 / 114 (61.40%) | 34 / 52 (65.38%) |
| Investigations | | | |
| Blood creatine phosphokinase increased | | | |
| subjects affected / exposed | 1 / 49 (2.04%) | 4 / 114 (3.51%) | 0 / 52 (0.00%) |
| occurrences (all) | 1 | 4 | 0 |
| Vascular disorders | | | |
| Hot flush | | | |
| subjects affected / exposed | 7 / 49 (14.29%) | 22 / 114 (19.30%) | 14 / 52 (26.92%) |
| occurrences (all) | 7 | 22 | 15 |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 10 / 49 (20.41%) | 23 / 114 (20.18%) | 12 / 52 (23.08%) |
| occurrences (all) | 29 | 37 | 16 |
| General disorders and administration site conditions | | | |
| Fatigue | | | |
| subjects affected / exposed | 1 / 49 (2.04%) | 0 / 114 (0.00%) | 3 / 52 (5.77%) |
| occurrences (all) | 1 | 0 | 3 |
| Gastrointestinal disorders | | | |
| Nausea | | | |
| subjects affected / exposed | 3 / 49 (6.12%) | 3 / 114 (2.63%) | 3 / 52 (5.77%) |
| occurrences (all) | 3 | 6 | 3 |
| Toothache | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 1 / 114 (0.88%) | 0 / 52 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Reproductive system and breast disorders | | | |
| Vulvovaginal dryness | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 1 / 114 (0.88%) | 2 / 52 (3.85%) |
| occurrences (all) | 0 | 1 | 2 |

| | | | |
|-----------------------------|----------------|-----------------|----------------|
| Psychiatric disorders | | | |
| Mood swings | | | |
| subjects affected / exposed | 2 / 49 (4.08%) | 2 / 114 (1.75%) | 2 / 52 (3.85%) |
| occurrences (all) | 2 | 2 | 2 |
| Infections and infestations | | | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 4 / 49 (8.16%) | 8 / 114 (7.02%) | 1 / 52 (1.92%) |
| occurrences (all) | 5 | 8 | 1 |
| Urinary tract infection | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 5 / 114 (4.39%) | 1 / 52 (1.92%) |
| occurrences (all) | 0 | 5 | 1 |
| Bronchitis | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 1 / 114 (0.88%) | 1 / 52 (1.92%) |
| occurrences (all) | 0 | 1 | 1 |

| Non-serious adverse events | Linzagolix 200 mg | Placebo | |
|---|-------------------|------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 41 / 57 (71.93%) | 30 / 55 (54.55%) | |
| Investigations | | | |
| Blood creatine phosphokinase increased | | | |
| subjects affected / exposed | 3 / 57 (5.26%) | 1 / 55 (1.82%) | |
| occurrences (all) | 3 | 1 | |
| Vascular disorders | | | |
| Hot flush | | | |
| subjects affected / exposed | 24 / 57 (42.11%) | 6 / 55 (10.91%) | |
| occurrences (all) | 28 | 6 | |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 17 / 57 (29.82%) | 14 / 55 (25.45%) | |
| occurrences (all) | 27 | 27 | |
| General disorders and administration site conditions | | | |
| Fatigue | | | |
| subjects affected / exposed | 2 / 57 (3.51%) | 0 / 55 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Gastrointestinal disorders | | | |
| Nausea | | | |

| | | | |
|--|--|--|--|
| <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Toothache</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>7 / 57 (12.28%)</p> <p>7</p> <p>1 / 57 (1.75%)</p> <p>2</p> | <p>1 / 55 (1.82%)</p> <p>1</p> <p>3 / 55 (5.45%)</p> <p>3</p> | |
| <p>Reproductive system and breast disorders</p> <p>Vulvovaginal dryness</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>3 / 57 (5.26%)</p> <p>3</p> | <p>0 / 55 (0.00%)</p> <p>0</p> | |
| <p>Psychiatric disorders</p> <p>Mood swings</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>2 / 57 (3.51%)</p> <p>2</p> | <p>5 / 55 (9.09%)</p> <p>6</p> | |
| <p>Infections and infestations</p> <p>Nasopharyngitis</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Urinary tract infection</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Bronchitis</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>1 / 57 (1.75%)</p> <p>1</p> <p>4 / 57 (7.02%)</p> <p>5</p> <p>3 / 57 (5.26%)</p> <p>3</p> | <p>3 / 55 (5.45%)</p> <p>4</p> <p>0 / 55 (0.00%)</p> <p>0</p> <p>0 / 55 (0.00%)</p> <p>0</p> | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|------------------|--|
| 25 November 2016 | <ul style="list-style-type: none">• Addition of an optional treatment extension phase.• Change in inclusion criterion: most recent surgical diagnosis was increased from 7 to 10 years.• Change in inclusion criterion: e-Diary completion compliance limit was reduced from 80% to 75% during the screening period. |
| 21 April 2017 | <ul style="list-style-type: none">• OATP1B1/1B3 inhibitors were prohibited during the treatment period.• The potential induction of CYP3A4 by linzagolix previously reported in Section 6.6.1 was removed.• Additional guidance was provided in the case of withdrawal from study during the first 4 weeks of treatment: Subjects should undergo the procedures required at Week 24 visit except the DXA.• Change in inclusion criterion: the lower limit of BMI ≥ 18 kg/m² was included, upper limit was removed. |
| 03 August 2017 | <ul style="list-style-type: none">• Clarification on sexual abstinence, as a birth control method (inclusion criteria for the main study and extension phase).• The washout period for the depot contraceptive, medroxyprogesterone acetate, was extended from 6 to 10 months.• Change in exclusion criterion for the extension phase: Subjects found to have had a BMD loss of $>7\%$ at any anatomic site or a Z-score ≤ -2.5 are to be excluded from the extension study.• Change in discontinuation criteria related to BMD loss: Subjects found to have a BMD loss of more than 7% at any anatomic site or a Z-score ≤ -2.5 should be discontinued from the study. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported