



Clinical trial results:

An exploratory single centre, open label, pilot study investigating the efficacy and safety of OBE2109 200 mg daily for 12 weeks followed by 100 mg daily for 12 weeks in uterine adenomyosis.

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2017-004042-14 |
| Trial protocol | FR |
| Global end of trial date | 20 May 2021 |

Results information

| | |
|--------------------------------|--------------|
| Result version number | v1 (current) |
| This version publication date | 09 June 2022 |
| First version publication date | 09 June 2022 |

Trial information

Trial identification

| | |
|-----------------------|----------------|
| Sponsor protocol code | 16-OBE2109-015 |
|-----------------------|----------------|

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, Geneva, Switzerland, |
| Public contact | Clinical Trials Information, ObsEva SA, +41 (0)225523840, clinicaltrials@obseva.ch |
| Scientific contact | Clinical Trials Information, ObsEva SA, +41 (0)225523840, 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 | 28 October 2021 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 20 May 2021 |
| Global end of trial reached? | Yes |
| Global end of trial date | 20 May 2021 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To assess the efficacy of 200 mg linzagolix (OBE2109) daily for 12 weeks followed by 100 mg linzagolix daily for 12 weeks on reduction of the volume of the uterus with adenomyosis. In addition, the overall safety of 24 weeks of daily administration of linzagolix in patients with uterine adenomyosis was assessed.

Protection of trial subjects:

The study was conducted in accordance with the ethical principles that have their origins in the Declaration of Helsinki, the ICH Harmonized Tripartite Guideline for Good Clinical Practice (GCP), and all applicable local regulatory requirements.

Background therapy: -

Evidence for comparator: -

| | |
|---|---------------|
| Actual start date of recruitment | 15 March 2019 |
| Long term follow-up planned | Yes |
| Long term follow-up rationale | Safety |
| Long term follow-up duration | 3 Months |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|-----------|
| Country: Number of subjects enrolled | France: 8 |
| Worldwide total number of subjects | 8 |
| EEA total number of subjects | 8 |

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) | 8 |

| | |
|---------------------|---|
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

The study was conducted at one clinical site in France.

Pre-assignment

Screening details:

The study started with a 4-week screening period evaluating the symptoms of uterine adenomyosis and assessing the volume of the adenomyosis affected uterus with MRI. During this period, the patients received no study drug.

A total of 10 patients were screened and 8 were enrolled in the study; 2 patients were not included because of screen failure.

Period 1

| | |
|------------------------------|----------------|
| Period 1 title | Baseline |
| Is this the baseline period? | Yes |
| Allocation method | Not applicable |
| Blinding used | Not blinded |

Arms

| | |
|--|--------------------|
| Arm title | Baseline |
| Arm description: - | |
| 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:

Once daily oral administration of linzagolix 200 mg for 12 weeks followed by 100 mg for 12 weeks.

| | |
|---------------------------------------|----------|
| Number of subjects in period 1 | Baseline |
| Started | 8 |
| Completed | 8 |

Period 2

| | |
|------------------------------|----------------|
| Period 2 title | Week 24 |
| Is this the baseline period? | No |
| Allocation method | Not applicable |
| Blinding used | Not blinded |

Arms

| | |
|---|--------------------|
| Arm title | Week 24 |
| Arm description: Patients received linzagolix 200 mg daily for 12 weeks followed by 100 mg 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:

Once daily oral administration of linzagolix 200 mg for 12 weeks followed by 100 mg for 12 weeks.

| Number of subjects in period 2 | Week 24 |
|---------------------------------------|---------|
| Started | 8 |
| Completed | 8 |

Period 3

| | |
|------------------------------|----------------|
| Period 3 title | Follow-up |
| Is this the baseline period? | No |
| Allocation method | Not applicable |
| Blinding used | Not blinded |

Arms

| | |
|------------------|-----------|
| Arm title | Follow-up |
|------------------|-----------|

Arm description:

At week 24, the patients entered a 12-week follow-up period without any active treatment.

| | |
|---|-----------------|
| Arm type | No intervention |
| No investigational medicinal product assigned in this arm | |

| Number of subjects in period 3 | Follow-up |
|---------------------------------------|-----------|
| Started | 8 |
| Completed | 8 |

Baseline characteristics

Reporting groups

| | |
|-----------------------|----------|
| Reporting group title | Baseline |
|-----------------------|----------|

Reporting group description: -

| Reporting group values | Baseline | Total | |
|---|----------|-------|--|
| Number of subjects | 8 | 8 | |
| Age categorical | | | |
| Units: Subjects | | | |
| In utero | 0 | 0 | |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | |
| Newborns (0-27 days) | 0 | 0 | |
| Infants and toddlers (28 days-23 months) | 0 | 0 | |
| Children (2-11 years) | 0 | 0 | |
| Adolescents (12-17 years) | 0 | 0 | |
| Adults (18-64 years) | 8 | 8 | |
| From 65-84 years | 0 | 0 | |
| 85 years and over | 0 | 0 | |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 42.0 | | |
| standard deviation | ± 2.8 | - | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 8 | 8 | |
| Male | 0 | 0 | |
| Uterine volume by MRI | | | |
| Volume of the uterus with adenomyosis as measured by MRI. | | | |
| Units: cm ³ | | | |
| arithmetic mean | 333.0 | | |
| standard deviation | ± 249.8 | - | |

End points

End points reporting groups

| | |
|---|-----------|
| Reporting group title | Baseline |
| Reporting group description: - | |
| Reporting group title | Week 24 |
| Reporting group description: Patients received linzagolix 200 mg daily for 12 weeks followed by 100 mg daily for 12 weeks. | |
| Reporting group title | Follow-up |
| Reporting group description: At week 24, the patients entered a 12-week follow-up period without any active treatment. | |

Primary: Change from baseline to week 24 in volume of the uterus with adenomyosis measured by MRI

| | |
|---------------------------------|--|
| End point title | Change from baseline to week 24 in volume of the uterus with adenomyosis measured by MRI |
| End point description: | |
| End point type | Primary |
| End point timeframe: Week 24 | |

| End point values | Baseline | Week 24 | | |
|--------------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 8 | 8 | | |
| Units: cm ³ | | | | |
| arithmetic mean (standard deviation) | 333.0 (± 249.8) | 203.9 (± 125.7) | | |

Statistical analyses

| | |
|--|--|
| Statistical analysis title | Week 24: Adjusted means for change from baseline |
| Statistical analysis description: The observed and change from baseline values were described using summary statistics (using appropriate transformations to normalise the data as necessary). A formal statistical assessment of change at each timepoint was carried out via a mixed model with repeated measures using two-sided 5% significance levels. | |
| Comparison groups | Baseline v Week 24 |

| | |
|---|--------------------------------|
| Number of subjects included in analysis | 16 |
| Analysis specification | Pre-specified |
| Analysis type | other ^[1] |
| P-value | = 0.0063 |
| Method | Mixed models analysis |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -135.44 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -216.19 |
| upper limit | -54.69 |

Notes:

[1] - Please note that the number of subjects in this analysis is 8, comparing baseline values to Week 24 values.

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From screening up to week 36.

Adverse event reporting additional description:

Data on adverse events were to be obtained at scheduled or unscheduled study visits, based on information spontaneously provided by the subject and/or through questioning of the subject. Only treatment-emergent adverse events are reported here.

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 22.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|-------------------|
| Reporting group title | Full analysis set |
|-----------------------|-------------------|

Reporting group description:

The Full Analysis Set (FAS) includes all screened patients and with at least one consumption of study drug.

| Serious adverse events | Full analysis set | | |
|---|-------------------|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | 0 | | |

Frequency threshold for reporting non-serious adverse events: 0 %

| Non-serious adverse events | Full analysis set | | |
|---|-------------------|--|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 8 / 8 (100.00%) | | |
| Vascular disorders | | | |
| Hot flush | | | |
| subjects affected / exposed | 6 / 8 (75.00%) | | |
| occurrences (all) | 7 | | |
| General disorders and administration site conditions | | | |
| Fatigue | | | |
| subjects affected / exposed | 3 / 8 (37.50%) | | |
| occurrences (all) | 3 | | |
| Pyrexia | | | |

| | | | |
|--|---------------------|--|--|
| subjects affected / exposed occurrences (all) | 1 / 8 (12.50%) 1 | | |
| Reproductive system and breast disorders | | | |
| Pelvic pain | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | | |
| occurrences (all) | 1 | | |
| Uterine polyp | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | | |
| occurrences (all) | 1 | | |
| Vaginal odour | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | | |
| occurrences (all) | 1 | | |
| Vulvovaginal dryness | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | | |
| occurrences (all) | 1 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Rhinitis allergic | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | | |
| occurrences (all) | 1 | | |
| Psychiatric disorders | | | |
| Anxiety | | | |
| subjects affected / exposed | 2 / 8 (25.00%) | | |
| occurrences (all) | 2 | | |
| Loss of libido | | | |
| subjects affected / exposed | 2 / 8 (25.00%) | | |
| occurrences (all) | 2 | | |
| Libido decreased | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | | |
| occurrences (all) | 1 | | |
| Investigations | | | |
| Gamma-glutamyltransferase increased | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | | |
| occurrences (all) | 1 | | |
| Nervous system disorders | | | |

| | | | |
|--|---------------------|--|--|
| Headache subjects affected / exposed occurrences (all) | 1 / 8 (12.50%) 2 | | |
| Anosmia subjects affected / exposed occurrences (all) | 1 / 8 (12.50%) 1 | | |
| Dizziness subjects affected / exposed occurrences (all) | 1 / 8 (12.50%) 1 | | |
| Migraine subjects affected / exposed occurrences (all) | 1 / 8 (12.50%) 1 | | |
| Sciatica subjects affected / exposed occurrences (all) | 1 / 8 (12.50%) 1 | | |
| Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all) | 1 / 8 (12.50%) 1 | | |
| Eye disorders Eye pain subjects affected / exposed occurrences (all) | 1 / 8 (12.50%) 1 | | |
| Gastrointestinal disorders Abdominal pain upper subjects affected / exposed occurrences (all) | 1 / 8 (12.50%) 2 | | |
| Abdominal discomfort subjects affected / exposed occurrences (all) | 1 / 8 (12.50%) 1 | | |
| Dyspepsia subjects affected / exposed occurrences (all) | 1 / 8 (12.50%) 1 | | |
| Nausea subjects affected / exposed occurrences (all) | 1 / 8 (12.50%) 1 | | |
| Skin and subcutaneous tissue disorders | | | |

| | | | |
|---|---------------------|--|--|
| Night sweats subjects affected / exposed occurrences (all) | 1 / 8 (12.50%) 1 | | |
| Paraesthesia subjects affected / exposed occurrences (all) | 1 / 8 (12.50%) 1 | | |
| Urticaria subjects affected / exposed occurrences (all) | 1 / 8 (12.50%) 1 | | |
| Musculoskeletal and connective tissue disorders | | | |
| Joint swelling subjects affected / exposed occurrences (all) | 1 / 8 (12.50%) 1 | | |
| Tendonitis subjects affected / exposed occurrences (all) | 1 / 8 (12.50%) 1 | | |
| Infections and infestations | | | |
| Nasopharyngitis subjects affected / exposed occurrences (all) | 1 / 8 (12.50%) 1 | | |
| Sinusitis subjects affected / exposed occurrences (all) | 1 / 8 (12.50%) 1 | | |
| Urinary tract infection subjects affected / exposed occurrences (all) | 1 / 8 (12.50%) 1 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|------------------|---|
| 04 June 2018 | Protocol version 2.0: 1. Addition of electrocardiogram (ECG) monitoring 2. Clarification of the fasting requirements 3. Change of urine pregnancy test to serum pregnancy test 4. Add possibility to perform Screening, Week 12, 24 and 36 visits over 2 days |
| 20 July 2018 | Protocol version 3.0: 1. Addition of electrocardiogram (ECG) monitoring at all visits apart from follow-up. 2. Addition of subject referral to a cardiologist. |
| 14 December 2020 | Protocol version 4.0: Addition of two interim analyses after last patient has reached week 12 and last patient has reached week 24. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

<http://www.ncbi.nlm.nih.gov/pubmed/34945090>

<http://www.ncbi.nlm.nih.gov/pubmed/32507315>

<http://www.ncbi.nlm.nih.gov/pubmed/34799277>