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: cm3			
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: cm3				
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	1 / 8 (12.50%)		
occurrences (all)	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) Anosmia subjects affected / exposed occurrences (all) Dizziness subjects affected / exposed occurrences (all) Migraine subjects affected / exposed occurrences (all) Sciatica subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 2 1 / 8 (12.50%) 1 1 / 8 (12.50%) 1 1 / 8 (12.50%) 1 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) Abdominal discomfort subjects affected / exposed occurrences (all) Dyspepsia subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 2 1 / 8 (12.50%) 1 1 / 8 (12.50%) 1 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