Clinical trial results:
A double-blind randomized extension study to assess the long-term efficacy and safety of linzagolix in subjects with endometriosis-associated pain.

Summary

EudraCT number	2019-002410-39
Trial protocol	FR CZ HU BG PL AT ES RO
Global end of trial date	15 December 2022

Results information

Result version number	v1 (current)
This version publication date	22 December 2023
First version publication date	22 December 2023

Trial information

Trial identification

Sponsor protocol code	19-OBE2109-006

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Kissei Pharmaceutical Co., Ltd.
Sponsor organisation address	3-1-3 Koishikawa, Bunkyo-ku, Tokyo, Japan, 112-002
Public contact	Clinical Projects Management, Kissei Pharmaceutical Co., Ltd., rinsyousiken@pharm.kissei.co.jp
Scientific contact	Clinical Projects Management, Kissei Pharmaceutical Co., Ltd., rinsyousiken@pharm.kissei.co.jp

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 March 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	15 September 2022
Global end of trial reached?	Yes
Global end of trial date	15 December 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the maintenance of efficacy of linzagolix administered orally once daily for up to an additional 6 months (for up to 12 months of treatment in total) in women who have already completed 6 months of linzagolix treatment at a dose of 75 mg alone or of 200 mg in combination with add-back therapy , in the management of moderate to severe EAP in women with surgically confirmed endometriosis.

Protection of trial subjects:

The study was conducted in accordance with Good Clinical Practice (GCP), local regulations, International Council for Harmonisation (ICH) notes for GCP (ICH/CPMP/135.95), internal standard operating procedures (SOPs) of ObsEva S.A. (=the former sponsor), and ethical principles that have their origin in the Declaration of Helsinki and its amendments.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	05 March 2020
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: 145
Country: Number of subjects enrolled	Romania: 20
Country: Number of subjects enrolled	Spain: 1
Country: Number of subjects enrolled	Austria: 1
Country: Number of subjects enrolled	Bulgaria: 6
Country: Number of subjects enrolled	Czechia: 4
Country: Number of subjects enrolled	Ukraine: 163
Country: Number of subjects enrolled	United States: 16
Worldwide total number of subjects	356
EEA total number of subjects	177

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)	356
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 43 clinical sites throughout the world, including centers in Austria, Bulgaria, Czech Republic, Spain, Romania, Poland, Ukraine, and United States.

Pre-assignment

Screening details:

Number of subjects:
- 356: Entered Extension Study
- 353: Treatment Extension Analysis Set (TEAS)
- 336: Per Protocol Extension Analysis Set (PP EAS)
- 356: Extension Safety Analysis Set (ESAF)
- 326: Follow-up Extension Analysis Set (FU EAS)
- 329: Follow-up Extension Safety Analysis Set (FU SAF)
- 354: Extension Pharmacokinetic Set

Period 1

Period 1 title	Extension Study 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	Placebo / LGX 75 mg group

Arm description:

- Main study (6 months): Linzagolix placebo + ABT placebo once daily
- Extension study (6 months): Linzagolix 75 mg + ABT Placebo once daily

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

Dosage and administration details:

75 mg

Investigational medicinal product name	ABT matching placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Estradiol (E2): 0 mg
Norethindrone acetate (NETA): 0 mg

Investigational medicinal product name	Linzagolix 75 mg matching placebo
Investigational medicinal product code	
Other name	OBE2109
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

0 mg

Arm title	Placebo / LGX 200 mg+ABT group
Arm description: - Main study (6 months): Linzagolix placebo + ABT placebo once daily - Extension study (6 months): Linzagolix 200 mg + ABT once daily	
Arm type	Experimental
Investigational medicinal product name	Linzagolix
Investigational medicinal product code	
Other name	OBE2109
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use
Dosage and administration details: 200 mg	
Investigational medicinal product name	Linzagolix 200 mg matching placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use
Dosage and administration details: 0 mg	
Investigational medicinal product name	ABT
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use
Dosage and administration details: Estradiol (E2): 1.0 mg Norethindrone acetate (NETA): 0.5 mg	
Investigational medicinal product name	ABT matching placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use
Dosage and administration details: Estradiol (E2): 0 mg Norethindrone acetate (NETA): 0 mg	
Arm title	LGX 75 mg group
Arm description: - Main study (6 months): Linzagolix 75 mg + Placebo ABT once daily - Extension study (6 months): Linzagolix 75 mg + Placebo ABT once daily	
Arm type	Experimental
Investigational medicinal product name	Linzagolix
Investigational medicinal product code	
Other name	OBE2109
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use
Dosage and administration details: 75 mg	
Investigational medicinal product name	ABT matching placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Estradiol (E2): 0 mg
Norethindrone acetate (NETA): 0 mg

Arm title	LGX 200 mg+ABT group

Arm description:

- Main study (6 months): Linzagolix 200 mg + ABT once daily
- Extension study (6 months): Linzagolix 200 mg + ABT once daily

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

Dosage and administration details:

200 mg

Investigational medicinal product name	ABT
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Estradiol (E2): 1.0 mg
Norethindrone acetate (NETA): 0.5 mg

Number of subjects in period 1	Placebo / LGX 75 mg group	Placebo / LGX 200 mg+ABT group	LGX 75 mg group
Started	58	57	119
Completed	49	50	101
Not completed	9	7	18
Consent withdrawn by subject	4	5	8
Ukrainian Russian war conflict	2	-	4
Adverse event, non-fatal	3	2	5
Subject planning pregnancy and AE-Nausea	-	-	-
Protocol deviation	-	-	1

Number of subjects in period 1	LGX 200 mg+ABT group
Started	122
Completed	110
Not completed	12
Consent withdrawn by subject	4
Ukrainian Russian war conflict	5
Adverse event, non-fatal	2
Subject planning pregnancy and AE-Nausea	1

Protocol deviation	-

Baseline characteristics

Reporting groups	
Reporting group title	Placebo / LGX 75 mg group
Reporting group description:	
- Main study (6 months): Linzagolix placebo + ABT placebo once daily - Extension study (6 months): Linzagolix 75 mg + ABT Placebo once daily	
Reporting group title	Placebo / LGX 200 mg+ABT group
Reporting group description:	
- Main study (6 months): Linzagolix placebo + ABT placebo once daily - Extension study (6 months): Linzagolix 200 mg + ABT once daily	
Reporting group title	LGX 75 mg group
Reporting group description:	
- Main study (6 months): Linzagolix 75 mg + Placebo ABT once daily - Extension study (6 months): Linzagolix 75 mg + Placebo ABT once daily	
Reporting group title	LGX 200 mg+ABT group
Reporting group description:	
- Main study (6 months): Linzagolix 200 mg + ABT once daily - Extension study (6 months): Linzagolix 200 mg + ABT once daily	

Reporting group values	Placebo / LGX 75 mg group	Placebo / LGX 200 mg+ABT group	LGX 75 mg group
Number of subjects	58	57	119
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)	58	57	119
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	34.3	35.0	35.1
standard deviation	± 6.6	± 7.7	± 6.3
Gender categorical Units: Subjects			
Female	58	57	119
Male	0	0	0

Reporting group values	LGX 200 mg+ABT group	Total	
Number of subjects	122	356	
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)	122	356	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous			
Units: years			
arithmetic mean	34.8		
standard deviation	± 6.9	-	
Gender categorical			
Units: Subjects			
Female	122	356	
Male	0	0	

End points

End points reporting groups

Reporting group title	Placebo / LGX 75 mg group
Reporting group description:	
- Main study (6 months): Linzagolix placebo + ABT placebo once daily - Extension study (6 months): Linzagolix 75 mg + ABT Placebo once daily	
Reporting group title	Placebo / LGX 200 mg+ABT group
Reporting group description:	
- Main study (6 months): Linzagolix placebo + ABT placebo once daily - Extension study (6 months): Linzagolix 200 mg + ABT once daily	
Reporting group title	LGX 75 mg group
Reporting group description:	
- Main study (6 months): Linzagolix 75 mg + Placebo ABT once daily - Extension study (6 months): Linzagolix 75 mg + Placebo ABT once daily	
Reporting group title	LGX 200 mg+ABT group
Reporting group description:	
- Main study (6 months): Linzagolix 200 mg + ABT once daily - Extension study (6 months): Linzagolix 200 mg + ABT once daily	

Primary: Proportion of subjects with reduction of DYS (Month 3 MCT) and stable or decreased use of analgesics for EAP at Month 12

End point title	Proportion of subjects with reduction of DYS (Month 3 MCT) and stable or decreased use of analgesics for EAP at Month 12[1]
End point description:	
End point type	Primary
End point timeframe:	
6-month extension study treatment period (from Month 6 to Month 12)	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Since the endpoint is the number of the responder who have a clinically meaningful reduction in DYS and the subjects with stable or decreased use of analgesics, no statistical analyses were done.

End point values	Placebo / LGX 75 mg group	Placebo / LGX 200 mg+ABT group	LGX 75 mg group	LGX 200 mg+ABT group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	57	55	111	111
Units: Percentage				
number (not applicable)	56.1	78.2	55.9	91.0

Statistical analyses

No statistical analyses for this end point

Primary: Proportion of subjects with reduction of NMPP (Month 3 MCT) and stable or

decreased use of analgesics

End point title	Proportion of subjects with reduction of NMPP (Month 3 MCT) and stable or decreased use of analgesics[2]

End point description:

End point type	Primary

End point timeframe:

6-month extension study treatment period (from Month 6 to Month 12)

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Since the endpoint is the number of the responder who have a clinically meaningful reduction in NMPP and the subjects with stable or decreased use of analgesics, no statistical analyses were done.

End point values	Placebo / LGX 75 mg group	Placebo / LGX 200 mg+ABT group	LGX 75 mg group	LGX 200 mg+ABT group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	57	55	111	111
Units: Percentage				
number (not applicable)	59.6	49.1	59.5	67.6

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: 6-month extension study treatment period (from Month 6 to Month 12)	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	23.0

Reporting groups	
Reporting group title	Placebo / LGX 75 mg group
Reporting group description: -	
Reporting group title	Placebo / LGX 200 mg+ABT group
Reporting group description: -	
Reporting group title	LGX 75 mg group
Reporting group description: -	
Reporting group title	LGX 200 mg+ABT group
Reporting group description: -	

Serious adverse events	Placebo / LGX 75 mg group	Placebo / LGX 200 mg+ABT group	LGX 75 mg group
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 58 (0.00%)	1 / 57 (1.75%)	3 / 119 (2.52%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Reproductive system and breast disorders			
Genital haemorrhage			
subjects affected / exposed	0 / 58 (0.00%)	1 / 57 (1.75%)	0 / 119 (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
Vaginal haemorrhage			
subjects affected / exposed	0 / 58 (0.00%)	0 / 57 (0.00%)	1 / 119 (0.84%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 58 (0.00%)	0 / 57 (0.00%)	1 / 119 (0.84%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 58 (0.00%)	0 / 57 (0.00%)	1 / 119 (0.84%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	LGX 200 mg+ABT group		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 122 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Reproductive system and breast disorders			
Genital haemorrhage			
subjects affected / exposed	0 / 122 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vaginal haemorrhage			
subjects affected / exposed	0 / 122 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 122 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 122 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Placebo / LGX 75 mg group	Placebo / LGX 200 mg+ABT group	LGX 75 mg group
Total subjects affected by non-serious adverse events			
subjects affected / exposed	15 / 58 (25.86%)	13 / 57 (22.81%)	26 / 119 (21.85%)
Vascular disorders			
Hot flush			
subjects affected / exposed	4 / 58 (6.90%)	0 / 57 (0.00%)	4 / 119 (3.36%)
occurrences (all)	4	0	4
Nervous system disorders			
Headache			
subjects affected / exposed	3 / 58 (5.17%)	3 / 57 (5.26%)	5 / 119 (4.20%)
occurrences (all)	6	4	5
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	3 / 58 (5.17%)	2 / 57 (3.51%)	7 / 119 (5.88%)
occurrences (all)	4	4	7
Reproductive system and breast disorders			
Vaginal haemorrhage			
subjects affected / exposed	1 / 58 (1.72%)	3 / 57 (5.26%)	3 / 119 (2.52%)
occurrences (all)	1	7	4
Infections and infestations			
COVID-19			
subjects affected / exposed	1 / 58 (1.72%)	2 / 57 (3.51%)	6 / 119 (5.04%)
occurrences (all)	1	2	6
Vulvovaginal mycotic infection			
subjects affected / exposed	3 / 58 (5.17%)	3 / 57 (5.26%)	1 / 119 (0.84%)
occurrences (all)	3	3	1

Non-serious adverse events	LGX 200 mg+ABT group		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	19 / 122 (15.57%)		
Vascular disorders			
Hot flush			
subjects affected / exposed	5 / 122 (4.10%)		
occurrences (all)	5		
Nervous system disorders			
Headache			
subjects affected / exposed	3 / 122 (2.46%)		
occurrences (all)	3		

Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all)	 0 / 122 (0.00%) 0		
Reproductive system and breast disorders Vaginal haemorrhage subjects affected / exposed occurrences (all)	 3 / 122 (2.46%) 5		
Infections and infestations COVID-19 subjects affected / exposed occurrences (all) Vulvovaginal mycotic infection subjects affected / exposed occurrences (all)	 6 / 122 (4.92%) 6 2 / 122 (1.64%) 2		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported