



Clinical trial results:

A Phase 3 multicenter, randomized, double-blind, placebo-controlled, clinical study to assess the efficacy and safety of linzagolix in subjects with moderate to severe endometriosis-associated pain.

Summary

EudraCT number	2019-000283-26
Trial protocol	FR HU AT CZ PL ES BG RO
Global end of trial date	28 June 2022

Results information

Result version number	v1 (current)
This version publication date	23 July 2023
First version publication date	23 July 2023

Trial information

Trial identification

Sponsor protocol code	18-OBE2109-003
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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, 112-0002
Public contact	Kissei Pharmaceutical Co., Ltd., Clinical Projects Management, rinsyousiken@pharm.kissei.co.jp
Scientific contact	Kissei Pharmaceutical Co., Ltd., Clinical Projects Management, 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	22 December 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	01 April 2022
Global end of trial reached?	Yes
Global end of trial date	28 June 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate the efficacy and safety of linzagolix administered orally once daily for 3 months at a dose of 75 mg alone or of 200 mg in combination with add-back therapy versus placebo, in the management of moderate to severe endometriosis-associated pain.

Protection of trial subjects:

The study was conducted in accordance with the ethical principles that have their origins in the Declaration of Helsinki and with Good Clinical Practice (GCP) rules and in line with local regulatory requirements.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	13 June 2019
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: 179
Country: Number of subjects enrolled	Romania: 49
Country: Number of subjects enrolled	Spain: 4
Country: Number of subjects enrolled	Austria: 1
Country: Number of subjects enrolled	Bulgaria: 13
Country: Number of subjects enrolled	Czechia: 6
Country: Number of subjects enrolled	France: 1
Country: Number of subjects enrolled	Hungary: 2
Country: Number of subjects enrolled	Ukraine: 205
Country: Number of subjects enrolled	United States: 26
Worldwide total number of subjects	486
EEA total number of subjects	255

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)	486
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 71 clinical sites throughout the world, including centers in Austria, Bulgaria, Czech Republic, France, Hungary, Poland, Romania, Spain, Ukraine, and United States

Pre-assignment

Screening details:

Number of subjects:

- 854 screened
- 486 randomized; 2 discontinued study between randomization and Day 1 due to protocol deviation
- 484 included in both of Full Analysis Set (FAS) and Safety Analysis Set (SAF)

Period 1

Period 1 title	Overall trial (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	LGX 75 mg group

Arm description:

Linzagolix 75 mg + Placebo ABT
Once daily for 6 months

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

Arm title	LGX 200 mg + ABT group
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Arm description:

Linzagolix 200 mg + ABT
Once daily for 6 months

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	ESTRADIOL HEMIHYDRATE/NORETHISTERONE ACETATE
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:
 ESTRADIOL HEMIHYDRATE: 1 mg
 NORETHISTERONE ACETATE: 0.5 mg

Arm title	Placebo group
Arm description: Placebo Linzagolix + Placebo ABT Once daily for 6 months	
Arm type	Placebo
Investigational medicinal product name	Placebo Linzagolix
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	Placebo ABT
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use
Dosage and administration details: 0 mg	

Number of subjects in period 1^[1]	LGX 75 mg group	LGX 200 mg + ABT group	Placebo group
Started	160	162	162
Day 1	160	162	162
Month 3	149	155	149
Month 6	140	143	137
Completed	140	143	137
Not completed	20	19	25
Consent withdrawn by subject	8	10	20
Adverse event, non-fatal	8	6	3
Other	1	-	-
Pregnancy	2	-	1
Lost to follow-up	-	1	1
Protocol deviation	1	2	-

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 Full Analysis Set (FAS). A total of 486 subjects were randomized, 484 subjects were included in the FAS. Two randomized subjects were excluded: these 2 subjects discontinued the study between randomization

and Day 1 due to protocol deviation.

Baseline characteristics

Reporting groups

Reporting group title	LGX 75 mg group
Reporting group description: Linzagolix 75 mg + Placebo ABT Once daily for 6 months	
Reporting group title	LGX 200 mg + ABT group
Reporting group description: Linzagolix 200 mg + ABT Once daily for 6 months	
Reporting group title	Placebo group
Reporting group description: Placebo Linzagolix + Placebo ABT Once daily for 6 months	

Reporting group values	LGX 75 mg group	LGX 200 mg + ABT group	Placebo group
Number of subjects	160	162	162
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)	160	162	162
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	35.1	34.6	34.9
standard deviation	± 6.4	± 6.8	± 6.8
Gender categorical Units: Subjects			
Female	160	162	162
Male	0	0	0

Reporting group values	Total		
Number of subjects	484		
Age categorical 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)	484		
From 65-84 years	0		
85 years and over	0		
Age continuous			
Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical			
Units: Subjects			
Female	484		
Male	0		

End points

End points reporting groups

Reporting group title	LGX 75 mg group
Reporting group description: Linzagolix 75 mg + Placebo ABT Once daily for 6 months	
Reporting group title	LGX 200 mg + ABT group
Reporting group description: Linzagolix 200 mg + ABT Once daily for 6 months	
Reporting group title	Placebo group
Reporting group description: Placebo Linzagolix + Placebo ABT Once daily for 6 months	

Primary: Reduction of DYS at Month 3 - Proportion of responders

End point title	Reduction of DYS at Month 3 - Proportion of responders
End point description:	
End point type	Primary
End point timeframe: 3 months	

End point values	LGX 75 mg group	LGX 200 mg + ABT group	Placebo group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	160	162	162	
Units: percent				
number (confidence interval 95%)	44.0 (36.3 to 52.0)	72.9 (65.3 to 79.4)	23.5 (17.5 to 30.7)	

Statistical analyses

Statistical analysis title	p-value of treatment effect
Comparison groups	LGX 75 mg group v Placebo group
Number of subjects included in analysis	322
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Bonferroni-corrected p-value

Statistical analysis title	p-value of treatment effect
Comparison groups	LGX 200 mg + ABT group v Placebo group
Number of subjects included in analysis	324
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Bonferroni-corrected p-value

Primary: Reduction of NMPP at Month 3 - Proportion of responders

End point title	Reduction of NMPP at Month 3 - Proportion of responders
End point description:	
End point type	Primary
End point timeframe:	
3 months	

End point values	LGX 75 mg group	LGX 200 mg + ABT group	Placebo group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	160	162	162	
Units: percent				
number (confidence interval 95%)	38.9 (31.5 to 46.9)	47.3 (39.5 to 55.3)	30.9 (24.1 to 38.6)	

Statistical analyses

Statistical analysis title	p-value of treatment effect
Comparison groups	LGX 75 mg group v Placebo group
Number of subjects included in analysis	322
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.279
Method	Bonferroni-corrected p-value

Statistical analysis title	p-value of treatment effect
Comparison groups	LGX 200 mg + ABT group v Placebo group

Number of subjects included in analysis	324
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.007
Method	Bonferroni-corrected p-value

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Day 1 to Month 6

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	23.0
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Reporting groups

Reporting group title	LGX 75 mg group
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Reporting group description: -

Reporting group title	LGX 200 mg + ABT group
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Reporting group description: -

Reporting group title	Placebo group
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Reporting group description: -

Serious adverse events	LGX 75 mg group	LGX 200 mg + ABT group	Placebo group
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 160 (1.25%)	2 / 162 (1.23%)	0 / 162 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 160 (0.00%)	1 / 162 (0.62%)	0 / 162 (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
Reproductive system and breast disorders			
Endometriosis			
subjects affected / exposed	1 / 160 (0.63%)	0 / 162 (0.00%)	0 / 162 (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
Infections and infestations			
Peritonitis			
subjects affected / exposed	1 / 160 (0.63%)	0 / 162 (0.00%)	0 / 162 (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
Pneumonia			

subjects affected / exposed	0 / 160 (0.00%)	1 / 162 (0.62%)	0 / 162 (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

Frequency threshold for reporting non-serious adverse events: 3 %

Non-serious adverse events	LGX 75 mg group	LGX 200 mg + ABT group	Placebo group
Total subjects affected by non-serious adverse events			
subjects affected / exposed	83 / 160 (51.88%)	94 / 162 (58.02%)	69 / 162 (42.59%)
Vascular disorders			
Hot flush			
subjects affected / exposed	12 / 160 (7.50%)	11 / 162 (6.79%)	4 / 162 (2.47%)
occurrences (all)	15	11	4
Nervous system disorders			
Headache			
subjects affected / exposed	13 / 160 (8.13%)	17 / 162 (10.49%)	13 / 162 (8.02%)
occurrences (all)	17	24	25
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	6 / 160 (3.75%)	11 / 162 (6.79%)	4 / 162 (2.47%)
occurrences (all)	6	11	4
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	5 / 160 (3.13%)	4 / 162 (2.47%)	10 / 162 (6.17%)
occurrences (all)	5	4	13
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	6 / 160 (3.75%)	6 / 162 (3.70%)	7 / 162 (4.32%)
occurrences (all)	6	6	7
Abdominal distension			
subjects affected / exposed	4 / 160 (2.50%)	6 / 162 (3.70%)	3 / 162 (1.85%)
occurrences (all)	4	6	4
Diarrhoea			
subjects affected / exposed	4 / 160 (2.50%)	2 / 162 (1.23%)	5 / 162 (3.09%)
occurrences (all)	4	2	5
Constipation			

subjects affected / exposed occurrences (all)	3 / 160 (1.88%) 3	5 / 162 (3.09%) 5	2 / 162 (1.23%) 2
Reproductive system and breast disorders Vaginal haemorrhage subjects affected / exposed occurrences (all)	4 / 160 (2.50%) 5	6 / 162 (3.70%) 7	1 / 162 (0.62%) 1
Breast pain subjects affected / exposed occurrences (all)	1 / 160 (0.63%) 1	2 / 162 (1.23%) 2	5 / 162 (3.09%) 5
Skin and subcutaneous tissue disorders Acne subjects affected / exposed occurrences (all)	1 / 160 (0.63%) 1	3 / 162 (1.85%) 3	5 / 162 (3.09%) 5
Psychiatric disorders Mood swings subjects affected / exposed occurrences (all)	8 / 160 (5.00%) 8	5 / 162 (3.09%) 6	3 / 162 (1.85%) 3
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all)	8 / 160 (5.00%) 8	3 / 162 (1.85%) 3	2 / 162 (1.23%) 2
Infections and infestations COVID-19 subjects affected / exposed occurrences (all)	5 / 160 (3.13%) 5	6 / 162 (3.70%) 6	5 / 162 (3.09%) 5
Urinary tract infection subjects affected / exposed occurrences (all)	3 / 160 (1.88%) 3	7 / 162 (4.32%) 7	0 / 162 (0.00%) 0

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