Clinical trial results:
An Open label, Multicenter, Single-arm and Prospective Study to Assess the Efficacy and Safety of Leuprorelin 3M in the Treatment of CPP

Summary

EudraCT number	2022-002471-11
Trial protocol	Outside EU/EEA
Global end of trial date	10 March 2025

Results information

Result version number	v1
This version publication date	23 October 2025
First version publication date	23 October 2025

Trial information

Trial identification

Sponsor protocol code	Leuprorelin-4002

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05341115
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Takeda (China) International Trading Co., Ltd.
Sponsor organisation address	37F, New Bund Center, NO.555 West Haiyang Rd, Pudong New Area, Shanghai, China, 200124
Public contact	Study Director, Takeda, TrialDisclosures@takeda.com
Scientific contact	Study Director, Takeda, TrialDisclosures@takeda.com

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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	10 March 2025
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	10 March 2025
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main aim of this study was to investigate the efficacy and safety of leuprolide acetate depot 11.25 milligrams (mg) 3-month formulations for the treatment of central precocious puberty (CPP) in children in China.

Protection of trial subjects:

Each participant or their legally authorised representative signed an informed consent form (ICF) before participating in the study.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	14 March 2023
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	China: 79
Worldwide total number of subjects	79
EEA total number of subjects	0

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)	79
Adolescents (12-17 years)	0
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 79 participants took part in the study at 5 investigative sites in China from 12 March 2023 to 10 March 2025.

Pre-assignment

Screening details:

A total of 79 participants with a diagnosis of CPP received leuprorelin acetate depot 11.25 mg.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Leuprorelin Acetate Depot 3M 11.25 mg

Arm description:

Participants with CPP having body weight greater than or equal to (≥)20 kilograms (kg) received the recommended dose of leuprorelin acetate depot 11.25 mg subcutaneous administration (SC) every 12 weeks based on the standard of 30180 micrograms (µg)/kg/4weeks for the 24-week Treatment Period. It was not recommended to exceed the dose above 180 µg/kg.

Arm type	Experimental
Investigational medicinal product name	Leuprorelin Acetate
Investigational medicinal product code	
Other name	Leuprorelin-4002
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Leuprorelin acetate depot 11.25 mg SC every 12 weeks based on the standard of 30180µg/kg/4weeks for the 24-week Treatment Period.

Number of subjects in period 1	Leuprorelin Acetate Depot 3M 11.25 mg
Started	79
Completed	77
Not completed	2
Adverse event, non-fatal	1
Lost to follow-up	1

Baseline characteristics

Reporting groups	
Reporting group title	Leuprorelin Acetate Depot 3M 11.25 mg
Reporting group description:	
Participants with CPP having body weight greater than or equal to (≥)20 kilograms (kg) received the recommended dose of leuprorelin acetate depot 11.25 mg subcutaneous administration (SC) every 12 weeks based on the standard of 30180 micrograms (µg)/kg/4weeks for the 24-week Treatment Period. It was not recommended to exceed the dose above 180 µg/kg.	

Reporting group values	Leuprorelin Acetate Depot 3M 11.25 mg	Total	
Number of subjects	79	79	
Age Categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	7.59		
standard deviation	± 1.019	-	
Gender categorical Units: Subjects			
Female	78	78	
Male	1	1	
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	79	79	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	0	0	
White	0	0	
More than one race	0	0	
Unknown or Not Reported	0	0	
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	0	0	
Not Hispanic or Latino	79	79	
Unknown or Not Reported	0	0	

End points

End points reporting groups

Reporting group title	Leuprorelin Acetate Depot 3M 11.25 mg

Reporting group description:

Participants with CPP having body weight greater than or equal to (≥)20 kilograms (kg) received the recommended dose of leuprorelin acetate depot 11.25 mg subcutaneous administration (SC) every 12 weeks based on the standard of 30180 micrograms (µg)/kg/4weeks for the 24-week Treatment Period. It was not recommended to exceed the dose above 180 µg/kg.

Primary: Percentage of Participants with Peak Luteinizing Hormone (LH) Suppression in Gonadotropin-Releasing Hormone (GnRH) Stimulation at Week 24

End point title	Percentage of Participants with Peak Luteinizing Hormone (LH) Suppression in Gonadotropin-Releasing Hormone (GnRH) Stimulation at Week 24 [1]

End point description:

The LH suppression was defined as LH peak value in GnRH stimulation ≤3.0 international units per liter (IU/L). The enrolled population set included all the eligible participants enrolled in this study, i.e., all participants enrolled in this study who met the inclusion criteria and did not meet any of the exclusion criteria, regardless of whether they received the study drug.

End point type	Primary

End point timeframe:

Week 24

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: Only descriptive analysis was planned for this endpoint.

End point values	Leuprorelin Acetate Depot 3M 11.25 mg			
Subject group type	Reporting group			
Number of subjects analysed	79			
Units: percentage of participants				
number (confidence interval 95%)	97.47 (91.15 to 99.69)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Tanner Stage Regression or No Progression at Week 24

End point title	Percentage of Participants with Tanner Stage Regression or No Progression at Week 24

End point description:

Tanner Stage was used to measure pubertal development. Tanner Stage is based on progression through 5-stages. Progression was defined as either breast/genitals or pubic hair score being increased compared with baseline score. Otherwise, the status was classified as regression or no progression. Baseline was defined as the assessment prior to the first dose of study drug. The enrolled population set included all the eligible participants enrolled in this study, i.e., all participants enrolled in this study who

met the inclusion criteria and did not meet any of the exclusion criteria, regardless of whether they received the study drug.

End point type	Secondary

End point timeframe:

Baseline and Week 24

End point values	Leuprorelin Acetate Depot 3M 11.25 mg			
Subject group type	Reporting group			
Number of subjects analysed	79			
Units: percentage of participants				
number (confidence interval 94%)	97.47 (91.15 to 99.69)			

Statistical analyses

No statistical analyses for this end point

Secondary: Concentrations of Basal Luteinizing Hormone (LH) and Follicle Stimulating Hormone (FSH)

End point title	Concentrations of Basal Luteinizing Hormone (LH) and Follicle Stimulating Hormone (FSH)

End point description:

Plasma LH and FSH basal concentrations were assessed. The enrolled population set included all the eligible participants enrolled in this study, i.e., all participants enrolled in this study who met the inclusion criteria and did not meet any of the exclusion criteria, regardless of whether they received the study drug. 'n' denotes number of participants with data available for analysis at the specified category and time-point.

End point type	Secondary

End point timeframe:

Baseline, Weeks 24 and 36

End point values	Leuprorelin Acetate Depot 3M 11.25 mg			
Subject group type	Reporting group			
Number of subjects analysed	79			
Units: International Units per liter (IU/L)				
arithmetic mean (standard deviation)				
LH: Baseline (n=67)	1.224 (± 1.410)			
LH: Week 24 (n=70)	0.454 (± 0.297)			
LH: Week 36 (n=75)	0.458 (± 0.293)			
FSH: Baseline (n=79)	3.213 (± 1.593)			

FSH: Week 24 (n=75) FSH: Week 36 (n=77)	1.457 (± 0.686) 1.569 (± 0.706)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Decreased Ratio of Bone Age Over Chronological Age at Week 24

End point title	Percentage of Participants With Decreased Ratio of Bone Age Over Chronological Age at Week 24

End point description:

Bone age was determined by Greulich and Pyle standards or Tanner-Whitehouse 3 (TW3) standards. The enrolled population set included all the eligible participants enrolled in this study, i.e., all participants enrolled in this study who met the inclusion criteria and did not meet any of the exclusion criteria, regardless of whether they received the study drug.

End point type	Secondary

End point timeframe:

Baseline and Week 24

End point values	Leuprorelin Acetate Depot 3M 11.25 mg			
Subject group type	Reporting group			
Number of subjects analysed	79			
Units: percentage of participants				
number (confidence interval 95%)	84.81 (74.97 to 91.90)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Treatment-Emergent Adverse Events (TEAE)

End point title	Number of Participants With Treatment-Emergent Adverse Events (TEAE)

End point description:

An AE is defined as any untoward medical occurrence in a clinical investigation participant administered a drug; it does not necessarily have to have a causal relationship with this treatment. An AE can therefore be any unfavorable and unintended sign (eg, a clinically significant abnormal laboratory finding), symptom, or disease temporally associated with the use of a drug, whether or not it is considered related to the drug. TEAE is defined as an adverse event with an onset that occurs after receiving study drug. Safety population set included all participants who had been under treatment with leuprorelin or who were first prescribed leuprorelin, received at least one dose and completed one follow-up visit.

End point type	Secondary

End point timeframe:

From first dose of study drug up to 12 weeks post last dose or early termination Visit (ET) (up to approximately 38 weeks)

End point values	Leuprorelin Acetate Depot 3M 11.25 mg			
Subject group type	Reporting group			
Number of subjects analysed	79			
Units: participants	27			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Decreased First Morning Voided (FMV) Urinary Gonadotropin (Gn) at Week 24

End point title	Percentage of Participants with Decreased First Morning Voided (FMV) Urinary Gonadotropin (Gn) at Week 24

End point description:

Percentage of participants with reductions from baseline FMV Gn urinary LH and urinary FSH values at Week 24 were reported. The enrolled population set included all the eligible participants enrolled in this study, i.e., all participants enrolled in this study who met the inclusion criteria and did not meet any of the exclusion criteria, regardless of whether they received the study drug.

End point type	Secondary

End point timeframe:

Baseline and Week 24

End point values	Leuprorelin Acetate Depot 3M 11.25 mg			
Subject group type	Reporting group			
Number of subjects analysed	79			
Units: percentage of participants				
number (confidence interval 95%)				
LH	62.03 (50.41 to 72.72)			
FSH	63.29 (51.69 to 73.86)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From first dose of study drug up to 12 weeks post last dose or early termination Visit (ET) (up to approximately 38 weeks)

Adverse event reporting additional description:

The safety population set included all included participants who had been under treatment with leuprorelin or who were first prescribed leuprorelin, received at least one dose and completed one follow-up visit.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	28.0

Reporting groups

Reporting group title	Leuprorelin Acetate Depot 3M 11.25 mg

Reporting group description:

Participants with CPP having body weight ≥20 kg received the recommended dose of leuprorelin acetate depot 11.25 mg SC every 12 weeks based on the standard of 30180 µg/kg/4weeks for the 24-week Treatment Period. It was not recommended to exceed the dose above 180 µg/kg.

Serious adverse events	Leuprorelin Acetate Depot 3M 11.25 mg		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 79 (1.27%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Infections and infestations			
Acute appendicitis			
subjects affected / exposed	1 / 79 (1.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Leuprorelin Acetate Depot 3M 11.25 mg		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 79 (5.06%)		
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	4 / 79 (5.06%)		
occurrences (all)	4		

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