Clinical trial results:
AN OPEN-LABEL, MULTICENTRE, SINGLE-ARM STUDY TO ASSESS THE EFFICACY AND SAFETY OF TRIPTORELIN 3-MONTH FORMULATION IN CHINESE CHILDREN WITH CENTRAL PRECOCIOUS PUBERTY

Summary

EudraCT number	2022-002963-31
Trial protocol	Outside EU/EEA
Global end of trial date	03 September 2022

Results information

Result version number	v1 (current)
This version publication date	20 March 2023
First version publication date	20 March 2023

Trial information

Trial identification

Sponsor protocol code	D-CN-52014-243

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04736602
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Ipsen Pharma
Sponsor organisation address	65, quai Georges Gorse, Boulogne Billancourt, France, 92100
Public contact	Medical Director, Ipsen Pharma, clinical.trials@ipsen.com
Scientific contact	Medical Director, Ipsen Pharma, clinical.trials@ipsen.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	03 September 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	03 September 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The purpose of this study was to assess the efficacy of the triptorelin 3-month prolonged release (PR) formulation in suppressing luteinising hormone (LH) levels to pre-pubertal levels [defined as a peak LH ≤3 international units per liter (IU/L)] after intravenous (IV) gonadotropin-releasing hormone (GnRH) stimulation at Month 3 in Chinese children with central precocious puberty (CPP).

Protection of trial subjects:

The study was conducted under the provisions of the Declaration of Helsinki, in accordance with the Good Clinical Practice of China and in compliance with ethics committee and informed consent regulations.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	27 March 2021
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: 32
Worldwide total number of subjects	32
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)	32
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:

This prospective, Phase 3, open-label, single arm, 2-phase (main study phase and an extension phase) study was conducted in children with central precocious puberty (CPP) at 6 investigational sites in China.

Pre-assignment

Screening details:

This study had two phases: main study phase and extension phase. Study consisted of screening period (up to 28 days), main study phase (6 months) and an extension phase (6 months). A total of 32 participants were enrolled in this study.

Period 1

Period 1 title	Main study phase
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	All Participants

Arm description:

Participants received triptorelin pamoate 15 milligrams (mg) intramuscular (IM) injection on Day 1 visit and Month 3 visit (Day 91) during the main study phase. Participants had an option to continue with the triptorelin pamoate in extension phase of the study. As per Investigator decision, eligible participants continued to receive IM injections of triptorelin pamoate on Month 6 (Day 182) and Month 9 (Day 271) during the extension phase.

Arm type	Experimental
Investigational medicinal product name	Triptorelin pamoate
Investigational medicinal product code	
Other name	Diphereline®
Pharmaceutical forms	Powder and solvent for suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Triptorelin pamoate was administered as an IM injection of 4 milliliter (mL) sterile lyophilizate of microparticles and 2 mL of sterile solvent, containing 15 mg dose.

Number of subjects in period 1	All Participants
Started	32
Completed	30
Not completed	2
Withdrawal by Parent/Guardian	2

Period 2

Period 2 title	Extension phase
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	All Participants

Arm description:

Participants received triptorelin pamoate 15 mg IM injection on Day 1 visit and Month 3 visit (Day 91) during the main study phase. Participants had an option to continue with the triptorelin pamoate in extension phase of the study. As per Investigator decision, eligible participants continued to receive IM injections of triptorelin pamoate on Month 6 (Day 182) and Month 9 (Day 271) during the extension phase.

Arm type	Experimental
Investigational medicinal product name	Triptorelin pamoate
Investigational medicinal product code	
Other name	Diphereline®
Pharmaceutical forms	Powder and solvent for suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Triptorelin pamoate was administered as an IM injection of 4 mL sterile lyophilizate of microparticles and 2 mL of sterile solvent, containing 15 mg dose.

Number of subjects in period 2	All Participants
Started	30
Completed	29
Not completed	1
Withdrawal by Parent/Guardian	1

Baseline characteristics

Reporting groups	
Reporting group title	All Participants
Reporting group description:	
Participants received triptorelin pamoate 15 milligrams (mg) intramuscular (IM) injection on Day 1 visit and Month 3 visit (Day 91) during the main study phase. Participants had an option to continue with the triptorelin pamoate in extension phase of the study. As per Investigator decision, eligible participants continued to receive IM injections of triptorelin pamoate on Month 6 (Day 182) and Month 9 (Day 271) during the extension phase.	

Reporting group values	All Participants	Total	
Number of subjects	32	32	
Age categorical Units: Subjects			
Age continuous Units: years arithmetic mean standard deviation	 7.6 ± 0.8	 -	
Gender categorical Units: Subjects			
Female	29	29	
Male	3	3	
Race Customized Units: Subjects			
Chinese	32	32	
Ethnicity Units: Subjects			
Hispanic or Latino	0	0	
Not Hispanic or Latino	32	32	

End points

End points reporting groups

Reporting group title	All Participants

Reporting group description:

Participants received triptorelin pamoate 15 milligrams (mg) intramuscular (IM) injection on Day 1 visit and Month 3 visit (Day 91) during the main study phase. Participants had an option to continue with the triptorelin pamoate in extension phase of the study. As per Investigator decision, eligible participants continued to receive IM injections of triptorelin pamoate on Month 6 (Day 182) and Month 9 (Day 271) during the extension phase.

Reporting group title	All Participants

Reporting group description:

Participants received triptorelin pamoate 15 mg IM injection on Day 1 visit and Month 3 visit (Day 91) during the main study phase. Participants had an option to continue with the triptorelin pamoate in extension phase of the study. As per Investigator decision, eligible participants continued to receive IM injections of triptorelin pamoate on Month 6 (Day 182) and Month 9 (Day 271) during the extension phase.

Primary: Percentage of Participants With LH Suppression After GnRH Stimulation

End point title	Percentage of Participants With LH Suppression After GnRH Stimulation[1]

End point description:

The LH suppression was defined as stimulated peak LH ≤3 IU/L. The GnRH stimulation test was performed by using an intravenous (IV) injection of gonadorelin (synthetic GnRH) to stimulate gonadotrophin release and blood samples were collected after the gonadorelin injection for central assessment of serum LH levels. The modified ITT (mITT) population consisted of all treated participants with at least 1 baseline and month 3 post-baseline assessment of the primary efficacy endpoint.

End point type	Primary

End point timeframe:

At Month 3

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: No additional statistical analysis was prespecified for this endpoint.

End point values	All Participants			
Subject group type	Reporting group			
Number of subjects analysed	31			
Units: percentage of participants				
number (confidence interval 90%)	100 (90.8 to 100)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Basal LH and Follicle-Stimulating Hormone (FSH) Serum Levels

End point title	Change From Baseline in Basal LH and Follicle-Stimulating Hormone (FSH) Serum Levels

End point description:

Basal LH and FSH serum concentrations were analyzed centrally. Change from baseline was defined as the values for LH and FSH at indicated timepoints minus the value at baseline. Baseline was defined as the last non-missing measurement taken prior to the first dose administered. The mITT population consisted of all treated participants with at least 1 baseline and Month 3 post-baseline assessment of the primary efficacy endpoint. Only data from the participants analyzed were reported. Here, 'n' = number of participants analyzed at specific time point.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and at Months 3, 6, 9 and 12

End point values	All Participants			
Subject group type	Reporting group			
Number of subjects analysed	31			
Units: IU/L				
arithmetic mean (standard deviation)				
LH, Month 3 (n = 31)	-0.6906 (± 1.6417)			
LH, Month 6 (n = 30)	-0.7411 (± 1.6606)			
LH, Month 9 (n = 28)	-0.7415 (± 1.6817)			
LH, Month 12 (n = 29)	-0.9310 (± 1.6367)			
FSH, Month 3 (n = 31)	-2.3531 (± 1.8079)			
FSH, Month 6 (n = 30)	-2.2307 (± 1.7445)			
FSH, Month 9 (n = 28)	-2.0740 (± 1.7979)			
FSH, Month 12 (n = 29)	-1.9413 (± 1.6996)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With LH Suppression After GnRH Stimulation

End point title	Percentage of Participants With LH Suppression After GnRH Stimulation

End point description:

A synthetic GnRH (gonadorelin) was used for gonadotrophin stimulation. Blood samples were collected prior to gonadorelin injection (timepoint T0) and at 30 minutes (T30), 60 minutes (T60) and 90 minutes (T90) (±5 minutes at each timepoint) after a single IV injection of gonadorelin. A suppressed LH response to GnRH stimulation test was defined as peak LH ≤3 IU/L among the 4 timepoints (T0, T30, T60 and T90). The mITT population consisted of all treated participants with at least 1 baseline and Month 3 post-baseline assessment of the primary efficacy endpoint. Here, 'n' = number of participants analyzed at specific time point.

End point type	Secondary

End point timeframe:

At Months 6 and 12

End point values	All Participants			
Subject group type	Reporting group			
Number of subjects analysed	31			
Units: percentage of participants				
number (confidence interval 90%)				
Month 6 (n = 29)	93.5 (81.1 to 98.8)			
Month 12 (n = 29)	93.5 (81.1 to 98.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Peak LH and FSH Level After GnRH Stimulation

End point title	Change From Baseline in Peak LH and FSH Level After GnRH Stimulation

End point description:

A synthetic GnRH were used for gonadotrophin stimulation. Blood samples were collected prior to gonadorelin injection (timepoint T0) and at 30 minutes (T30), 60 minutes (T60) and 90 minutes (T90) (±5 minutes at each timepoint) after a single IV injection of gonadorelin. The FSH response to GnRH stimulation was the peak FSH level among the 4 timepoints (T0, T30, T60 and T90). The LH response to GnRH stimulation test was defined as peak LH ≤3 IU/L among the 4 timepoints T0, T30, T60 and T90). Baseline was defined as the last non-missing measurement taken prior to the first dose administered. The mITT population consisted of all treated participants with at least 1 baseline and Month 3 post-baseline assessment of the primary efficacy endpoint. Only data from the participants analyzed were reported. Here, 'n' = number of participants analyzed at specific time point.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and at Months 3, 6 and 12

End point values	All Participants			
Subject group type	Reporting group			
Number of subjects analysed	31			
Units: IU/L				
arithmetic mean (standard deviation)				
LH, Month 3 (n = 31)	-23.0969 (± 17.9856)			
LH, Month 6 (n = 29)	-24.3596 (± 17.9180)			
LH, Month 12 (n = 29)	-23.7221 (± 18.3669)			
FSH, Month 3 (n = 31)	-11.2757 (± 4.5026)			
FSH, Month 6 (n = 29)	-11.2536 (± 4.5267)			

FSH, Month 12 (n = 29)	-10.4701 (± 4.8424)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Prepubertal Levels of Sex Steroids

End point title	Percentage of Participants With Prepubertal Levels of Sex Steroids

End point description:

Prepubertal sex steroids assessment included estradiol in female participants and testosterone in male participants. Prepubertal sex steroids levels were defined as: estradiol ≤20 picogram (pg)/mL in female participants and testosterone ≤0.3 nanogram (ng)/mL in male participants. The mITT population consisted of all treated participants with at least 1 baseline and Month 3 post-baseline assessment of the primary efficacy endpoint. Only data from the participants analyzed were reported. Here, 'n' = number of participants analyzed at specific time point.

End point type	Secondary

End point timeframe:

At Months 3, 6, 9 and 12

End point values	All Participants			
Subject group type	Reporting group			
Number of subjects analysed	31			
Units: percentage of participants				
number (confidence interval 90%)				
Month 3 (n = 31)	100 (90.8 to 100)			
Month 6 (n = 30)	96.8 (85.6 to 99.8)			
Month 9 (n = 28)	90.3 (76.8 to 97.3)			
Month 12 (n = 29)	93.5 (81.1 to 98.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Estradiol Levels

End point title	Change From Baseline in Estradiol Levels

End point description:

Estradiol serum concentration was analyzed centrally. Change from baseline was defined as the value for estradiol levels at indicated timepoints minus the value at baseline. Baseline was defined as the last non-missing measurement taken prior to the first dose administered. The mITT population consisted of all treated participants with at least 1 baseline and Month 3 post-baseline assessment of the primary

efficacy endpoint. Only data for female participants were analyzed. Here, 'n' = number of participants analyzed at specific time point.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and at Months 3, 6 ,9 and 12

End point values	All Participants			
Subject group type	Reporting group			
Number of subjects analysed	28			
Units: pg/mL				
arithmetic mean (standard deviation)				
Month 3 (n = 28)	-8.0047 (± 15.6905)			
Month 6 (n = 27)	-8.3011 (± 15.9093)			
Month 9 (n = 25)	-7.7458 (± 15.8683)			
Month 12 (n = 26)	-8.6204 (± 16.1359)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Testosterone Levels

End point title	Change From Baseline in Testosterone Levels

End point description:

Testosterone serum concentration was analyzed centrally. Change from baseline was defined as the value for testosterone levels at indicated timepoints minus the value at baseline. Baseline was defined as the last non-missing measurement taken prior to the first dose administered. The mITT population consisted of all treated participants with at least 1 baseline and Month 3 post-baseline assessment of the primary efficacy endpoint. Only data for male participants were analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and at Months 3, 6 ,9 and 12

End point values	All Participants			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: ng/mL				
median (standard deviation)				
Month 3	-1.3650 (± 1.1734)			
Month 6	-1.3650 (± 1.1734)			

Month 9	-1.3650 (± 1.1734)			
Month 12	-1.3650 (± 1.1734)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Change From Baseline in Pubertal Stage

End point title	Percentage of Participants With Change From Baseline in Pubertal Stage

End point description:

Pubertal stage parameters were analyzed using Tanner method. Pubertal stage parameters included genital stage in male participants, breast stage in female participants and pubic hair stage in both sexes. The mITT population consisted of all treated participants with at least 1 baseline and Month 3 post-baseline assessment of the primary efficacy endpoint. Only data from the participants analyzed were reported. Here, 'n' = number of participants analyzed at specific time point. Breast development stage (BDS), Genital development stage (GDS), Pubic hair development (PHD), Month 6 (M6), Month 12 (M12).

End point type	Secondary

End point timeframe:

Baseline (Day 1) and at Months 6 and 12

End point values	All Participants			
Subject group type	Reporting group			
Number of subjects analysed	31			
Units: percentage of participants				
number (not applicable)				
BDS for female participants, M6, No change (n=10)	35.7			
BDS for female participants, M6, Reduced (n=16)	57.1			
BDS for female participants, M6, Increased (n=1)	3.6			
BDS for female participants, M6, Missing (n=1)	3.6			
GDS for male participants, M6, No change (n=1)	33.3			
GDS for male participants, M6, Reduced (n=2)	66.7			
GDS for male participants, M6, Increased (n=0)	0			
GDS for male participants, M6, Missing (n=0)	0			
PHD for female participants, M6, No change (n=27)	96.4			
PHD for female participants, M6, Reduced (n=0)	0			
PHD for female participants, M6, Increased (n=0)	0			
PHD for female participants, M6, Missing (n=1)	3.6			

PHD for male participants, M6, No change (n=2)	66.7			
PHD for male participants, M6, Reduced (n=1)	33.3			
PHD for male participants, M6, Increased (n=0)	0			
PHD for male participants, M6, Missing (n=0)	0			
BDS for female participants, M12, No change (n=11)	39.3			
BDS for female participants, M12, Reduced (n=14)	50.0			
BDS for female participants, M12, Increased (n=1)	3.6			
BDS for female participants, M12, Missing (n=2)	7.1			
GDS for male participants, M12, No change (n=0)	0			
GDS for male participants, M12, Reduced (n=3)	100			
GDS for male participants, M12, Increased (n=0)	0			
GDS for male participants, M12, Missing (n=0)	0			
PHD for female participants, M12, No change (n=23)	82.1			
PHD for female participants, M12, Reduced (n=0)	0			
PHD for female participants, M12, Increased (n=3)	10.7			
PHD for female participants, M12, Missing (n=2)	7.1			
PHD for male participants, M12, No change (n=2)	66.7			
PHD for male participants, M12, Reduced (n=1)	33.3			
PHD for male participants, M12, Increased (n=0)	0			
PHD for male participants, M12, Missing (n=0)	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Stabilized Pubertal Stage Compared to Baseline

End point title	Percentage of Participants With Stabilized Pubertal Stage Compared to Baseline

End point description:

Pubertal stage parameters were analyzed using Tanner method. Pubertal stage parameters included genital stage in male participants, breast stage in female participants and pubic hair stage in both sexes. The mITT population consisted of all treated participants with at least 1 baseline and Month 3 post-baseline assessment of the primary efficacy endpoint.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and at Months 6 and 12

End point values	All Participants			
Subject group type	Reporting group			
Number of subjects analysed	31			
Units: percentage of participants				
number (confidence interval 90%)				
BDS for female participants, Month 6	92.9 (79.2 to 98.7)			
GDS for male participants, Month 6	100 (36.8 to 100)			
PHD for female participants, Month 6	96.4 (84.1 to 99.8)			
PHD for male participants, Month 6	100 (36.8 to 100)			
BDS for female participants, Month 12	89.3 (74.6 to 97.0)			
GDS for male participants, Month 12	100 (36.8 to 100)			
PHD for female participants, Month 12	82.1 (66.1 to 92.7)			
PHD for male participants, Month 12	100 (36.8 to 100)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Auxological Parameter: Height

End point title	Change From Baseline in Auxological Parameter: Height

End point description:

Auxological parameter including height was analyzed. Change from baseline was defined as the value for each auxological parameter at indicated timepoints minus the value at baseline. Baseline was defined as the last non-missing measurement taken prior to the first dose administered. The mITT population consisted of all treated participants with at least 1 baseline and Month 3 post-baseline assessment of the primary efficacy endpoint. Only data from the participants analyzed were reported. Here, 'n' = number of participants analyzed at specific time point.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and at Months 3, 6, 9 and 12

End point values	All Participants			
Subject group type	Reporting group			
Number of subjects analysed	31			
Units: centimeter (cm)				
arithmetic mean (standard deviation)				
Month 3 (n = 31)	2.24 (± 0.62)			
Month 6 (n = 30)	3.55 (± 0.69)			

Month 9 (n = 30) Month 12 (n = 29)	4.63 (± 0.81) 6.54 (± 0.88)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Auxological Parameter: Weight

End point title	Change From Baseline in Auxological Parameter: Weight

End point description:

Auxological parameter including weight was analyzed. Change from baseline was defined as the value for each auxological parameter at indicated timepoints minus the value at baseline. Baseline was defined as the last non-missing measurement taken prior to the first dose administered. The mITT population consisted of all treated participants with at least 1 baseline and Month 3 post-baseline assessment of the primary efficacy endpoint. Only data from the participants analyzed were reported. Here, 'n' = number of participants analyzed at specific time point.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and at Months 3, 6, 9 and 12

End point values	All Participants			
Subject group type	Reporting group			
Number of subjects analysed	31			
Units: kilogram (kg)				
arithmetic mean (standard deviation)				
Month 3 (n = 31)	1.284 (± 1.319)			
Month 6 (n = 30)	2.533 (± 1.647)			
Month 9 (n = 30)	3.290 (± 1.899)			
Month 12 (n = 29)	4.818 (± 2.385)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Auxological Parameter: Growth Velocity

End point title	Change From Baseline in Auxological Parameter: Growth Velocity

End point description:

Auxological parameter including growth velocity was analyzed. Change from baseline was defined as the value for each auxological parameter at indicated timepoints minus the value at baseline. Baseline was defined as the last non-missing measurement taken prior to the first dose administered. The mITT population consisted of all treated participants with at least 1 baseline and Month 3 post-baseline

assessment of the primary efficacy endpoint. Only data from the participants analyzed were reported. Here, 'n' = number of participants analyzed at specific time point.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and at Months 3, 6, 9 and 12

End point values	All Participants			
Subject group type	Reporting group			
Number of subjects analysed	31			
Units: cm/year				
arithmetic mean (standard deviation)				
Month 3 (n = 31)	-0.895 (± 3.637)			
Month 6 (n = 30)	-3.769 (± 2.806)			
Month 9 (n = 30)	-4.804 (± 2.927)			
Month 12 (n = 29)	-2.052 (± 3.089)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Auxological Parameter: Body Mass Index (BMI)

End point title	Change From Baseline in Auxological Parameter: Body Mass Index (BMI)

End point description:

Auxological parameter including BMI was analyzed. Change from baseline was defined as the value for each auxological parameter at indicated timepoints minus the value at baseline. Baseline was defined as the last non-missing measurement taken prior to the first dose administered. The mITT population consisted of all treated participants with at least 1 baseline and Month 3 post-baseline assessment of the primary efficacy endpoint. Only data from the participants analyzed were reported. Here, 'n' = number of participants analyzed at specific time point.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and at Months 3, 6, 9 and 12

End point values	All Participants			
Subject group type	Reporting group			
Number of subjects analysed	31			
Units: kg/meter square				
arithmetic mean (standard deviation)				
Month 3 (n = 31)	0.142 (± 0.702)			
Month 6 (n = 30)	0.470 (± 0.791)			

Month 9 (n = 30) Month 12 (n = 29)	0.585 (± 0.849) 0.895 (± 1.081)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Bone Age (BA)

End point title	Change From Baseline in Bone Age (BA)

End point description:

BA was determined using X-rays of the hand and wrist. Change from baseline was defined as the value for BA at indicated timepoints minus the value at baseline. Baseline was defined as the last non-missing measurement taken prior to the first dose administered. The mITT population consisted of all treated participants with at least 1 baseline and Month 3 post-baseline assessment of the primary efficacy endpoint. Only data from the participants analyzed were reported. Here, 'n' = number of participants analyzed at specific time point.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and at Months 6 and 12

End point values	All Participants			
Subject group type	Reporting group			
Number of subjects analysed	30			
Units: years				
arithmetic mean (standard deviation)				
Month 6 (n = 30) Month 12 (n = 29)	0.233 (± 0.307) 0.586 (± 0.544)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline Difference Between BA and Chronological Age (CA)

End point title	Change From Baseline Difference Between BA and Chronological Age (CA)

End point description:

BA was determined using X-rays of the hand and wrist. Change from baseline was defined as the difference between BA and CA value at indicated timepoints minus the value at baseline. Baseline was defined as the last non-missing measurement taken prior to the first dose administered. The mITT population consisted of all treated participants with at least 1 baseline and Month 3 post-baseline assessment of the primary efficacy endpoint. Only data from the participants analyzed were reported. Here, 'n' = number of participants analyzed at specific time point.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and at Months 6 and 12

End point values	All Participants			
Subject group type	Reporting group			
Number of subjects analysed	30			
Units: years				
arithmetic mean (standard deviation)				
Month 6 (n = 30) Month 12 (n = 29)	-0.44 (± 0.53) -0.48 (± 0.57)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Uterine Length

End point title	Change From Baseline in Uterine Length

End point description:

Uterine length was determined by type B ultrasound. Change from baseline was defined as the value of uterine length at indicated timepoints minus the value at baseline. Baseline was defined as the last non-missing measurement taken prior to the first dose administered. The mITT population consisted of all treated participants with at least 1 baseline and Month 3 post-baseline assessment of the primary efficacy endpoint. Only data from the female participants analyzed were reported. Here, 'n' = number of participants analyzed at specific time point.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and at Months 6 and12

End point values	All Participants			
Subject group type	Reporting group			
Number of subjects analysed	28			
Units: cm				
arithmetic mean (standard deviation)				
Month 6 (n = 26) Month 12 (n = 24)	-0.4012 (± 0.4391) -0.3771 (± 0.6534)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline of Testicular Volume

End point title	Change From Baseline of Testicular Volume

End point description:

Testicular volume was determined by type B ultrasound. Change from baseline was defined as the value of testicular volume at indicated timepoints minus the value at baseline. Baseline was defined as the last non-missing measurement taken prior to the first dose administered. The mITT population consisted of all treated participants with at least 1 baseline and Month 3 post-baseline assessment of the primary efficacy endpoint. Only data from the male participants analyzed were reported. 9999 indicates that standard deviation could not be calculated as only 1 participant was analyzed. Here, 'n' = number of participants analyzed at specific time point.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and at Months 6 and 12

End point values	All Participants			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: mL				
arithmetic mean (standard deviation)				
Left, Month 6 (n = 2)	-2.4022 (± 1.7109)			
Right, Month 6 (n = 3)	-4.7334 (± 4.4222)			
Left, Month 12 (n = 1)	-2.8840 (± 9999)			
Right, Month 12 (n = 2)	-6.7975 (± 6.3958)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Treatment-emergent adverse events were reported from the first dose of study treatment (Day 1) up to end of extension phase, a maximum of approximately 368 days.

Adverse event reporting additional description:

Safety population consisted of all participants who received at least 1 dose of study medication and had at least 1 post-baseline safety assessment.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.0

Reporting groups

Reporting group title	All Participants

Reporting group description:

Participants received triptorelin pamoate 15 mg IM injection on Day 1 visit and Month 3 visit (Day 91) during the main study phase. Participants had an option to continue with the triptorelin pamoate in extension phase of the study. As per Investigator decision, eligible participants continued to receive IM injections of triptorelin pamoate on Month 6 (Day 182) and Month 9 (Day 271) during the extension phase.

Serious adverse events	All Participants		
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 32 (6.25%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Infections and infestations			
Pneumonia			
subjects affected / exposed	2 / 32 (6.25%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	All Participants		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	27 / 32 (84.38%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Pyogenic granuloma			

subjects affected / exposed	1 / 32 (3.13%)		
occurrences (all)	1		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	2 / 32 (6.25%)		
occurrences (all)	2		
Chest discomfort			
subjects affected / exposed	1 / 32 (3.13%)		
occurrences (all)	2		
Condition aggravated			
subjects affected / exposed	1 / 32 (3.13%)		
occurrences (all)	1		
Reproductive system and breast disorders			
Vaginal haemorrhage			
subjects affected / exposed	1 / 32 (3.13%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	3 / 32 (9.38%)		
occurrences (all)	3		
Rhinorrhoea			
subjects affected / exposed	3 / 32 (9.38%)		
occurrences (all)	4		
Rhinitis allergic			
subjects affected / exposed	2 / 32 (6.25%)		
occurrences (all)	2		
Nasal congestion			
subjects affected / exposed	1 / 32 (3.13%)		
occurrences (all)	1		
Nasal obstruction			
subjects affected / exposed	1 / 32 (3.13%)		
occurrences (all)	2		
Psychiatric disorders			
Tic			

subjects affected / exposed occurrences (all)	1 / 32 (3.13%) 1		
Investigations Blood creatinine increased subjects affected / exposed occurrences (all) Red blood cells urine subjects affected / exposed occurrences (all) Red blood cells urine positive subjects affected / exposed occurrences (all)	 1 / 32 (3.13%) 1 1 / 32 (3.13%) 1 1 / 32 (3.13%) 1		
Injury, poisoning and procedural complications Foot fracture subjects affected / exposed occurrences (all)	 1 / 32 (3.13%) 1		
Congenital, familial and genetic disorders Dermoid cyst subjects affected / exposed occurrences (all)	 1 / 32 (3.13%) 1		
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all)	 1 / 32 (3.13%) 1		
Eye disorders Myopia subjects affected / exposed occurrences (all)	 1 / 32 (3.13%) 1		
Gastrointestinal disorders Abdominal discomfort subjects affected / exposed occurrences (all) Abdominal pain upper subjects affected / exposed occurrences (all) Abdominal pain	 1 / 32 (3.13%) 1 1 / 32 (3.13%) 1		

subjects affected / exposed occurrences (all)	1 / 32 (3.13%) 1		
Dental caries subjects affected / exposed occurrences (all)	1 / 32 (3.13%) 1		
Dyspepsia subjects affected / exposed occurrences (all)	1 / 32 (3.13%) 1		
Gastritis subjects affected / exposed occurrences (all)	1 / 32 (3.13%) 1		
Retained deciduous tooth subjects affected / exposed occurrences (all)	1 / 32 (3.13%) 1		
Vomiting subjects affected / exposed occurrences (all)	1 / 32 (3.13%) 2		
Skin and subcutaneous tissue disorders			
Rash subjects affected / exposed occurrences (all)	2 / 32 (6.25%) 2		
Urticaria subjects affected / exposed occurrences (all)	2 / 32 (6.25%) 2		
Dermatitis subjects affected / exposed occurrences (all)	1 / 32 (3.13%) 1		
Dermatitis allergic subjects affected / exposed occurrences (all)	1 / 32 (3.13%) 1		
Renal and urinary disorders			
Proteinuria subjects affected / exposed occurrences (all)	1 / 32 (3.13%) 1		
Infections and infestations			

Upper respiratory tract infection			
subjects affected / exposed	10 / 32 (31.25%)		
occurrences (all)	15		
Bronchitis			
subjects affected / exposed	3 / 32 (9.38%)		
occurrences (all)	4		
Tonsillitis			
subjects affected / exposed	2 / 32 (6.25%)		
occurrences (all)	2		
Gastroenteritis			
subjects affected / exposed	1 / 32 (3.13%)		
occurrences (all)	1		
Gingivitis			
subjects affected / exposed	1 / 32 (3.13%)		
occurrences (all)	1		
Hordeolum			
subjects affected / exposed	1 / 32 (3.13%)		
occurrences (all)	1		
Parotitis			
subjects affected / exposed	1 / 32 (3.13%)		
occurrences (all)	1		
Pneumonia			
subjects affected / exposed	1 / 32 (3.13%)		
occurrences (all)	1		
Respiratory tract infection			
subjects affected / exposed	1 / 32 (3.13%)		
occurrences (all)	1		
Rhinitis			
subjects affected / exposed	1 / 32 (3.13%)		
occurrences (all)	1		
Metabolism and nutrition disorders			
Abnormal weight gain			
subjects affected / exposed	7 / 32 (21.88%)		
occurrences (all)	7		
Overweight			

subjects affected / exposed	3 / 32 (9.38%)		
occurrences (all)	3		
Vitamin D deficiency			
subjects affected / exposed	3 / 32 (9.38%)		
occurrences (all)	3		
Obesity			
subjects affected / exposed	2 / 32 (6.25%)		
occurrences (all)	2		
Hypovitaminosis			
subjects affected / exposed	1 / 32 (3.13%)		
occurrences (all)	1		
Impaired fasting glucose			
subjects affected / exposed	1 / 32 (3.13%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
28 October 2020	Introduction of extension study available for participants. Clarified how safety profile were analyzed. Extra assessments were removed since the population was at very low risk of pregnancy. For participant centricity to reduced blood draw burden and removed the requirement for children to fast. Measurement of uterine length as measurement of gonad development was normal clinical practice. For participant centricity, increasing the larger window was maximize flexibility for children at school. To clarify timing of this assessment.
16 March 2021	Added information regarding the extension phase and provide other minor changes to improved clarity regarding the main and extension phases of the study. Amended to provided distinction between the main study phase and the extension study phase. Added the requirement of reporting serious adverse events with the electronic data collection tool. The blood chemistry was to be done at site local lab, it may be different practice in different sites.
09 July 2021	Additional ±5 minutes time window for blood sample collection time point for GnRH stimulation test was added. Added temporary discontinuation due to COVID-19. Added the definition of lost follow-up and the action to be taken. Added requirement to record information on subjects who failed screening. Added medication or procedure that are not permitted. Added operational requirements for on-site administration.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported