Clinical trial results:
Phase III, multicentre, non comparative, open and single stage study to assess the efficacy and safety of pamoate of triptorelin 11.25 mg in children with precocious puberty.

Summary

EudraCT number	2005-005644-11
Trial protocol	FR
Global end of trial date	27 October 2010

Results information

Result version number	v2 (current)
This version publication date	05 September 2024
First version publication date	12 August 2015
Version creation reason	• Correction of full data set Data validation

Trial information

Trial identification

Sponsor protocol code	2-54-52014-143

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00564850
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Ipsen
Sponsor organisation address	65 Quai Georges Gorse, Boulogne-Billancourt Cedex, France, 92650
Public contact	Medical Director, Endocrinology, Ipsen, clinical.trials@ipsen.com
Scientific contact	Medical Director, Endocrinology, Ipsen, 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	24 November 2011
Is this the analysis of the primary completion data?	Yes
Primary completion date	27 October 2010
Global end of trial reached?	Yes
Global end of trial date	27 October 2010
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the efficacy of Triptorelin 11.25 mg pamoate with respect to the proportion of children with suppressed Luteinizing Hormone (LH) response (LH < or =3 UI/l) to Gonadotropin Releasing Hormone (GnRH) test performed 3 months (M3) after injection with Triptorelin 11.25 mg.

Protection of trial subjects:

This clinical study was designed and implemented and reported in accordance with the International Conference on Harmonisation (ICH) Harmonized Tripartite Guidelines for Good Clinical Practice (GCP), with applicable local regulations (including European Directive 2001/20/EC, US Code of Federal Regulations Title 21, and Japanese Ministry of Health, Labor, and Welfare), and with the ethical principles laid down in the Declaration of Helsinki.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	03 October 2007
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	France: 37
Worldwide total number of subjects	37
EEA total number of subjects	37

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)	37
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:

62 participants were screened, of which 37 met the study's entry criteria and received at least one dose of investigational medicinal product. 25 participants failed screening. Participants were recruited from October 2007 at 18 Hospital clinics across France.

Pre-assignment

Screening details: -

Pre-assignment period milestones

Number of subjects started	62[1]
Number of subjects completed	37

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Physician decision: 2
Reason: Number of subjects	Three Criteria Failed: 3
Reason: Number of subjects	Two Criteria Failed: 7
Reason: Number of subjects	One Criterion Failed: 13

Notes:

[1] - The number of subjects reported to have started the pre-assignment period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: World-wide subject number (N=62) includes screen failure subjects and pre-assignment period does not include screen failure subjects.

Period 1

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

Arms

Arm title	Triptorelin pamoate 11.25 mg

Arm description:

Triptorelin pamoate 11.25 mg two intramuscular injections at baseline and month 3

Arm type	Experimental
Investigational medicinal product name	Decapeptyl PR
Investigational medicinal product code	
Other name	triptorelin pamoate
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

11.25 mg two intramuscular injections at baseline and month 3

Number of subjects in period 1	Triptorelin pamoate 11.25 mg
Started	37
Completed	35
Not completed	2
Protocol deviation	2

Baseline characteristics

Reporting groups	
Reporting group title	Treatment phase

Reporting group description: -

Reporting group values	Treatment phase	Total	
Number of subjects	37	37	
Age categorical Units: Subjects			
Children (2-11 years)	37	37	
Age continuous Units: years			
arithmetic mean	8.2		
standard deviation	± 1.1	-	
Gender categorical Units: Subjects			
Female	36	36	
Male	1	1	
Weight Units: kg			
arithmetic mean	32.76		
standard deviation	± 7.36	-	

End points

End points reporting groups

Reporting group title	Triptorelin pamoate 11.25 mg
Reporting group description:	
Triptorelin pamoate 11.25 mg two intramuscular injections at baseline and month 3	

Primary: Number of Participants With a GnRH-stimulated LH Level ≤3 IU/L

End point title	Number of Participants With a GnRH-stimulated LH Level ≤3 IU/L[1]
End point description:	
Analyses performed on: Intention to Treat (ITT): All patients having received ≥1 injection. Any subject with missing data is considered a non-responder. Modified ITT (mITT): All ITT patients with ≥ Month 3 post-baseline assessment of primary efficacy criterion. Per Protocol (PP): All mITT patients without major protocol deviations.	
End point type	Primary
End point timeframe:	
3 months after the first injection of triptorelin pamoate 11.25 mg	

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 for the primary endpoint was provided with 95% confidence interval to give an indication of the magnitude for the population mean.

End point values	Triptorelin pamoate 11.25 mg			
Subject group type	Reporting group			
Number of subjects analysed	37			
Units: Participants				
Yes [ITT (n=37)]	31			
No [ITT (n=37)]	6			
Yes [mITT (n=34)]	31			
No [mITT (n=34)]	3			
Yes [PP (n=32)]	30			
No [PP (n=32)]	2			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants Whose Intravenous (i.v.) GnRH-stimulated LH Response Was ≤3 IU/L

End point title	Number of Participants Whose Intravenous (i.v.) GnRH-

	stimulated LH Response Was ≤3 IU/L

End point description:

Analysis was performed on Intention to Treat population (ITT) defined as all participants having received at least one injection of 11.25 mg triptorelin pamoate. "n" indicates the number of patients who had an assessment at the visit

End point type	Secondary

End point timeframe:

Month 6

End point values	Triptorelin pamoate 11.25 mg			
Subject group type	Reporting group			
Number of subjects analysed	37			
Units: Participants				
Yes (n=37)	32			
No (n=37)	5			

Statistical analyses

No statistical analyses for this end point

Secondary: Follicle Stimulating Hormone (FSH) Level Following GnRH Test

End point title	Follicle Stimulating Hormone (FSH) Level Following GnRH Test

End point description:

Analysis was performed on the ITT population. 3 participants and 2 participants had missing data at month 3 and month 6 respectively.

End point type	Secondary

End point timeframe:

Screening, month 3 and 6

End point values	Triptorelin pamoate 11.25 mg			
Subject group type	Reporting group			
Number of subjects analysed	37			
Units: IU/L				
arithmetic mean (standard deviation)				
Screening (n=37)	11.84 (± 3.23)			
Month 3 (n=34)	2.26 (± 2.5)			
Month 6 (n=35)	2.34 (± 1.65)			

Statistical analyses

No statistical analyses for this end point

Secondary: Basal FSH Level

End point title	Basal FSH Level

End point description:

Analysis was performed on the ITT population. 2 participants had missing data at month 1, 3, 4 and 6. 1 and 3 participants had missing data at month 2 and month 5 respectively.

End point type	Secondary

End point timeframe:

Month 0, 1, 2, 3, 4, 5, and 6

End point values	Triptorelin pamoate 11.25 mg			
Subject group type	Reporting group			
Number of subjects analysed	37			
Units: IU/L				
arithmetic mean (standard deviation)				
Month 0 (screening, n=37)	4.13 (± 2.65)			
Month 1 (n=35)	0.67 (± 0.53)			
Month 2 (n=36)	1.07 (± 0.82)			
Month 3 (n=35)	1.11 (± 0.73)			
Month 4 (n=35)	0.78 (± 0.39)			
Month 5 (n=34)	1.41 (± 2.09)			
Month 6 (n=35)	1.36 (± 1.24)			

Statistical analyses

No statistical analyses for this end point

Secondary: Basal LH Level

End point title	Basal LH Level

End point description:

Analysis was performed on ITT population. 2 participants had missing data at month 1, 3, 4 and 6. 1 and 3 participants had missing data at month 2 and month 5 respectively.

End point type	Secondary

End point timeframe:

Month 0, 1, 2, 3, 4, 5 and 6

End point values	Triptorelin pamoate 11.25 mg			
Subject group type	Reporting group			
Number of subjects analysed	37			
Units: IU/L				
arithmetic mean (standard deviation)				
Month 0 (screening, n=37)	1.49 (± 1.78)			
Month 1 (n=35)	0.42 (± 0.22)			
Month 2 (n=36)	0.42 (± 0.31)			
Month 3 (n=35	0.43 (± 0.27)			
Month 4 (n=35)	0.43 (± 0.23)			
Month 5 (n=34)	0.48 (± 0.7)			
Month 6 (n=35)	0.44 (± 0.42)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Girls With Oestradiol Levels ≤ 20 pg/ml

End point title	Number of Girls With Oestradiol Levels ≤ 20 pg/ml

End point description:

Analysis was performed on female patients in the ITT population. 2 participants had missing data at month 1, 3, 4 and 6. 1 participant and 3 participants had missing data at month 2 and 5 respectively.

End point type	Secondary

End point timeframe:

Month 0, 1, 2, 3, 4, 5 and 6

End point values	Triptorelin pamoate 11.25 mg			
Subject group type	Reporting group			
Number of subjects analysed	36			
Units: Participants				
Yes - month 0 (n=36)	22			
No - month 0 (n=36)	14			
Yes - month 1 (n=34)	34			
No - month 1 (n=34)	0			
Yes - month 2 (n=35)	34			
No - month 2 (n=35)	1			
Yes - month 3 (n=34)	33			
No - month 3 (n=34)	1			
Yes - month 4 (n=34)	34			
No - month 4 (n=34)	0			
Yes - month 5 (n=33)	33			
No - month 5 (n=33)	0			
Yes - month 6 (n=34)	33			
No - month 6 (n=34)	1			

Statistical analyses

No statistical analyses for this end point

Secondary: Testosterone Level

End point title	Testosterone Level

End point description:

Testosterone level from the male patient in the ITT population.

End point type	Secondary

End point timeframe:

Month 0, 3 and 6

End point values	Triptorelin pamoate 11.25 mg			
Subject group type	Reporting group			
Number of subjects analysed	1			
Units: ng/ml				
number (not applicable)				
Month 0 (screening)	2			
Month 3	0.12			
Month 6	0.16			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Girls With Inhibin B Levels < 6 pg/ml

End point title	Number of Girls With Inhibin B Levels < 6 pg/ml

End point description:

Analysis was performed on female patients in the ITT population. 2 participants had missing data at month 3 and month 6.

End point type	Secondary

End point timeframe:

Month 0, 3 and 6

End point values	Triptorelin pamoate 11.25 mg			
Subject group type	Reporting group			
Number of subjects analysed	36			
Units: Participants				
Yes - month 0 (screening, n=36)	18			
No - month 0 (screening, n=36)	18			
Yes - month 3 (n=34)	33			
No - month 3 (n=34)	1			
Yes - month 6 (n=34)	32			
No - month 6 (n=34)	2			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Screening in Pubertal Stage (Tanner Method) at Month 6

End point title	Change From Screening in Pubertal Stage (Tanner Method) at Month 6

End point description:

Pubertal stage (graded from 1 to 5 for penis and breast development, graded from 1 to 6 for pubic hair development) according to the Tanner method was collected. A low stage (i.e. 1) corresponds to a pre-pubertal stage and a high stage (i.e. 5 or 6) to an adult stage. Any increase of grade was defined as 'increased' and no change in grade or a reduced grade was defined as 'stabilised or reduced'.

Analysis was performed on the ITT population. 2 participants had missing data for pubic hair stage and breast stage.

End point type	Secondary

End point timeframe:

Between screening and month 6

End point values	Triptorelin pamoate 11.25 mg			
Subject group type	Reporting group			
Number of subjects analysed	37			
Units: Participants				
Pubic hair stage stabilised or reduced (n=35)	30			
Pubic hair stage increased (n=35)	5			
Breast stage stabilised or reduced (n=34)	32			
Breast stage increased (n=34)	2			
Penis stage stabilised or reduced (n=1)	1			
Penis stage increased (n=1)	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Height Standard Deviation Score (SDS)

End point title	Height Standard Deviation Score (SDS)

End point description:

Standard deviation (SD) is a standard term used in growth studies and represents Standard Deviations calculated as the patient value minus the mean divided by the standard deviation. Standard Deviation Scores vary depending on the age and sex of the child.

Analysis was performed on the ITT population. 2 participants had missing data at month 6.

End point type	Secondary

End point timeframe:

Month 0, 3 and 6

End point values	Triptorelin pamoate 11.25 mg			
Subject group type	Reporting group			
Number of subjects analysed	37			
Units: SD score				
arithmetic mean (standard deviation)				
Month 0 (baseline, n=37)	1.25 (± 1.14)			
Month 3 (n=37)	1.32 (± 1.16)			
Month 6 (n=35)	1.32 (± 1.16)			

Statistical analyses

No statistical analyses for this end point

Secondary: Body Mass Index (BMI) SDS

End point title	Body Mass Index (BMI) SDS

End point description:

Analysis was performed on the ITT population. 1 and 2 participants had missing data at month 0 and month 6 respectively.

End point type	Secondary

End point timeframe:

Month 0, 3 and 6

End point values	Triptorelin pamoate 11.25 mg			
Subject group type	Reporting group			
Number of subjects analysed	37			
Units: SD score				
arithmetic mean (standard deviation)				
Month 0 (baseline, n=36)	0.58 (± 0.85)			
Month 3 (n=37)	0.64 (± 0.89)			
Month 6 (n=35)	0.6 (± 0.78)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Growth Velocity (GV) SDS at Month 6

End point title	Change From Baseline in Growth Velocity (GV) SDS at Month 6

End point description:

Change from baseline of GV was calculated as: GV at month 6 - GV at baseline. GV SDS was calculated using SAS algorithm.

Growth velocity during the study was calculated using the two height measures as: GV = (Height at baseline - Height at screening)*365/delay between two height measures.

Analysis was performed on the ITT population. If GV at screening was missing, the value was derived from data recorded between 5 to 19 months ago otherwise GV at screening was considered missing. 9 participants had missing data.

End point type	Secondary

End point timeframe:

Baseline and month 6

End point values	Triptorelin pamoate 11.25 mg			
Subject group type	Reporting group			
Number of subjects analysed	37			
Units: SD score				
arithmetic mean (standard deviation)				
Change From Baseline in GV SDS at Month 6	-1.95 (± 2.07)			

Statistical analyses

No statistical analyses for this end point

Secondary: Difference Between Bone Age and Chronological Age

End point title	Difference Between Bone Age and Chronological Age

End point description:

Bone age was defined according to Greulich and Pyle method. Chronological age was calculated using the date of birth.

Analysis was performed on the ITT population. 33 participants were assessed. 4 participants had missing data at month 6.

End point type	Secondary

End point timeframe:

Month 0 and 6

End point values	Triptorelin pamoate 11.25 mg			
Subject group type	Reporting group			
Number of subjects analysed	37			
Units: Years				
arithmetic mean (standard deviation)				
Month 0 (screening, n=37)	2.09 (± 0.91)			
Month 6 (n=33)	2.02 (± 0.88)			

Statistical analyses

No statistical analyses for this end point

Secondary: Uterine Length

End point title	Uterine Length

End point description:

Analysis was performed on female patients in the ITT population. 2 participants had missing data at month 3 and 6.

End point type	Secondary

End point timeframe:

Month 0, 3 and 6

End point values	Triptorelin pamoate 11.25 mg			
Subject group type	Reporting group			
Number of subjects analysed	36			
Units: mm				
arithmetic mean (standard deviation)				
Month 0 (screening, n=35)	37.6 (± 10.6)			
Month 3 (n=34)	37.4 (± 8.2)			
Month 6 (n=34)	36.8 (± 6.9)			

Statistical analyses

No statistical analyses for this end point

Secondary: Triptorelin Plasma Levels

End point title	Triptorelin Plasma Levels

End point description:

Analysis was performed on the Pharmacokinetics (PK) Valid population defined as all participants who received at least one injection of 11.25 mg triptorelin pamoate and had at least one PK assessment. 2 participants had data missing at month 1,3 and 6. 1, 3 and 4 participants had data missing at month 2, 4 and 5 respectively.

End point type	Secondary

End point timeframe:

Month 1, 2, 3, 4, 5 and 6

End point values	Triptorelin pamoate 11.25 mg			
Subject group type	Reporting group			
Number of subjects analysed	37			
Units: ng/mL				
arithmetic mean (standard deviation)				
Month 1 (n=35)	0.187 (± 0.115)			
Month 2 (n=36)	0.048 (± 0.023)			
Month 3 (n=35)	0.034 (± 0.018)			
Month 4 (n=34)	0.201 (± 0.120)			
Month 5 (n=33)	0.045 (± 0.023)			
Month 6 (n=35)	0.03 (± 0.017)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to month 6

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	13.1

Reporting groups

Reporting group title	Triptorelin pamoate 11.25 mg

Reporting group description: -

Serious adverse events	Triptorelin pamoate 11.25 mg		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 37 (2.70%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Injury, poisoning and procedural complications			
Foot fracture			
subjects affected / exposed	1 / 37 (2.70%)		
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	Triptorelin pamoate 11.25 mg		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	8 / 37 (21.62%)		
Vascular disorders			
Hot Flush			
subjects affected / exposed	2 / 37 (5.41%)		
occurrences (all)	2		
General disorders and administration site conditions			
Injection site pain			

subjects affected / exposed occurrences (all)	2 / 37 (5.41%) 2		
Gastrointestinal disorders Abdominal pain subjects affected / exposed occurrences (all)	 4 / 37 (10.81%) 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