Clinical trial results:
A phase III single arm study to evaluate the efficacy, safety and local tolerability of a subcutaneous 3month formulation of triptorelin pamoate (11.25 mg) in patients with locally advanced or metastatic prostate cancer.

Summary

EudraCT number	2012-001279-35
Trial protocol	LV PL BG
Global end of trial date	09 October 2013

Results information

Result version number	v2 (current)
This version publication date	27 February 2016
First version publication date	01 August 2015
Version creation reason	• Correction of full data set Review and correction.

Trial information

Trial identification

Sponsor protocol code	8-55-52014-200

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
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, Oncology, Ipsen, clinical.trials@ipsen.com
Scientific contact	Medical Director, Oncology, 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?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	03 April 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	09 October 2013
Global end of trial reached?	Yes
Global end of trial date	09 October 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To confirm the efficacy of triptorelin pamoate (11.25 mg) prolonged release (PR) formulation by inducing castration (defined as serum testosterone level of <50 ng/dL or <1.735 nmol/L) at Day 29 and maintaining castration at Day 183 (after receiving two subcutaneous (s.c.) administrations of triptorelin pamoate, 3 months apart).

Protection of trial subjects:

The study was conducted under the provisions of the Declaration of Helsinki, and in accordance with the International Conference on Harmonisation (ICH) Consolidated Guideline on Good Clinical Practice (GCP). The local tolerance of the s.c. route of administration, was evaluated in animals before the start of the clinical trial. This local tolerance study, conducted in rabbits comparing s.c. and i.m. single dose of triptorelin pamoate 11.25 mg 3 month formulation, demonstrated that the local tolerance of the compound was slightly better when administered subcutaneously.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	25 October 2012
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	Poland: 19
Country: Number of subjects enrolled	Bulgaria: 40
Country: Number of subjects enrolled	France: 6
Country: Number of subjects enrolled	Latvia: 21
Country: Number of subjects enrolled	Romania: 40
Worldwide total number of subjects	126
EEA total number of subjects	126

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	0

months)	
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	25
From 65 to 84 years	99
85 years and over	2

Subject disposition

Recruitment

Recruitment details:

A total of 139 subjects were screened. 13 subjects were screen failures. 126 subjects were randomized. 126 subjects were treated and 9 subjects withdrawn. 117 completed the study.

Pre-assignment

Screening details: -

Pre-assignment period milestones

Number of subjects started	139[1]
Number of subjects completed	126

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Screen failure: 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: Pre-assignment period includes screen failure subjects

Period 1

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

Arms

Arm title	Triptorelin Pamoate

Arm description:

Triptorelin Pamoate corresponding to 11.25 mg of triptorelin administered subcutaneously on Day 1 and 92

Arm type	Experimental
Investigational medicinal product name	Triptorelin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Each subject received two successive s.c. administrations of triptorelin pamoate corresponding to 11.25 mg triptorelin on Day 1 and Day 92

Number of subjects in period 1	Triptorelin Pamoate
Started	126
Completed	117
Not completed	9
Adverse event, serious fatal	1
Consent withdrawn by subject	2
Unspecified	1

Lost to follow-up	1
Lack of efficacy	3
Protocol deviation	1

Baseline characteristics

Reporting groups	
Reporting group title	Triptorelin pamoate

Reporting group description: -

Reporting group values	Triptorelin pamoate	Total	
Number of subjects	126	126	
Age categorical Units: Subjects			
Age continuous Units: years arithmetic mean standard deviation	 70.4 ± 7.3	 -	
Gender categorical Units: Subjects			
Female Male	0 126	0 126	
Race Units: Subjects			
Caucasian / White Missing	120 6	120 6	
Height Units: cm arithmetic mean standard deviation	 172.2 ± 6.7	 -	
Weight Units: kg arithmetic mean standard deviation	 80.6 ± 12.8	 -	
BMI Units: kg/m²			
arithmetic mean standard deviation	27.16 ± 3.96	 -	
Prostate Specific Antigen (PSA) Units: ng/mL arithmetic mean standard deviation	 133.53 ± 385.6	 -	

End points

End points reporting groups

Reporting group title	Triptorelin Pamoate

Reporting group description:

Triptorelin Pamoate corresponding to 11.25 mg of triptorelin administered subcutaneously on Day 1 and 92

Primary: Percentage of Subjects Demonstrating Castration at Day 29 and Maintaining Castration at Day 183

End point title	Percentage of Subjects Demonstrating Castration at Day 29 and Maintaining Castration at Day 183[1]

End point description:

Percentage of subjects castrated (i.e. with serum testosterone <50 ng/dL or 1.735 nmol/L, using the LC-MS/MS method
and missing data imputed by immunoassay method (at time points when LC-MS/MS data was planned to be available
only) and the proportion with castration maintained at Day 183 (after receiving 2 S.C. administrations of triptorelin
pamoate, three months apart); they were calculated along with their respective 95% confidence intervals (CI) using
exact methods on the ITT population at Day 29 and on the initially castrated (IC) population at Day 183

N = Number of subjects attending the visit; n = Number of subjects castrated (serum testosterone level of <50 ng/dL at the visit)

End point type	Primary

End point timeframe:

At Day 29 and 183

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 statistical analyses reported for this endpoint

End point values	Triptorelin Pamoate			
Subject group type	Reporting group			
Number of subjects analysed	126			
Units: Percentage of subjects				
number (confidence interval 95%)				
Day 29 (n/N=123/126)	97.6 (93.2 to 99.5)			
Day 183 (n/N=115/119)	96.6 (91.6 to 99.1)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Demonstrating Castration Before Administration of the Second Dose

End point title	Percentage of Subjects Demonstrating Castration Before

	Administration of the Second Dose

End point description:

Percentage of subjects demonstrating castration at Day 92 (before administration of the second dose) were also
assessed using the LC-MS/MS method and missing data imputed by immunoassay method (at time points when
LC-MS/MS data was planned to be available only) and summarised using descriptive statistics on the ITT and IC
populations.

Initially Castrated (IC1) population: All treated subjects with testosterone levels <50 ng/dL at Day 29 or at Day 36, assessed with the LC-MS/MS method and missing data imputed by immunoassay method.

End point type	Secondary

End point timeframe:

At Day 92

End point values	Triptorelin Pamoate			
Subject group type	Reporting group			
Number of subjects analysed	120			
Units: Percentage of subjects				
number (confidence interval 95%)	99.2 (95.4 to 100)			

Statistical analyses

No statistical analyses for this end point

Secondary: Probability of testosterone <50 ng/dL

End point title	Probability of testosterone <50 ng/dL

End point description:

Intention-to-treat (ITT) population: All treated subjects

Probability of testosterone <50 ng/dL from Day 29 to Day 183 was assessed as a secondary endpoint using the time to
event from first administration date to first observed (and subsequently confirmed if assessment not performed at end
of study or early withdrawal visits) serum testosterone level ≥50 ng/dL or ≥1.735 nmol/L at or after Day 29, assessed
using the LC-MS/MS Method and Missing Data imputed by immunoassay method Kaplan-Meier Analysis.

LC-MS/MS: Liquid Chromatography–Tandem Mass Spectrometry

End point type	Secondary

End point timeframe:

Day 29 through Day 183

End point values	Triptorelin Pamoate			
Subject group type	Reporting group			
Number of subjects analysed	126			
Units: Proportion of subjects				
number (confidence interval 95%)	0.96 (0.92 to 0.99)			

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of subjects demonstrating castration with Testosterone Level <50 ng/dL at Day 95

End point title	Proportion of subjects demonstrating castration with Testosterone Level <50 ng/dL at Day 95

End point description:

IC1 population.

Proportion of subjects demonstrating castration at Day 95 (3-4 days after administration of the second dose to assess the suppression of acute-on-chronic effect following the second administration) were also assessed using the LC-MS/MS method and missing data imputed by immunoassay method (at time points when LC-MS/MS data was planned to be available only), then using the LC-MS/MS method only and the immunoassay method only and summarised using descriptive statistics on the ITT and IC populations.

End point type	Secondary

End point timeframe:

Day 95

End point values	Triptorelin Pamoate			
Subject group type	Reporting group			
Number of subjects analysed	119			
Units: Percentage of subjects				
number (confidence interval 95%)	98.3 (94.1 to 99.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: Time to achieve castration (Tcast)

End point title	Time to achieve castration (Tcast)

End point description:

ITT population

Time to castration (Tcast) from first administration date until first observed serum testosterone level <50 ng/dL or <1.735 nmol/L evaluated using the immunoassay method only (i.e. defined as the number of days between the injection time at Day 1 and castration achievement)

End point type	Secondary

End point timeframe:

Up to Day 36

End point values	Triptorelin Pamoate			
Subject group type	Reporting group			
Number of subjects analysed	126			
Units: Day				
median (confidence interval 95%)	22 (22 to 23)			

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma Triptorelin levels (Cmin)

End point title	Plasma Triptorelin levels (Cmin)

End point description:

ITT population.

No samples were collected from 4 subjects at Day 92 and 9 subjects at Day 183.

Minimal triptorelin plasma concentration at the end of each dosage interval just before the next dose injection (Cmin) for
Days 92 and 183 were assessed.

End point type	Secondary

End point timeframe:

At Day 92 and 183

End point values	Triptorelin Pamoate			
Subject group type	Reporting group			
Number of subjects analysed	122			
Units: ng/mL				
arithmetic mean (standard deviation)				
Day 92 Day 183 (N=117)	0.062 (± 0.031) 0.049 (± 0.027)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage Change in Prostate Specific Antigen (PSA) Levels From Baseline in All Subjects

End point title	Percentage Change in Prostate Specific Antigen (PSA) Levels From Baseline in All Subjects

End point description:

ITT population at End of Study (Day 183). One subject had no data.

Serum PSA level was presented throughout the study using descriptive statistics displaying raw values, change from
Baseline and percentage change from Baseline at each visit in all subjects from the ITT population only. Additionally,
the PSA level was described in subjects with elevated PSA levels (i.e. >4 ng/mL) at study entry, and the proportion of
subjects with normal PSA levels (i.e. [0-4] ng/mL) at Day 183 compared to Baseline was presented.

End point type	Secondary

End point timeframe:

From Day 1 (Baseline) to Day 183 (End of study)

End point values	Triptorelin Pamoate			
Subject group type	Reporting group			
Number of subjects analysed	116			
Units: Percentage Change				
arithmetic mean (standard deviation)	-85.503 (± 42.41)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Normal and Abnormal PSA Levels at Day 183 (End of Study Visit)

End point title	Percentage of Subjects With Normal and Abnormal PSA Levels at Day 183 (End of Study Visit)

End point description:

0-4 ng/mL (normal PSA value)

>4 ng/mL (abnormal PSA levels)

Subjects completed Day 183 visit (End of Study)

End point type	Secondary

End point timeframe:

At Day 183

End point values	Triptorelin Pamoate			
Subject group type	Reporting group			
Number of subjects analysed	117			
Units: Percentage of subjects				
number (not applicable)				
End of Study (0-4 ng/mL)	84.6			
End of Study (>4 ng/mL)	15.4			

Statistical analyses

No statistical analyses for this end point

Secondary: Clinically Apparent Tumor Progression

End point title	Clinically Apparent Tumor Progression

End point description:

ITT population.

Tumour progression was recorded according to the Investigator’s clinical judgement, considering the PSA levels and
any other indications of disease; the clinical confirmation might be supplemented by radiological or other investigations
or scans if required. The lack of clinically apparent tumour progression was assessed at Day 92 (prior to administration
of the second dose) and Day 183 (end of study visit).

End point type	Secondary

End point timeframe:

Day 92 and 183

End point values	Triptorelin Pamoate			
Subject group type	Reporting group			
Number of subjects analysed	126			
Units: Number of subjects				
number (not applicable)				
Day 92: Non Progressive Disease	122			
Day 92: Progressive Disease	0			
Day 183: Non Progressive Disease	114			
Day 183: Progressive Disease	3			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Adverse Events

End point title	Percentage of Subjects With Adverse Events

End point description:	
All subjects who received at least one dose of study treatment were included in safety population.	
End point type	Secondary
End point timeframe:	
Up to Day 183	

End point values	Triptorelin Pamoate			
Subject group type	Reporting group			
Number of subjects analysed	126			
Units: Percentage of subjects				
number (not applicable)				
Any Adverse Events	35.7			
Any Serious Adverse Events (SAEs)	4.8			
Any Treatment Emergent Adverse Events (TEAEs)	35.7			
TEAEs Leading to Withdrawal	0.8			
TEAEs Leading to Death	0.8			
Maximum Grade NCI-CTC of TEAEs: Grade 5	0.8			
Maximum Grade NCI-CTC of TEAEs: Grade 4	0			
Maximum Grade NCI-CTC of TEAEs: Grade 3	4			
Maximum Grade NCI-CTC of TEAEs: Grade 2	13.5			
Maximum Grade NCI-CTC of TEAEs: Grade 1	27.8			
Most serious causality of TEAEs: Related	21.4			
Most serious causality of TEAEs: Not related	26.2			

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Cmax (Tmax) of triptorelin

End point title	Time to Cmax (Tmax) of triptorelin
End point description:	
Pharmacokinetic (PK) profile was assessed in a subset of 18 subjects.	
End point type	Secondary
End point timeframe:	
At 1, 2, 3, 4, 5, 6, 7, 8 and 24 hours after first dose on Day 1	

End point values	Triptorelin Pamoate			
Subject group type	Reporting group			
Number of subjects analysed	18			
Units: Hours				
median (full range (min-max))	4.5 (1.01 to 24)			

Statistical analyses

No statistical analyses for this end point

Secondary: Peak plasma concentration value (Cmax) of triptorelin

End point title	Peak plasma concentration value (Cmax) of triptorelin
End point description:	
PK profile was assessed in a subset of 18 subjects.	
End point type	Secondary
End point timeframe:	
At 1, 2, 3, 4, 5, 6, 7, 8 and 24 hours after first dose on Day 1	

End point values	Triptorelin Pamoate			
Subject group type	Reporting group			
Number of subjects analysed	18			
Units: ng/mL				
arithmetic mean (standard deviation)	18.58 (± 7.35)			

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Concentration Versus Time Curve Between 0 and 24 Hours (AUC0-24) of Triptorelin

End point title	Area Under the Concentration Versus Time Curve Between 0 and 24 Hours (AUC0-24) of Triptorelin
End point description:	
PK profile was assessed in a subset of 18 subjects.	
End point type	Secondary
End point timeframe:	
At 1, 2, 3, 4, 5, 6, 7, 8 and 24 hours after first dose on Day 1	

End point values	Triptorelin Pamoate			
Subject group type	Reporting group			
Number of subjects analysed	18			
Units: h*ng/mL				
arithmetic mean (standard deviation)	304.6 (± 103.7)			

Statistical analyses

No statistical analyses for this end point

Secondary: Cmin of Triptorelin in Subset of 18 Subjects

End point title	Cmin of Triptorelin in Subset of 18 Subjects

End point description:

End point type	Secondary

End point timeframe:

At Day 92 and 183

End point values	Triptorelin Pamoate			
Subject group type	Reporting group			
Number of subjects analysed	18			
Units: ng/mL				
arithmetic mean (standard deviation)				
Day 92 (N=14)	0.078 (± 0.038)			
Day 183 (N=18)	0.062 (± 0.023)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to Day 183

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	16.1

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	6 / 126 (4.76%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events	0		
Injury, poisoning and procedural complications			
Fibula Fracture			
subjects affected / exposed	1 / 126 (0.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Cardiac Failure			
subjects affected / exposed	1 / 126 (0.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Myocardial infarction			
subjects affected / exposed	1 / 126 (0.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Blood and lymphatic system disorders			
Anaemia			

subjects affected / exposed	1 / 126 (0.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Chronic Obstructive Pulmonary Disease			
subjects affected / exposed	1 / 126 (0.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Pneumonia			
subjects affected / exposed	2 / 126 (1.59%)		
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	Triptorelin pamoate 11.25 mg		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	45 / 126 (35.71%)		
Vascular disorders			
Hot Flush			
subjects affected / exposed	13 / 126 (10.32%)		
occurrences (all)	13		
Hypertension			
subjects affected / exposed	6 / 126 (4.76%)		
occurrences (all)	8		
Flushing			
subjects affected / exposed	1 / 126 (0.79%)		
occurrences (all)	1		
Haematoma			
subjects affected / exposed	1 / 126 (0.79%)		
occurrences (all)	1		
General disorders and administration site conditions			

Oedema Peripheral subjects affected / exposed occurrences (all)	2 / 126 (1.59%) 2		
Asthenia subjects affected / exposed occurrences (all)	1 / 126 (0.79%) 1		
Chills subjects affected / exposed occurrences (all)	1 / 126 (0.79%) 1		
Fatigue subjects affected / exposed occurrences (all)	1 / 126 (0.79%) 1		
Hyperthermia subjects affected / exposed occurrences (all)	1 / 126 (0.79%) 1		
Injection Site Haematoma subjects affected / exposed occurrences (all)	1 / 126 (0.79%) 1		
Injection Site Pain subjects affected / exposed occurrences (all)	1 / 126 (0.79%) 1		
Injection Site Swelling subjects affected / exposed occurrences (all)	1 / 126 (0.79%) 1		
Reproductive system and breast disorders			
Erectile Dysfunction subjects affected / exposed occurrences (all)	3 / 126 (2.38%) 3		
Breast Pain subjects affected / exposed occurrences (all)	2 / 126 (1.59%) 2		
Breast Swelling subjects affected / exposed occurrences (all)	1 / 126 (0.79%) 1		
Breast Tenderness			

subjects affected / exposed	1 / 126 (0.79%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Chronic Obstructive Pulmonary Disease			
subjects affected / exposed	1 / 126 (0.79%)		
occurrences (all)	1		
Cough			
subjects affected / exposed	1 / 126 (0.79%)		
occurrences (all)	1		
Dyspnoea			
subjects affected / exposed	1 / 126 (0.79%)		
occurrences (all)	1		
Haemoptysis			
subjects affected / exposed	1 / 126 (0.79%)		
occurrences (all)	1		
Psychiatric disorders			
Anger			
subjects affected / exposed	1 / 126 (0.79%)		
occurrences (all)	1		
Nervousness			
subjects affected / exposed	1 / 126 (0.79%)		
occurrences (all)	1		
Investigations			
Weight Increased			
subjects affected / exposed	12 / 126 (9.52%)		
occurrences (all)	12		
Weight Decreased			
subjects affected / exposed	7 / 126 (5.56%)		
occurrences (all)	7		
Blood Pressure Increased			
subjects affected / exposed	1 / 126 (0.79%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			
Fall			

subjects affected / exposed occurrences (all) Fibula Fracture subjects affected / exposed occurrences (all) Wound subjects affected / exposed occurrences (all) Wrist Fracture subjects affected / exposed occurrences (all)	2 / 126 (1.59%) 2 1 / 126 (0.79%) 1 1 / 126 (0.79%) 1 1 / 126 (0.79%) 1		
Cardiac disorders Cardiac Failure subjects affected / exposed occurrences (all) Myocardial Infarction subjects affected / exposed occurrences (all)	 1 / 126 (0.79%) 1 1 / 126 (0.79%) 1		
Nervous system disorders Headache subjects affected / exposed occurrences (all) Loss Of Consciousness subjects affected / exposed occurrences (all)	 4 / 126 (3.17%) 12 1 / 126 (0.79%) 1		
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all)	 1 / 126 (0.79%) 1		
Eye disorders Conjunctivitis subjects affected / exposed occurrences (all)	 2 / 126 (1.59%) 2		
Skin and subcutaneous tissue disorders Hyperhidrosis subjects affected / exposed occurrences (all)	 3 / 126 (2.38%) 3		

Night Sweats subjects affected / exposed occurrences (all)	2 / 126 (1.59%) 2		
Hypotrichosis subjects affected / exposed occurrences (all)	1 / 126 (0.79%) 1		
Pruritus subjects affected / exposed occurrences (all)	1 / 126 (0.79%) 1		
Renal and urinary disorders			
Dysuria subjects affected / exposed occurrences (all)	1 / 126 (0.79%) 1		
Haematuria subjects affected / exposed occurrences (all)	1 / 126 (0.79%) 1		
Nocturia subjects affected / exposed occurrences (all)	1 / 126 (0.79%) 1		
Pollakiuria subjects affected / exposed occurrences (all)	1 / 126 (0.79%) 1		
Urinary Retention subjects affected / exposed occurrences (all)	1 / 126 (0.79%) 1		
Musculoskeletal and connective tissue disorders			
Arthralgia subjects affected / exposed occurrences (all)	1 / 126 (0.79%) 1		
Back Pain subjects affected / exposed occurrences (all)	1 / 126 (0.79%) 1		
Haemarthrosis subjects affected / exposed occurrences (all)	1 / 126 (0.79%) 1		
Pain In Extremity			

subjects affected / exposed	1 / 126 (0.79%)		
occurrences (all)	1		
Infections and infestations			
Pneumonia			
subjects affected / exposed	2 / 126 (1.59%)		
occurrences (all)	2		
Bronchitis			
subjects affected / exposed	1 / 126 (0.79%)		
occurrences (all)	1		
Ear Infection			
subjects affected / exposed	1 / 126 (0.79%)		
occurrences (all)	1		
Influenza			
subjects affected / exposed	1 / 126 (0.79%)		
occurrences (all)	1		
Nasopharyngitis			
subjects affected / exposed	1 / 126 (0.79%)		
occurrences (all)	1		
Tooth Abscess			
subjects affected / exposed	1 / 126 (0.79%)		
occurrences (all)	1		
Metabolism and nutrition disorders			
Hypokalaemia			
subjects affected / exposed	1 / 126 (0.79%)		
occurrences (all)	2		
Hyperglycaemia			
subjects affected / exposed	1 / 126 (0.79%)		
occurrences (all)	1		
Hyperkalaemia			
subjects affected / exposed	1 / 126 (0.79%)		
occurrences (all)	1		
Hypomagnesaemia			
subjects affected / exposed	1 / 126 (0.79%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
24 June 2013	The protocol was amended to include an additional secondary endpoints, the probability of testosterone <50 ng/dL from Day 29 through Day 183, in order to obtain a reliable estimation of the full maintenance of the castration between Day 29 and Day 183.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported