Clinical trial results:
An open label, one-arm, multiple dose study in patients with prostate cancer to demonstrate efficacy of a one month goserelin 3.6 mg implant in a two months treatment (2 application periods) and PK/PD analysis of Zoladex® 3.6 mg implant in additional 12 patients.

Summary

EudraCT number	2011-001193-26
Trial protocol	DE CZ PL
Global end of trial date	15 July 2015

Results information

Result version number	v1 (current)
This version publication date	30 July 2016
First version publication date	30 July 2016

Trial information

Trial identification

Sponsor protocol code	C_30050_P3_02

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Acino Supply AG
Sponsor organisation address	Pfeffingerring 205, Aesch, Switzerland,
Public contact	Ulrike Seminati (Head of Corporate Communications), Acino International AG, Thurgauerstrasse 36/38, Zürich, Switzerland, +41 44 555 22 00,
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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	06 October 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	19 March 2013
Global end of trial reached?	Yes
Global end of trial date	15 July 2015
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To demonstrate that Acino Goserelin 3.6 mg implant is effective in achieving and maintaining castration levels of testosterone.

Protection of trial subjects:

Patients could be hospitalized for 2 or more days at the beginning of the study (first implantation of study medication at Day 0), if required, or if more convenient for the patient.

An independent Medical Monitor was implemented to evaluate the safety of the patients on an ongoing basis.

Background therapy: -

Evidence for comparator:

A small comparator group receiving Zoladex 3.6 mg implant was used to compare pharmacokinetic and pharmacodynamic data of Acino Goserelin with a marketed and well established reference product.

Actual start date of recruitment	11 September 2012
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Poland: 26
Country: Number of subjects enrolled	Czech Republic: 14
Country: Number of subjects enrolled	Germany: 44
Worldwide total number of subjects	84
EEA total number of subjects	84

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0

Adults (18-64 years)	12
From 65 to 84 years	69
85 years and over	3

Subject disposition

Recruitment

Recruitment details:

Patients were enrolled from 11-Sep-2012 to 07-Feb-2013 at 10 sites in 3 countries.

Pre-assignment

Screening details:

Screening was conducted up to 2 weeks prior to injection of the first implant. 96 patients were screened; 84 patients were randomized.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Acino Goserelin

Arm description:

Patients received Acino Goserelin 3.6 mg implant at Day 0 and Day 28.

Arm type	Experimental
Investigational medicinal product name	Acino Goserelin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Implant
Routes of administration	Implantation

Dosage and administration details:

Patients received Acino Goserelin 3.6 mg implant subcutaneously with a special applicator at Days 0 and Day 28. During administration a second staff person had to be present to confirm that the administration was done correctly.

Arm title	Zoladex

Arm description:

Patients received Zoladex 3.6 mg implant at Day 0 and Day 28.

Arm type	Active comparator
Investigational medicinal product name	Zoladex
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Implant
Routes of administration	Implantation

Dosage and administration details:

Patients received Zoladex 3.6 mg implants subcutaneously with a special applicator at Day 0 and Day 28. During administration a second staff person had to be present to confirm that the administration was done correctly.

Number of subjects in period 1	Acino Goserelin	Zoladex
Started	76	8
Completed	53	8
Not completed	23	0
Study was set on hold.	23	-

Baseline characteristics

Reporting groups

Reporting group title	Overall study

Reporting group description: -

Reporting group values	Overall study	Total	
Number of subjects	84	84	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	12	12	
From 65-84 years	69	69	
85 years and over	3	3	
Gender categorical Units: Subjects			
Female	0	0	
Male	84	84	

End points

End points reporting groups

Reporting group title	Acino Goserelin
Reporting group description:	
Patients received Acino Goserelin 3.6 mg implant at Day 0 and Day 28.	
Reporting group title	Zoladex
Reporting group description:	
Patients received Zoladex 3.6 mg implant at Day 0 and Day 28.	
Subject analysis set title	FAS - Acino Goserelin
Subject analysis set type	Full analysis
Subject analysis set description:	
The full analysis set (FAS: N = 61) included all randomized patients to whom at least 1 implant had succesfully been administered. Patients who prematurely discontinued the study due to the study being on hold were excluded. Patients of the FAS who received the Acino Goserelin implant (N = 53) are defined as FAS - Acino Goserelin.	
Subject analysis set title	PK/PD analysis set - Acino Goserelin
Subject analysis set type	Modified intention-to-treat
Subject analysis set description:	
All patients of the FAS who receiced Acino-Goserelin and had at least one post-baseline pharmacokinetic/pharmacodynamic (PK/PD) measurement (N = 53). Patients who early discontinued the study because the study was set on hold were excluded.	
Subject analysis set title	PK/PD analysis set - Zoladex
Subject analysis set type	Modified intention-to-treat
Subject analysis set description:	
All patients of the FAS who received Zoladex and had at least one post-baseline PK/PD measurement (N = 8). Patients who early discontinued the study because the study was set on hold were excluded.	

Primary: Testosterone response rate at and after Day 28 until Day 56

End point title	Testosterone response rate at and after Day 28 until Day 56[1]
End point description:	
Testosterone response rate was defined as the rate of patients with testosterone values sustained below castration level (0.5 ng/mL) at and after Day 28 until Day 56.	
End point type	Primary
End point timeframe:	
Day 28 to Day 56	

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: The primary endpoint, testosterone response rate, was evaluated using exact 95% confidence intervals (CI) according to Clopper-Pearson. The study objective was to show that the lower bound of this confidence interval was >90%.

End point values	FAS - Acino Goserelin			
Subject group type	Subject analysis set			
Number of subjects analysed	53			
Units: percent				
number (confidence interval 95%)	92.5 (81.8 to 97.9)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of patients who reached castration level of testosterone (< 0.5 ng/mL) at the last visit (Day 56)

End point title	Percentage of patients who reached castration level of testosterone (< 0.5 ng/mL) at the last visit (Day 56)

End point description:

End point type	Secondary

End point timeframe:

At Day 56

End point values	FAS - Acino Goserelin			
Subject group type	Subject analysis set			
Number of subjects analysed	53			
Units: percent				
number (confidence interval 95%)	98.1 (89.9 to 100)			

Statistical analyses

No statistical analyses for this end point

Secondary: Time after first implantation until castration level of testosterone (< 0.5 ng/mL) was achieved for the first time

End point title	Time after first implantation until castration level of testosterone (< 0.5 ng/mL) was achieved for the first time

End point description:

End point type	Secondary

End point timeframe:

Day 0 to Day 56

End point values	FAS - Acino Goserelin			
Subject group type	Subject analysis set			
Number of subjects analysed	52			
Units: Days				
median (full range (min-max))	21 (14 to 35)			

Statistical analyses

No statistical analyses for this end point

Secondary: Rate of patients with testosterone values sustained below 0.2 ng/mL at and after Day 28 until Day 56

End point title	Rate of patients with testosterone values sustained below 0.2 ng/mL at and after Day 28 until Day 56

End point description:

End point type	Secondary

End point timeframe:

Day 28 to Day 56

End point values	FAS - Acino Goserelin			
Subject group type	Subject analysis set			
Number of subjects analysed	53			
Units: percent				
number (confidence interval 95%)	54.7 (40.4 to 68.4)			

Statistical analyses

No statistical analyses for this end point

Secondary: Results of clinical examination of the prostate

End point title	Results of clinical examination of the prostate

End point description:

The prostate was examined by the investigator via a digital rectal examination and classified according to the categories listed below.

End point type	Secondary

End point timeframe:

At Day 56

End point values	FAS - Acino Goserelin			
Subject group type	Subject analysis set			
Number of subjects analysed	53			
Units: percent				
number (not applicable)				
Normal	20.8			
Hard	34			
Hard, Asymmetrical	9.4			
Hard, Asymmetrical, Enlarged	15.1			

Hard, Enlarged	3.8			
Enlarged	13.2			
Asymmetrical, Enlarged	3.8			
Missing	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Prostate specific antigen (PSA) levels

End point title	Prostate specific antigen (PSA) levels

End point description:

End point type	Secondary

End point timeframe:

Time course from Day 0 to Day 56

End point values	FAS - Acino Goserelin			
Subject group type	Subject analysis set			
Number of subjects analysed	53			
Units: µg/L				
median (full range (min-max))				
Day 0	7.4 (0.1 to 2735.2)			
Day 28	3.1 (0.1 to 822.2)			
Day 31	2.4 (0.1 to 722.2)			
Day 35	2.3 (0.1 to 610.5)			
Day 42	2 (0.1 to 497.2)			
Day 49	1.3 (0.1 to 417.3)			
Day 56	0.9 (0.1 to 396.5)			

Statistical analyses

No statistical analyses for this end point

Secondary: PK - Goserelin concentration

End point title	PK - Goserelin concentration

End point description:

End point type	Secondary
End point timeframe:	
Time course from Day 0 to Day 56	

End point values	PK/PD analysis set - Acino Goserelin	PK/PD analysis set - Zoladex		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	53	8		
Units: ng/mL				
median (full range (min-max))				
Day 0	0 (0 to 0)	0 (0 to 0)		
Day 1	0.71 (0 to 2)	0.36 (0.2 to 0.55)		
Day 2	0.43 (0 to 0.89)	0.31 (0.17 to 0.48)		
Day 4	0.23 (0 to 0.48)	0.17 (0.1 to 0.24)		
Day 7	0.37 (0 to 0.95)	0.1 (0.1 to 0.12)		
Day 14	0.59 (0 to 3.45)	1.19 (0.25 to 2.83)		
Day 21	0.51 (0 to 1.09)	0.44 (0.29 to 0.86)		
Day 28	0.25 (0 to 0.87)	0.21 (0.14 to 0.48)		
Day 31	0.46 (0 to 1.12)	0.3 (0.21 to 0.65)		
Day 35	0.47 (0 to 1.38)	0.21 (0.1 to 0.95)		
Day 42	0.61 (0 to 1.61)	0.8 (0.1 to 4.62)		
Day 49	0.53 (0 to 1.38)	0.43 (0.14 to 0.86)		
Day 56	0.25 (0 to 0.75)	0.18 (0.1 to 0.74)		

Statistical analyses

No statistical analyses for this end point

Secondary: PD - Plasma levels of luteinizing hormone (LH) between Day 0 and Day 56

End point title	PD - Plasma levels of luteinizing hormone (LH) between Day 0 and Day 56
End point description:	

End point type	Secondary
End point timeframe:	
Time course from Day 0 to Day 56	

End point values	PK/PD analysis set - Acino Goserelin	PK/PD analysis set - Zoladex		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	53	8		
Units: IU/L				
median (full range (min-max))				
Day 0	6.5 (1.1 to 37.3)	8.3 (2.9 to 16.5)		
Day 1	36.4 (6.6 to 124.4)	30.9 (17.5 to 55.2)		
Day 2	21.4 (5.9 to 58.2)	18.1 (12.1 to 28.4)		
Day 4	14 (4 to 39.5)	17 (7.2 to 25.2)		
Day 7	9.3 (2.7 to 28.9)	8.8 (4.8 to 12.4)		
Day 14	3.4 (1.1 to 10.8)	4.3 (1.9 to 5.2)		
Day 21	1.4 (0.4 to 5.1)	1.45 (0.8 to 2)		
Day 28	0.5 (0.1 to 2.7)	0.6 (0.2 to 0.9)		
Day 31	0.4 (0.1 to 3.3)	0.4 (0.1 to 0.7)		
Day 35	0.3 (0.1 to 5.5)	0.2 (0.1 to 0.4)		
Day 42	0.1 (0.1 to 4.3)	0.1 (0.1 to 0.4)		
Day 49	0.1 (0.1 to 5.2)	0.1 (0.1 to 0.2)		
Day 56	0.1 (0.1 to 5.6)	0.1 (0.1 to 0.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: PD - Plasma levels of follicle stimulating hormone (FSH) between Day and Day 56

End point title	PD - Plasma levels of follicle stimulating hormone (FSH) between Day and Day 56

End point description:

End point type	Secondary

End point timeframe:

Time course from Day 0 to Day 56

End point values	PK/PD analysis set - Acino Goserelin	PK/PD analysis set - Zoladex		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	53	8		
Units: IU/L				
median (full range (min-max))				
Day 0	9.5 (1.7 to 49.3)	9.5 (5 to 27.8)		
Day 1	24.1 (4.8 to 104.6)	19.8 (10.3 to 55.8)		
Day 2	15 (3.3 to 59.5)	13.3 (7.7 to 31.2)		
Day 4	9.4 (2.1 to 44.3)	8.3 (5.8 to 17.9)		
Day 7	4.8 (1.1 to 25.3)	4.1 (2.2 to 10.9)		
Day 14	2.9 (0.8 to 11.7)	2.7 (1.4 to 4.4)		
Day 21	2.7 (0.9 to 7.3)	2.2 (1 to 4.3)		
Day 28	3.4 (0.9 to 7.8)	2.7 (1.1 to 5.8)		
Day 31	3.2 (1 to 7.7)	2.7 (1 to 5)		
Day 35	3.6 (0.9 to 9.6)	3.7 (1.5 to 5.7)		
Day 42	3.3 (0.6 to 10.6)	3.4 (1.2 to 5.9)		
Day 49	3.8 (0.9 to 11.7)	3.3 (1 to 6.9)		
Day 56	4.2 (0.6 to 13.7)	4.4 (1.2 to 6.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time course of testosterone levels on Day 28, 31, 35, 42, 49, and 56

End point title	Time course of testosterone levels on Day 28, 31, 35, 42, 49, and 56

End point description:

End point type	Secondary

End point timeframe:

On Days 28, 31, 35, 42, 49, and 56

End point values	PK/PD analysis set - Acino Goserelin	PK/PD analysis set - Zoladex		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	53	8		
Units: ng/mL				
median (full range (min-max))				

Day 28	0.19 (0.1 to 2.24)	0.13 (0.1 to 0.33)		
Day 31	0.15 (0.1 to 2.68)	0.11 (0.1 to 0.2)		
Day 35	0.11 (0.1 to 2.07)	0.1 (0.1 to 0.19)		
Day 42	0.11 (0.1 to 3.23)	0.1 (0.1 to 0.16)		
Day 49	0.1 (0.1 to 2.37)	0.1 (0.1 to 0.21)		
Day 56	0.1 (0.1 to 3.01)	0.1 (0.1 to 0.19)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were documented starting at Screening until study Day 56. Serious adverse events still ongoing at Day 56 were followed-up after the end of the study.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	15.1

Reporting groups

Reporting group title	Acino Goserelin

Reporting group description:

Patients received Acino Goserelin 3.6 mg implant on Day 0 and Day 28.

Reporting group title	Zoladex

Reporting group description:

Patients received Zoladex 3.6 mg implant on Day 0 and Day 28.

Serious adverse events	Acino Goserelin	Zoladex	
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 76 (3.95%)	0 / 8 (0.00%)	
number of deaths (all causes)	1	0	
number of deaths resulting from adverse events	0	0	
Cardiac disorders			
Arrhythmia			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 76 (1.32%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Ischaemic stroke			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 76 (1.32%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Disease progression			
alternative assessment type: Systematic			

subjects affected / exposed	1 / 76 (1.32%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Dehydration			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 76 (1.32%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Acino Goserelin	Zoladex	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	34 / 76 (44.74%)	4 / 8 (50.00%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Metastases to bone			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 76 (2.63%)	0 / 8 (0.00%)	
occurrences (all)	2	0	
Vascular disorders			
Hot flush			
alternative assessment type: Systematic			
subjects affected / exposed	13 / 76 (17.11%)	3 / 8 (37.50%)	
occurrences (all)	13	3	
Hypertension			
alternative assessment type: Systematic			
subjects affected / exposed	4 / 76 (5.26%)	0 / 8 (0.00%)	
occurrences (all)	4	0	
General disorders and administration site conditions			
Asthenia			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 76 (1.32%)	1 / 8 (12.50%)	
occurrences (all)	1	1	
Fatigue			

alternative assessment type: Systematic			
subjects affected / exposed	3 / 76 (3.95%)	1 / 8 (12.50%)	
occurrences (all)	4	2	
Implant site pruritus			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 76 (2.63%)	0 / 8 (0.00%)	
occurrences (all)	2	0	
Influenza like illness			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 76 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Injection site erythema			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 76 (1.32%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Injection site haematoma			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 76 (1.32%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Pain			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 76 (2.63%)	0 / 8 (0.00%)	
occurrences (all)	2	0	
Vessel puncture site haematoma			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 76 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Reproductive system and breast disorders			
Gynaecomastia			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 76 (1.32%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Cough			
alternative assessment type: Systematic			

subjects affected / exposed	1 / 76 (1.32%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea exertional			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 76 (1.32%)	0 / 8 (0.00%)	
occurrences (all)	2	0	
Psychiatric disorders			
Depression			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 76 (1.32%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Insomnia			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 76 (1.32%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Investigations			
Alanine aminotransferase increased			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 76 (1.32%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Aspartate aminotransferase increased			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 76 (1.32%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Blood follicle stimulating hormone increased			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 76 (1.32%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Blood luteinising hormone decreased			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 76 (1.32%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Blood luteinising hormone increased			

alternative assessment type: Systematic			
subjects affected / exposed	1 / 76 (1.32%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Blood pressure increased			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 76 (2.63%)	0 / 8 (0.00%)	
occurrences (all)	2	0	
Injury, poisoning and procedural complications			
Contusion			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 76 (2.63%)	1 / 8 (12.50%)	
occurrences (all)	2	1	
Cardiac disorders			
Atrioventricular block first degree			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 76 (1.32%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			
Burning sensation			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 76 (1.32%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Dizziness			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 76 (1.32%)	0 / 8 (0.00%)	
occurrences (all)	2	0	
Headache			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 76 (1.32%)	1 / 8 (12.50%)	
occurrences (all)	1	1	
Hyperaesthesia			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 76 (1.32%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Tension headache			

alternative assessment type: Systematic			
subjects affected / exposed	0 / 76 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Constipation			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 76 (1.32%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Diarrhoea			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 76 (1.32%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Melaena			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 76 (1.32%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Skin and subcutaneous tissue disorders			
Erythema			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 76 (1.32%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Hyperhidrosis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 76 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Pruritus			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 76 (1.32%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Renal and urinary disorders			
Urethral stenosis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 76 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Urinary retention			

alternative assessment type: Systematic			
subjects affected / exposed	1 / 76 (1.32%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			
Bone pain			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 76 (1.32%)	0 / 8 (0.00%)	
occurrences (all)	2	0	
Musculoskeletal discomfort			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 76 (1.32%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Myalgia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 76 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Pain in extremity			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 76 (3.95%)	0 / 8 (0.00%)	
occurrences (all)	3	0	
Rhabdomyolysis			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 76 (1.32%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			
Cystitis			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 76 (1.32%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Nasopharyngitis			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 76 (3.95%)	0 / 8 (0.00%)	
occurrences (all)	3	0	
Rhinitis			
alternative assessment type:			

Systematic subjects affected / exposed occurrences (all)	1 / 76 (1.32%) 1	0 / 8 (0.00%) 0	
Metabolism and nutrition disorders Hypocalcaemia alternative assessment type: Systematic subjects affected / exposed occurrences (all)	1 / 76 (1.32%) 1	0 / 8 (0.00%) 0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
03 February 2012	This amendment stated that only the testosterone values at Screening (and not Baseline) would be used to decide if a patient was eligible for participation in the study, as it was assumed that testosterone values would not change from Screening to Baseline (maximum of 2 weeks).
04 February 2013	This amendment - changed the planned number of recruited patients from 130 to 145 because it was considered that the percentage of patients expected to be excluded from the analysis is rather 10% than 4% as initially assumed; - changed the definitions of analysis populations and primary analysis set from the per protocol to the full analysis set; - included some clarifications and editorial changes;
20 June 2013	This amendment - specified an interim analysis of the primary efficacy endpoint and the main safety data due to an unconfirmed out-of-specification (OOS) result for the Acino implant that was noticed during stability testing. Further investigations showed that the non-confirmed OOS-result was not related to the analytical procedure, the manufacturing process, or to the product an its quality. Nevertheless, an interim analysis was to provide a risk/benefit assessment whether to stop the study due to futility or continue the study without changes; - included some clarifications and editorial changes;
06 October 2014	- Androgen deprivation therapy was added to exclusion criteria (i.e. treatment with gonadotropin releasing hormone (GnRH) analogs, treatment with antiandrogens or androgen receptor blockers within 3 months before baseline was not allowed); - A number of exclusion criteria were changed in accordance with scientific advices from FDA for a similar study;
06 May 2015	A statement regarding the study medication administration was added that administration was to be supervised by a further person, who confirmed a correct administration in the Case Report Form as well as in the patient file. It also added that the blood samples taken for goserelin levels would be analyzed shortly after implantation of study medication to ensure that the study medication administration was successful.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date

15 July 2015	The study C_30050_P3_02 was on hold since 08 February 2013 due to an unconfirmed out-of-specification result of Acino Goserelin that was noticed during stability testing. A not pre-planned interim analysis by an independant Data Monitoring Committee, and additional testing justified the conclusion that the benfit/risk ratio in case of study re-start remained positive. Nevertheless, due to a change in the portfolio strategy of the sponsor Acino it was decided not to pursue the Goserelin study C_30050_P3_02.	-

Notes:

Limitations and caveats

None reported