



Clinical trial results:

A Phase II, Open Label, Active Control, Multi-National, Multi-Centre, Randomized, Parallel Group Study Assessing Pharmacokinetics, Pharmacodynamics, Efficacy and Safety of CAM2032 q1m (Leuprolide Acetate FluidCrystal® Injection Depot once monthly) after Repeat Doses of 3.75 mg and 7.5 mg of Leuprolide Acetate vs. Eligard® 7.5 mg in Patients with Prostate Cancer

Summary

EudraCT number	2014-001074-34
Trial protocol	FI HU
Global end of trial date	10 November 2015

Results information

Result version number	v1 (current)
This version publication date	25 November 2016
First version publication date	25 November 2016

Trial information

Trial identification

Sponsor protocol code	HS-12-460
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02212197
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Camurus AB
Sponsor organisation address	Ideon Science Park, Gamma Building, Sölvegatan 41, Sweden, SE-223 70 Lund
Public contact	Director, Clinical Programme Management, Camurus AB, +46 46286 3852, Hakan.Olsson@camurus.com
Scientific contact	CRA, TFS, +358 4450 6 6323, heidi.oksama@tfscro.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	10 November 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	10 November 2015
Global end of trial reached?	Yes
Global end of trial date	10 November 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To characterize the pharmacokinetic (PK) profiles after repeated administration of CAM2032 at doses of 3.75 mg and 7.5 mg leuprolide acetate, in patients with prostate cancer.

Protection of trial subjects:

The trial was conducted in compliance with the approved clinical trial protocol and its amendments, regulatory requirements, Good Clinical Practice and the ethical principles of the latest revision of the Declaration of Helsinki as adopted by the World Medical Association.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	17 September 2014
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	Finland: 31
Country: Number of subjects enrolled	Hungary: 20
Worldwide total number of subjects	51
EEA total number of subjects	51

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)	9
From 65 to 84 years	42
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 57 participants were screened, out of which 51 participants were randomized and treated in this trial, which was conducted at 7 trial sites (4 in Finland and 3 in Hungary).

Pre-assignment

Screening details:

Participants were screened within 14 days of first dose of trial drug and eligible participants enrolled.

Period 1

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

Blinding implementation details:

This trial was an open-label trial. The randomization was used to assign the participants to one of the three treatment groups.

Arms

Are arms mutually exclusive?	Yes
Arm title	CAM2032 3.75 mg

Arm description:

Participants were administered single subcutaneous buttock injections of CAM2032 3.75 mg on Days 0, 28 and 56.

Arm type	Experimental
Investigational medicinal product name	CAM2032 3.75 mg
Investigational medicinal product code	
Other name	Leuprolide Acetate FluidCrystal® Injection Depot
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants were administered single subcutaneous buttock injections of CAM2032 3.75 mg on Days 0, 28 and 56.

Arm title	CAM2032 7.5 mg
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Arm description:

Participants were administered single subcutaneous buttock injections of CAM2032 7.5 mg on Days 0, 28 and 56.

Arm type	Experimental
Investigational medicinal product name	CAM2032 7.5 mg
Investigational medicinal product code	
Other name	Leuprolide Acetate FluidCrystal® Injection Depot
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants were administered single subcutaneous buttock injections of CAM2032 7.5 mg on Days 0, 28 and 56.

Arm title	Eligard 7.5 mg
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Arm description:

Participants were administered single subcutaneous buttock injections of Eligard 7.5 mg on Days 0, 28 and 56.

Arm type	Active comparator
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Investigational medicinal product name	Eligard 7.5 mg
Investigational medicinal product code	
Other name	Leuprolide acetate
Pharmaceutical forms	Powder and solution for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants were administered single subcutaneous buttock injections of Eligard 7.5 mg on Days 0, 28 and 56.

Number of subjects in period 1	CAM2032 3.75 mg	CAM2032 7.5 mg	Eligard 7.5 mg
Started	19	15	17
Completed	18	15	17
Not completed	1	0	0
Due to need for radiotherapy	1	-	-

Baseline characteristics

Reporting groups

Reporting group title	CAM2032 3.75 mg
Reporting group description:	
Participants were administered single subcutaneous buttock injections of CAM2032 3.75 mg on Days 0, 28 and 56.	
Reporting group title	CAM2032 7.5 mg
Reporting group description:	
Participants were administered single subcutaneous buttock injections of CAM2032 7.5 mg on Days 0, 28 and 56.	
Reporting group title	Eligard 7.5 mg
Reporting group description:	
Participants were administered single subcutaneous buttock injections of Eligard 7.5 mg on Days 0, 28 and 56.	

Reporting group values	CAM2032 3.75 mg	CAM2032 7.5 mg	Eligard 7.5 mg
Number of subjects	19	15	17
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	6	1	2
From 65-84 years	13	14	15
85 years and over	0	0	0
Age continuous			
Units: years			
arithmetic mean	69.7	71.9	70.9
standard deviation	± 9.5	± 6.3	± 7
Gender categorical			
Units: Subjects			
Female	0	0	0
Male	19	15	17

Reporting group values	Total		
Number of subjects	51		
Age categorical			
Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	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)	9		
From 65-84 years	42		
85 years and over	0		
Age continuous			
Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical			
Units: Subjects			
Female	0		
Male	51		

End points

End points reporting groups

Reporting group title	CAM2032 3.75 mg
Reporting group description: Participants were administered single subcutaneous buttock injections of CAM2032 3.75 mg on Days 0, 28 and 56.	
Reporting group title	CAM2032 7.5 mg
Reporting group description: Participants were administered single subcutaneous buttock injections of CAM2032 7.5 mg on Days 0, 28 and 56.	
Reporting group title	Eligard 7.5 mg
Reporting group description: Participants were administered single subcutaneous buttock injections of Eligard 7.5 mg on Days 0, 28 and 56.	
Subject analysis set title	CAM2032/Eligard
Subject analysis set type	Per protocol
Subject analysis set description: The Per-protocol Set consisted of all randomized participants in the safety population who had a complete PK profile.	

Primary: Observed maximum serum concentration (C_{max}) for Dose 1 and Dose 3

End point title	Observed maximum serum concentration (C _{max}) for Dose 1 and Dose 3 ^[1]
End point description: Blood samples for analysis of serum leuprolide concentrations were collected at pre-determined time points throughout the trial (with full PK profiles after Dose 1 and Dose 3). The PK parameter, C _{max} was derived for Doses 1 and 3 of the investigational medicinal products (IMPs).	
End point type	Primary
End point timeframe: Days 0 and 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: No inferential statistical analysis was done for this primary endpoint.	

End point values	CAM2032 3.75 mg	CAM2032 7.5 mg	Eligard 7.5 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	15	15	17	
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
Dose 1 (n= 15, 15, 17)	6.14 (± 41.1)	9.66 (± 31.5)	13.6 (± 54.7)	
Dose 3 (n= 15, 15, 17)	5.36 (± 33.3)	11.3 (± 36.8)	12.1 (± 47.3)	

Statistical analyses

No statistical analyses for this end point

Primary: Apparent terminal half-life (t_{1/2}) for Dose 1 and Dose 3

End point title	Apparent terminal half-life (t _{1/2}) for Dose 1 and Dose 3 ^[2]
End point description: Blood samples for analysis of serum leuprolide concentrations were collected at pre-determined time points throughout the trial (with full PK profiles after Dose 1 and Dose 3). The PK parameter, t _{1/2} was derived for Doses 1 and 3 of the IMPs.	
End point type	Primary
End point timeframe: Days 0 and 56	

Notes:

[2] - 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 inferential statistical analysis was done for this primary endpoint.

End point values	CAM2032 3.75 mg	CAM2032 7.5 mg	Eligard 7.5 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	15	15	17	
Units: hour				
arithmetic mean (standard deviation)				
Dose 1 (n= 14, 14, 9)	205 (± 113)	231 (± 142)	743 (± 1677)	
Dose 3 (n= 11, 11, 15)	299 (± 277)	434 (± 867)	378 (± 570)	

Statistical analyses

No statistical analyses for this end point

Primary: Area under the serum concentration-time curve (AUC), computed using the linear/log trapezoidal rule, linear up to C_{max} and thereafter log transformed concentration over the dosing interval (tau = 28 days) (AUC_{tau}) for Dose 1 and Dose 3

End point title	Area under the serum concentration-time curve (AUC), computed using the linear/log trapezoidal rule, linear up to C _{max} and thereafter log transformed concentration over the dosing interval (tau = 28 days) (AUC _{tau}) for Dose 1 and Dose 3 ^[3]
End point description: Blood samples for analysis of serum leuprolide concentrations were collected at pre-determined time points throughout the trial (with full PK profiles after Dose 1 and Dose 3). The PK parameter, AUC _{tau} was derived for Doses 1 and 3 of the IMPs.	
End point type	Primary
End point timeframe: Days 0 and 56	

Notes:

[3] - 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 inferential statistical analysis was done for this primary endpoint.

End point values	CAM2032 3.75 mg	CAM2032 7.5 mg	Eligard 7.5 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	15	15	17	
Units: h*ng/mL				
geometric mean (geometric coefficient of variation)				
Dose 1 (n= 15, 15, 17)	329 (± 37.6)	622 (± 45.2)	397 (± 45.3)	
Dose 3 (n= 15, 15, 17)	343 (± 24.7)	757 (± 53.4)	460 (± 62.2)	

Statistical analyses

No statistical analyses for this end point

Secondary: Relative bioavailability of leuprolide following injections of the IMP for Dose 3

End point title	Relative bioavailability of leuprolide following injections of the IMP for Dose 3
End point description:	
Dose adjusted AUCtau values after Dose 3 were compared for CAM2032 and Eligard in the evaluation of relative bioavailability. The dose adjusted AUCtau values of CAM2032 3.75 mg and CAM2032 7.5 mg were merged in the comparison with Eligard. ANOVA of log transformed AUCtau adjusted for nominal dose, including treatment group and country as factors. The measure type number defined below is the ratio of relative bioavailability of leuprolide for CAM2032 vs Eligard.	
End point type	Secondary
End point timeframe:	
Day 56	

End point values	CAM2032/Eligard			
Subject group type	Subject analysis set			
Number of subjects analysed	47			
Units: percentage				
number (confidence interval 90%)	1.5 (1.19 to 1.9)			

Statistical analyses

No statistical analyses for this end point

Secondary: Profiles of testosterone concentration (ng/dL) following injections of the IMP

End point title	Profiles of testosterone concentration (ng/dL) following injections of the IMP
End point description:	
The Pharmacodynamic (PD) effects of leuprolide were assessed by measuring serum testosterone concentrations during the trial. The following PD variable was analyzed: The profiles of testosterone concentration (ng/dL) following injections of the IMP. Blood samples for analyses of serum testosterone	

concentrations were collected at Screening and on Days 0 to 126/early termination (ET).

End point type	Secondary
End point timeframe:	
Days 0 to 126/ET	

End point values	CAM2032 3.75 mg	CAM2032 7.5 mg	Eligard 7.5 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	15	15	17	
Units: ng/dL				
median (inter-quartile range (Q1-Q3))				
Day 0 (predose) (n= 15, 15, 17)	443 (369 to 546)	321 (269 to 439)	350 (240 to 465)	
Day 28 (predose) (n= 15, 15, 17)	20.9 (18.3 to 47)	24.5 (16.1 to 210)	18.1 (11.1 to 28.1)	
Day 56 (predose) (n= 15, 15, 17)	14.6 (10.7 to 19.3)	13.8 (7.8 to 22)	12 (9.29 to 15)	
Day 84 (n= 15, 15, 17)	14.8 (9.17 to 27.6)	10.6 (7.5 to 18.8)	12.4 (9.92 to 13.8)	
Day 126 (n= 15, 15, 17)	423 (258 to 526)	278 (124 to 470)	85.8 (16 to 280)	

Statistical analyses

No statistical analyses for this end point

Secondary: Time (days) to Testosterone Recovery after Dose 3

End point title	Time (days) to Testosterone Recovery after Dose 3
End point description:	
The PD effects of leuprolide were assessed by measuring serum testosterone during the trial. Time to testosterone recovery after last injection of the IMP. Blood samples for analyses of serum testosterone concentrations were collected at Screening and on Days 0 to 126/ET.	
End point type	Secondary
End point timeframe:	
Day 56	

End point values	CAM2032 3.75 mg	CAM2032 7.5 mg	Eligard 7.5 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	15	15	17	
Units: days				
arithmetic mean (standard deviation)	46.2 (± 13.6)	52.3 (± 20.6)	65 (± 5.7)	

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Prostate Specific Antigen (PSA) Concentration

End point title	Mean Prostate Specific Antigen (PSA) Concentration
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End point description:

The PD effects of leuprolide were assessed by measuring serum PSA concentrations during the trial. The following PD variable was analyzed: PSA (ng/mL) response to IMP. Blood samples for analyses of plasma PSA concentrations were collected at Screening and on Days 0 to 126/ET.

End point type	Secondary
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End point timeframe:

Days 0 to 126/ET

End point values	CAM2032 3.75 mg	CAM2032 7.5 mg	Eligard 7.5 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	15	15	17	
Units: ng/mL				
median (inter-quartile range (Q1-Q3))				
Day 0 (predose) (n= 15, 15, 17)	14.9 (5.8 to 85.4)	18.8 (9.6 to 93.5)	14.6 (4.7 to 32.9)	
Day 28 (predose) (n= 15, 15, 17)	9 (2.8 to 19)	8.3 (5.9 to 31.5)	4.6 (2.3 to 8)	
Day 56 (predose) (n= 15, 15, 17)	3.6 (1.1 to 8.4)	5.8 (1.1 to 11.2)	2.1 (0.8 to 4.1)	
Day 84 (n= 15, 15, 17)	2.3 (1.1 to 5.6)	2.6 (0.8 to 14)	1.6 (0.4 to 2.7)	
Day 126 (n= 15, 15, 17)	4.7 (2.9 to 19.9)	3.1 (1.5 to 19.1)	1.6 (0.5 to 3.8)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Participants were carefully monitored for the occurrence of adverse events during the trial from Day 0 to the completion of the follow-up visit (Day 126/early termination), up to 18 weeks.

Assessment type	Non-systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	17.0
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Reporting groups

Reporting group title	CAM2032 3.75 mg
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Reporting group description:

Participants were administered single subcutaneous buttock injections of CAM2032 3.75 mg on Days 0, 28 and 56.

Reporting group title	CAM2032 7.5 mg
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Reporting group description:

Participants were administered single subcutaneous buttock injections of CAM2032 7.5 mg on Days 0, 28 and 56.

Reporting group title	Eligard 7.5 mg
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Reporting group description:

Participants were administered single subcutaneous buttock injections of Eligard 7.5 mg on Days 0, 28 and 56.

Serious adverse events	CAM2032 3.75 mg	CAM2032 7.5 mg	Eligard 7.5 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 19 (0.00%)	1 / 15 (6.67%)	0 / 17 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Psychiatric disorders			
Disorientation			
subjects affected / exposed	0 / 19 (0.00%)	1 / 15 (6.67%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Calculus urinary			
subjects affected / exposed	0 / 19 (0.00%)	1 / 15 (6.67%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Urinary tract infection			

subjects affected / exposed	0 / 19 (0.00%)	1 / 15 (6.67%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	CAM2032 3.75 mg	CAM2032 7.5 mg	Eligard 7.5 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	14 / 19 (73.68%)	12 / 15 (80.00%)	10 / 17 (58.82%)
Vascular disorders			
Hot flush			
subjects affected / exposed	8 / 19 (42.11%)	4 / 15 (26.67%)	5 / 17 (29.41%)
occurrences (all)	8	4	5
Hypertension			
subjects affected / exposed	3 / 19 (15.79%)	1 / 15 (6.67%)	0 / 17 (0.00%)
occurrences (all)	3	1	0
Haematoma			
subjects affected / exposed	1 / 19 (5.26%)	0 / 15 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 19 (0.00%)	0 / 15 (0.00%)	2 / 17 (11.76%)
occurrences (all)	0	0	3
Injection site erythema			
subjects affected / exposed	0 / 19 (0.00%)	1 / 15 (6.67%)	0 / 17 (0.00%)
occurrences (all)	0	2	0
Fatigue			
subjects affected / exposed	0 / 19 (0.00%)	0 / 15 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Injection site nodule			
subjects affected / exposed	0 / 19 (0.00%)	1 / 15 (6.67%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Oedema peripheral			
subjects affected / exposed	0 / 19 (0.00%)	0 / 15 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Pain			

subjects affected / exposed occurrences (all)	0 / 19 (0.00%) 0	1 / 15 (6.67%) 1	0 / 17 (0.00%) 0
Reproductive system and breast disorders			
Prostatic pain			
subjects affected / exposed	1 / 19 (5.26%)	0 / 15 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Erectile dysfunction			
subjects affected / exposed	0 / 19 (0.00%)	1 / 15 (6.67%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Genital pain			
subjects affected / exposed	0 / 19 (0.00%)	0 / 15 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			
Epistaxis			
subjects affected / exposed	0 / 19 (0.00%)	1 / 15 (6.67%)	0 / 17 (0.00%)
occurrences (all)	0	2	0
Rhinitis allergic			
subjects affected / exposed	1 / 19 (5.26%)	0 / 15 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Dyspnoea			
subjects affected / exposed	0 / 19 (0.00%)	0 / 15 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 19 (0.00%)	0 / 15 (0.00%)	2 / 17 (11.76%)
occurrences (all)	0	0	2
Depressed mood			
subjects affected / exposed	0 / 19 (0.00%)	1 / 15 (6.67%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Investigations			
Blood creatine phosphokinase increased			
subjects affected / exposed	1 / 19 (5.26%)	0 / 15 (0.00%)	1 / 17 (5.88%)
occurrences (all)	1	0	1
Gamma-glutamyltransferase increased			

subjects affected / exposed	1 / 19 (5.26%)	0 / 15 (0.00%)	1 / 17 (5.88%)
occurrences (all)	1	0	1
Alanine aminotransferase increased			
subjects affected / exposed	1 / 19 (5.26%)	0 / 15 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Blood glucose increased			
subjects affected / exposed	1 / 19 (5.26%)	0 / 15 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Blood urine			
subjects affected / exposed	0 / 19 (0.00%)	0 / 15 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
C-reactive protein increased			
subjects affected / exposed	0 / 19 (0.00%)	0 / 15 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	3 / 19 (15.79%)	0 / 15 (0.00%)	1 / 17 (5.88%)
occurrences (all)	3	0	1
Ligament sprain			
subjects affected / exposed	1 / 19 (5.26%)	0 / 15 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Muscle strain			
subjects affected / exposed	0 / 19 (0.00%)	1 / 15 (6.67%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	1 / 19 (5.26%)	0 / 15 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Arrhythmia			
subjects affected / exposed	1 / 19 (5.26%)	0 / 15 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 19 (0.00%)	1 / 15 (6.67%)	3 / 17 (17.65%)
occurrences (all)	0	2	6
Sciatica			

subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 1	0 / 15 (0.00%) 0	0 / 17 (0.00%) 0
Syncope subjects affected / exposed occurrences (all)	0 / 19 (0.00%) 0	0 / 15 (0.00%) 0	1 / 17 (5.88%) 1
Eye disorders Vision blurred subjects affected / exposed occurrences (all)	0 / 19 (0.00%) 0	1 / 15 (6.67%) 1	1 / 17 (5.88%) 1
Conjunctival haemorrhage subjects affected / exposed occurrences (all)	0 / 19 (0.00%) 0	0 / 15 (0.00%) 0	1 / 17 (5.88%) 1
Eye pain subjects affected / exposed occurrences (all)	0 / 19 (0.00%) 0	1 / 15 (6.67%) 1	0 / 17 (0.00%) 0
Gastrointestinal disorders Nausea subjects affected / exposed occurrences (all)	4 / 19 (21.05%) 5	0 / 15 (0.00%) 0	0 / 17 (0.00%) 0
Diarrhoea subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 1	0 / 15 (0.00%) 0	0 / 17 (0.00%) 0
Inguinal hernia subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 1	0 / 15 (0.00%) 0	0 / 17 (0.00%) 0
Dry mouth subjects affected / exposed occurrences (all)	0 / 19 (0.00%) 0	1 / 15 (6.67%) 1	0 / 17 (0.00%) 0
Skin and subcutaneous tissue disorders Eczema subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 1	1 / 15 (6.67%) 1	0 / 17 (0.00%) 0
Renal and urinary disorders Urinary retention subjects affected / exposed occurrences (all)	0 / 19 (0.00%) 0	2 / 15 (13.33%) 2	2 / 17 (11.76%) 2
Haematuria			

subjects affected / exposed	1 / 19 (5.26%)	1 / 15 (6.67%)	0 / 17 (0.00%)
occurrences (all)	1	1	0
Nocturia			
subjects affected / exposed	0 / 19 (0.00%)	2 / 15 (13.33%)	0 / 17 (0.00%)
occurrences (all)	0	2	0
Haemorrhage urinary tract			
subjects affected / exposed	1 / 19 (5.26%)	0 / 15 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Micturition urgency			
subjects affected / exposed	1 / 19 (5.26%)	0 / 15 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Bladder pain			
subjects affected / exposed	0 / 19 (0.00%)	0 / 15 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Incontinence			
subjects affected / exposed	0 / 19 (0.00%)	0 / 15 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Urethral pain			
subjects affected / exposed	0 / 19 (0.00%)	1 / 15 (6.67%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 19 (0.00%)	3 / 15 (20.00%)	1 / 17 (5.88%)
occurrences (all)	0	4	1
Pain in extremity			
subjects affected / exposed	1 / 19 (5.26%)	1 / 15 (6.67%)	2 / 17 (11.76%)
occurrences (all)	1	1	2
Musculoskeletal pain			
subjects affected / exposed	1 / 19 (5.26%)	0 / 15 (0.00%)	1 / 17 (5.88%)
occurrences (all)	2	0	1
Arthralgia			
subjects affected / exposed	0 / 19 (0.00%)	2 / 15 (13.33%)	1 / 17 (5.88%)
occurrences (all)	0	2	1
Muscle spasms			

subjects affected / exposed	0 / 19 (0.00%)	1 / 15 (6.67%)	1 / 17 (5.88%)
occurrences (all)	0	1	1
Intervertebral disc disorder			
subjects affected / exposed	1 / 19 (5.26%)	0 / 15 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Myalgia			
subjects affected / exposed	1 / 19 (5.26%)	0 / 15 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Neck pain			
subjects affected / exposed	1 / 19 (5.26%)	0 / 15 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Bone pain			
subjects affected / exposed	0 / 19 (0.00%)	0 / 15 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Bursitis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 15 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Groin pain			
subjects affected / exposed	0 / 19 (0.00%)	1 / 15 (6.67%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 19 (0.00%)	0 / 15 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Infections and infestations			
Influenza			
subjects affected / exposed	3 / 19 (15.79%)	3 / 15 (20.00%)	1 / 17 (5.88%)
occurrences (all)	6	3	1
Abscess			
subjects affected / exposed	1 / 19 (5.26%)	0 / 15 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Bronchitis			
subjects affected / exposed	1 / 19 (5.26%)	0 / 15 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Gastroenteritis			
subjects affected / exposed	1 / 19 (5.26%)	0 / 15 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0

Localised infection			
subjects affected / exposed	1 / 19 (5.26%)	0 / 15 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Nasopharyngitis			
subjects affected / exposed	1 / 19 (5.26%)	0 / 15 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Sinusitis			
subjects affected / exposed	1 / 19 (5.26%)	0 / 15 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Gastroenteritis viral			
subjects affected / exposed	0 / 19 (0.00%)	0 / 15 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Herpes zoster			
subjects affected / exposed	0 / 19 (0.00%)	0 / 15 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Upper respiratory tract infection			
subjects affected / exposed	0 / 19 (0.00%)	1 / 15 (6.67%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Metabolism and nutrition disorders			
Hypercholesterolaemia			
subjects affected / exposed	1 / 19 (5.26%)	0 / 15 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
18 June 2014	This amendment was prepared after request from the Hungarian Authorities to add the analysis of HbA1c. In addition, changes to sampling time points for testosterone and time windows for deviations from sampling times were made. Minor errors in the text were also corrected.
26 November 2014	This amendment was issued to clarify the visit window of ± 1 day for the visits on Days 21, 49, 77, 84, 91, 98, 105, 112, 119, and 126, and to provide an updated instruction for the preparation of CAM2032 before administration (included in Appendix C in the clinical trial protocol).

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

The endpoints 1) days of suppression of s-T below 50 ng/dL after repeated injection of the study medication and 2) percentage of patients with s-T control escapes after injection of study medication were not investigated.

Notes: