Clinical trial results:
A Multi-Center, Randomized, Assessor-Blind, Controlled Trial Comparing the Occurrence of Major Adverse Cardiovascular Events (MACEs) in Patients with Prostate Cancer and Cardiovascular Disease Receiving Degarelix (GnRH Receptor Antagonist) or Leuprolide (GnRH Receptor Agonist)

Summary

EudraCT number	2017-002495-20
Trial protocol	SK CZ DE GB FR GR FI PL
Global end of trial date	29 March 2021

Results information

Result version number	v1 (current)
This version publication date	06 April 2022
First version publication date	06 April 2022

Trial information

Trial identification

Sponsor protocol code	000108

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02663908
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Ferring Pharmaceuticals A/S
Sponsor organisation address	International PharmaScience Center, Amager Strandvej 405, Kastrup, Denmark, 2770
Public contact	Global Clinical Compliance, Ferring Pharmaceuticals, DK0-Disclosure@ferring.com
Scientific contact	Global Clinical Compliance, Ferring Pharmaceuticals, DK0-Disclosure@ferring.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	27 May 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	29 March 2021
Global end of trial reached?	Yes
Global end of trial date	29 March 2021
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objective is to assess the effect of a gonadotropin-releasing hormone (GnRH) receptor antagonist (degarelix) on the risk of occurrence of major adverse cardiovascular events (MACEs) (a composite of death due to any cause, non-fatal myocardial infarction or non-fatal stroke) as compared to a GnRH receptor agonist (leuprolide) in subjects with prostate cancer and concomitant cardiovascular disease (CVD).

Protection of trial subjects:

The trial was performed in compliance with International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) guideline on Good Clinical Practice (GCP).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	19 April 2016
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: 8
Country: Number of subjects enrolled	Slovakia: 82
Country: Number of subjects enrolled	United Kingdom: 15
Country: Number of subjects enrolled	Czechia: 47
Country: Number of subjects enrolled	Finland: 1
Country: Number of subjects enrolled	France: 30
Country: Number of subjects enrolled	Germany: 19
Country: Number of subjects enrolled	Greece: 30
Country: Number of subjects enrolled	Canada: 51
Country: Number of subjects enrolled	United States: 213
Country: Number of subjects enrolled	South Africa: 2
Country: Number of subjects enrolled	Russian Federation: 47
Worldwide total number of subjects	545
EEA total number of subjects	217

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)	64
From 65 to 84 years	450
85 years and over	31

Subject disposition

Recruitment

Recruitment details:

The trial was performed at 113 investigational sites in 12 countries between Apr 2016 to Mar 2021.

Pre-assignment

Screening details:

In total, 702 subjects were screened of which 545 subjects were randomised. Of the randomised subjects, 544 subjects were exposed to investigational medicinal product (IMP): 275 to Degarelix and 269 to Leuprolide. One subject was randomised in error and was not exposed to IMP.

Period 1

Period 1 title	Randomised Treatment Period (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Single blind
Roles blinded	Assessor[1]

Blinding implementation details:

A true double-blind design was considered difficult to apply, most importantly because of factors such as different doses and treatment regimens as well as expected differences in incidence of injection-site reactions. Instead, an assessor-blinded design was applied.

Arms

Are arms mutually exclusive?	Yes
Arm title	Degarelix 240 mg/80 mg

Arm description:

Degarelix 240 mg/80 mg: Degarelix at a starting dose of 240 mg administered as two subcutaneous (SC) depot injections, each containing 120 mg of degarelix; followed by up to 11 maintenance doses of 80 mg degarelix administered as single SC depot injections at monthly (28-day) intervals.

Arm type	Experimental
Investigational medicinal product name	Degarelix 240 mg/80 mg
Investigational medicinal product code	
Other name	FIRMAGON
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Degarelix 240 mg/80 mg: Degarelix at a starting dose of 240 mg administered as two subcutaneous (SC) depot injections, each containing 120 mg of degarelix; followed by up to 11 maintenance doses of 80 mg degarelix administered as single SC depot injections at monthly (28-day) intervals.

Arm title	Leuprolide 22.5 mg

Arm description:

Leuprolide 22.5 mg: Leuprolide at dose of 22.5 mg administered as intramuscular depot injection every 3 months throughout the trial.

Arm type	Active comparator
Investigational medicinal product name	Leuprolide 22.5 mg
Investigational medicinal product code	
Other name	LUPRON DEPOT
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Leuprolide at dose of 22.5 mg administered as intramuscular depot injection every 3 months throughout the trial.

Notes:

[1] - The roles blinded appear inconsistent with a simple blinded trial.

Justification: A true double-blind design was considered difficult to apply, most importantly because of factors such as different doses and treatment regimens as well as expected differences in incidence of injection-site reactions. Instead, an assessor-blinded design was implemented.

Number of subjects in period 1[2]	Degarelix 240 mg/80 mg	Leuprolide 22.5 mg
Started	275	269
Completed	244	245
Not completed	31	24
Consent withdrawn by subject	8	5
Lack of therapeutic response	2	-
Adverse event, non-fatal	13	11
Protocol violation	1	2
COVID-19	1	-
Death	1	-
Subject discontinued treatment	-	1
Subject ended trial (prohibited medication)	1	-
Intolerance to FIRMAGON therapy	1	-
Site closed	1	-
Lost to follow-up	1	5
Subject treated with an exclusionary medication	1	-

Notes:

[2] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: In total, 702 subjects were screened of which 545 subjects were randomised. Of the randomised subjects, 544 subjects were exposed to the IMP: 275 to Degarelix and 269 to Leuprolide. One subject was randomised in error and did not receive the IMP.

Baseline characteristics

Reporting groups	
Reporting group title	Degarelix 240 mg/80 mg
Reporting group description:	
Degarelix 240 mg/80 mg: Degarelix at a starting dose of 240 mg administered as two subcutaneous (SC) depot injections, each containing 120 mg of degarelix; followed by up to 11 maintenance doses of 80 mg degarelix administered as single SC depot injections at monthly (28-day) intervals.	

Reporting group title	Leuprolide 22.5 mg
Reporting group description:	
Leuprolide 22.5 mg: Leuprolide at dose of 22.5 mg administered as intramuscular depot injection every 3 months throughout the trial.	

Reporting group values	Degarelix 240 mg/80 mg	Leuprolide 22.5 mg	Total
Number of subjects	275	269	544
Age categorical Units: Subjects			
< 75 years	153	151	304
>= 75 years	122	118	240
Age continuous Units: years			
arithmetic mean	73.3	73.1	
standard deviation	± 7.28	± 7.16	-
Gender categorical Units: Subjects			
Female	0	0	0
Male	275	269	544
Ethnicity Units: Subjects			
Hispanic or Latino	16	14	30
Not Hispanic or Latino	256	254	510
Unknown or Not Reported	3	1	4
Stage of prostate cancer Units: Subjects			
Localised	138	133	271
Locally Advanced	63	80	143
Metastatic	63	48	111
Not classifiable	11	8	19
Race Units: Subjects			
American Indian or Alaska Native	2	0	2
Asian	3	5	8
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	16	12	28
White	252	251	503
Unknown or Not Reported	2	1	3
Eastern Cooperative Oncology Group			

(ECOG) performance score Units: Subjects			
0 score	178	167	345
1 score	75	80	155
2 score	8	11	19
Unknown or Not Reported	14	11	25
Baseline body mass index (BMI)			
Degarelix 240 mg/80 mg: n=273; Leuprolide 22.5 mg: n=268			
Units: kg/m^2			
arithmetic mean	28.38	28.58	
standard deviation	± 5.057	± 4.589	-
Testosterone levels			
Degarelix 240 mg/80 mg: n=274			
Units: ng/dL			
arithmetic mean	353.6	351.6	
standard deviation	± 150.49	± 140.32	-
Prostate Specific Antigen (PSA)			
Leuprolide 22.5 mg: n=268			
Units: ng/mL			
arithmetic mean	119.7	59.9	
standard deviation	± 472.10	± 236.68	-

End points

End points reporting groups

Reporting group title	Degarelix 240 mg/80 mg

Reporting group description:

Degarelix 240 mg/80 mg: Degarelix at a starting dose of 240 mg administered as two subcutaneous (SC) depot injections, each containing 120 mg of degarelix; followed by up to 11 maintenance doses of 80 mg degarelix administered as single SC depot injections at monthly (28-day) intervals.

Reporting group title	Leuprolide 22.5 mg

Reporting group description:

Leuprolide 22.5 mg: Leuprolide at dose of 22.5 mg administered as intramuscular depot injection every 3 months throughout the trial.

Subject analysis set title	Full analysis set (FAS)
Subject analysis set type	Full analysis

Subject analysis set description:

The FAS consisted of all randomised and treated subjects (who received at least one dose of IMP) and was analysed based on the planned (randomised) treatment.

Primary: Time From Randomisation to the First Confirmed (Adjudicated) Occurrence of the Composite MACE Endpoint; Percentage of Observed Subjects With Outcome Measure Events During the Trial

End point title	Time From Randomisation to the First Confirmed (Adjudicated) Occurrence of the Composite MACE Endpoint; Percentage of Observed Subjects With Outcome Measure Events During the Trial

End point description:

Composite MACE endpoint was defined as: death due to any cause, non-fatal myocardial infarction or non-fatal stroke.

Kaplan Meier plots of the cumulative incidence rate by treatment groups were used to depict first confirmed (adjudicated) occurrence of composite MACE over time. Percentage of observed subjects with outcome measure events during the trial are reported.

Subjects were censored at the time a subject discontinued the trial, was lost to follow-up, discontinued treatment with IMP, initiated treatment with prohibited medication (including hormonal combination therapy), or at Day 336, whichever occurred first.

The analysis population consisted of the FAS which comprised all randomised and treated subjects (who received at least one dose of IMP) and was analysed based on the planned (randomised) treatment.

End point type	Primary

End point timeframe:

Randomisation to Day 336 (end-of-trial)

End point values	Degarelix 240 mg/80 mg	Leuprolide 22.5 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	275	269		
Units: percentage of subjects				
number (not applicable)	5.5	4.1		

Statistical analyses

Statistical analysis title	Degarelix 240 mg/80 mg, Leuprolide 22.5 mg
Comparison groups	Degarelix 240 mg/80 mg v Leuprolide 22.5 mg
Number of subjects included in analysis	544
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.5294 [1]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.283
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.589
upper limit	2.794

Notes:

[1] - The p-value of the log-rank test is based on comparison of the treatment groups stratified for age group and region.

Secondary: Time From Randomisation to the First Confirmed (Adjudicated) Occurrence of Cardiovascular (CV)-Related Death, Non-fatal Myocardial Infarction, Non-fatal Stroke; Percentage of Observed Subjects With Outcome Measure Events During the Trial

End point title	Time From Randomisation to the First Confirmed (Adjudicated) Occurrence of Cardiovascular (CV)-Related Death, Non-fatal Myocardial Infarction, Non-fatal Stroke; Percentage of Observed Subjects With Outcome Measure Events During the Trial

End point description:

Kaplan Meier plots of the cumulative incidence rate by treatment groups were used to depict confirmed (adjudicated) occurrence of CV-related death, non-fatal myocardial infarction, non-fatal stroke. Percentage of observed subjects with outcome measure events during the trial are reported.

Subjects were censored at the time a subject discontinued the trial, was lost to follow-up, discontinued treatment with IMP, initiated treatment with prohibited medication (including hormonal combination therapy), or at Day 336, whichever occurred first.

The analysis population consisted of the FAS which comprised all randomised and treated subjects (who received at least one dose of IMP) and was analysed based on the planned (randomised) treatment.

End point type	Secondary

End point timeframe:

Randomisation to Day 336 (end-of-trial)

End point values	Degarelix 240 mg/80 mg	Leuprolide 22.5 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	275	269		
Units: percentage of subjects				
number (not applicable)	3.3	2.6		

Statistical analyses

Statistical analysis title	Degarelix 240 mg/80 mg, Leuprolide 22.5 mg
Comparison groups	Degarelix 240 mg/80 mg v Leuprolide 22.5 mg
Number of subjects included in analysis	544
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.7126
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.204
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.448
upper limit	3.234

Secondary: Time From Randomisation to Confirmed (Adjudicated) CV-related Death; Percentage of Observed Subjects With Outcome Measure Events During the Trial

End point title	Time From Randomisation to Confirmed (Adjudicated) CV-related Death; Percentage of Observed Subjects With Outcome Measure Events During the Trial

End point description:

Kaplan Meier plots of the cumulative incidence rate by treatment groups were used to depict confirmed (adjudicated) CV-related death. Percentage of observed subjects with outcome measure events during the trial are reported. Percentage of observed subjects with outcome measure events during the trial are reported.

Subjects were censored at the time a subject discontinued the trial, was lost to follow-up, discontinued treatment with IMP, initiated treatment with prohibited medication (including hormonal combination therapy), or at Day 336, whichever occurred first.

The analysis population consisted of the FAS which comprised all randomised and treated subjects (who received at least one dose of IMP) and was analysed based on the planned (randomised) treatment.

End point type	Secondary

End point timeframe:

Randomisation to Day 336 (end-of-trial)

End point values	Degarelix 240 mg/80 mg	Leuprolide 22.5 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	275	269		
Units: percentage of subjects				
number (not applicable)	0.4	1.9		

Statistical analyses

Statistical analysis title	Degarelix 240 mg/80 mg, Leuprolide 22.5 mg
Comparison groups	Degarelix 240 mg/80 mg v Leuprolide 22.5 mg
Number of subjects included in analysis	544
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0853
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.186
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.022
upper limit	1.595

Secondary: Time From Randomisation to the First Confirmed (Adjudicated) Myocardial Infarction; Percentage of Observed Subjects With Outcome Measure Events During the Trial

End point title	Time From Randomisation to the First Confirmed (Adjudicated) Myocardial Infarction; Percentage of Observed Subjects With Outcome Measure Events During the Trial

End point description:

Kaplan Meier plots of the cumulative incidence rate by treatment groups were used to depict first confirmed (adjudicated) myocardial infarction. Percentage of observed subjects with outcome measure events during the trial are reported.

Subjects were censored at the time a subject discontinued the trial, was lost to follow-up, discontinued treatment with IMP, initiated treatment with prohibited medication (including hormonal combination therapy), or at Day 336, whichever occurred first.

The analysis population consisted of the FAS which comprised all randomised and treated subjects (who received at least one dose of IMP) and was analysed based on the planned (randomised) treatment.

End point type	Secondary

End point timeframe:

Randomisation to Day 336 (end-of-trial)

End point values	Degarelix 240 mg/80 mg	Leuprolide 22.5 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	275	269		
Units: percentage of subjects				
number (not applicable)	1.8	1.1		

Statistical analyses

Statistical analysis title	Degarelix 240 mg/80 mg, Leuprolide 22.5 mg
Comparison groups	Degarelix 240 mg/80 mg v Leuprolide 22.5 mg
Number of subjects included in analysis	544
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.5196
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.594
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.381
upper limit	6.673

Secondary: Time From Randomisation to the First Confirmed (Adjudicated) Stroke; Percentage of Observed Subjects With Outcome Measure Events During the Trial

End point title	Time From Randomisation to the First Confirmed (Adjudicated) Stroke; Percentage of Observed Subjects With Outcome Measure Events During the Trial

End point description:

Kaplan Meier plots of the cumulative incidence rate by treatment groups were used to depict first confirmed (adjudicated) stroke. Percentage of observed subjects with outcome measure events during the trial are reported.

Subjects were censored at the time a subject discontinued the trial, was lost to follow-up, discontinued treatment with IMP, initiated treatment with prohibited medication (including hormonal combination therapy), or at Day 336, whichever occurred first.

The analysis population consisted of the FAS which comprised all randomised and treated subjects (who received at least one dose of IMP) and was analysed based on the planned (randomised) treatment.

End point type	Secondary

End point timeframe:

Randomisation to Day 336 (end-of-trial)

End point values	Degarelix 240 mg/80 mg	Leuprolide 22.5 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	275	269		
Units: percentage of subjects				
number (not applicable)	1.1	1.1		

Statistical analyses

Statistical analysis title	Degarelix 240 mg/80 mg, Leuprolide 22.5 mg
Comparison groups	Degarelix 240 mg/80 mg v Leuprolide 22.5 mg
Number of subjects included in analysis	544
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.8966
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.899
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.181
upper limit	4.457

Secondary: Time From Randomisation to the First Confirmed (Adjudicated) Unstable Angina Requiring Hospitalisation; Percentage of Observed Subjects With Outcome Measure Events During the Trial

End point title	Time From Randomisation to the First Confirmed (Adjudicated) Unstable Angina Requiring Hospitalisation; Percentage of Observed Subjects With Outcome Measure Events During the Trial

End point description:

Kaplan Meier plots of the cumulative incidence rate by treatment groups were used to depict first confirmed (adjudicated) unstable angina requiring hospitalisation. Percentage of observed subjects with outcome measure events during the trial are reported.

Subjects were censored at the time a subject discontinued the trial, was lost to follow-up, discontinued treatment with IMP, initiated treatment with prohibited medication (including hormonal combination therapy), or at Day 336, whichever occurred first.

The analysis population consisted of the FAS which comprised all randomised and treated subjects (who received at least one dose of IMP) and was analysed based on the planned (randomised) treatment.

End point type	Secondary

End point timeframe:

Randomisation to Day 336 (end-of-trial)

End point values	Degarelix 240 mg/80 mg	Leuprolide 22.5 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	275	269		
Units: percentage of subjects				
number (not applicable)	0.7	1.5		

Statistical analyses

Statistical analysis title	Degarelix 240 mg/80 mg, Leuprolide 22.5 mg
Comparison groups	Degarelix 240 mg/80 mg v Leuprolide 22.5 mg
Number of subjects included in analysis	544
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.3857
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.48
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.088
upper limit	2.62

Secondary: Time From Randomisation to Death Due to Any Cause; Percentage of Observed Subjects With Outcome Measure Events During the Trial

End point title	Time From Randomisation to Death Due to Any Cause; Percentage of Observed Subjects With Outcome Measure Events During the Trial

End point description:

Kaplan Meier plots of the cumulative incidence rate by treatment groups were used to depict death due to any cause. Percentage of observed subjects with outcome measure events during the trial are reported.

Subjects were censored at the time a subject discontinued the trial, was lost to follow-up, discontinued treatment with IMP, initiated treatment with prohibited medication (including hormonal combination therapy), or at Day 336, whichever occurred first.

The analysis population consisted of the FAS which comprised all randomised and treated subjects (who received at least one dose of IMP) and was analysed based on the planned (randomised) treatment.

End point type	Secondary

End point timeframe:

Randomisation to Day 336 (end-of-trial)

End point values	Degarelix 240 mg/80 mg	Leuprolide 22.5 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	275	269		
Units: percentage of subjects				
number (not applicable)	2.9	3.3		

Statistical analyses

Statistical analysis title	Degarelix 240 mg/80 mg, Leuprolide 22.5 mg
Comparison groups	Degarelix 240 mg/80 mg v Leuprolide 22.5 mg
Number of subjects included in analysis	544
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.718
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.839
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.324
upper limit	2.176

Secondary: Testosterone Levels at Days 28, 168 and 336 in the Degarelix and Leuprolide treatment groups

End point title	Testosterone Levels at Days 28, 168 and 336 in the Degarelix and Leuprolide treatment groups

End point description:

Median levels and interquartile ranges for serum testosterone at Days 28, 168, and 336 are presented.

The analysis population consisted of the FAS which comprised all randomised and treated subjects (who received at least one dose of IMP) and was analysed based on the planned (randomised) treatment.

End point type	Secondary

End point timeframe:

Days 28, 168 and 336 (end-of-trial)

Degarelix 240 mg/80 mg: Day 28 (n=264) , Day 168 (n=247) , Day 336 (n=234)
Leuprolide 22.5 mg: Day 28 (n=257) , Day 168 (n=248) , Day 336 (n=228)

End point values	Degarelix 240 mg/80 mg	Leuprolide 22.5 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	275	269		
Units: ng/dL				
median (inter-quartile range (Q1-Q3))				

Day 28	8.650 (6.810 to 13.960)	14.410 (10.910 to 20.170)		
Day 168	8.650 (5.760 to 12.750)	8.475 (5.760 to 11.530)		
Day 336	9.855 (5.760 to 14.410)	8.650 (5.760 to 11.530)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time From Randomisation to Failure in Progression-free Survival (PFS); Percentage of Observed Subjects With Outcome Measure Events During the Trial

End point title	Time From Randomisation to Failure in Progression-free Survival (PFS); Percentage of Observed Subjects With Outcome Measure Events During the Trial

End point description:

Time to failure in PFS was defined as the time, measured in days, from randomisation to the first occurrence of either death, radiographic disease progression, introduction of additional prostate cancer therapies for progression, or PSA failure.

Subjects who discontinued treatment with IMP or withdrew from the trial were censored at the time of discontinuation/withdrawal.

Kaplan Meier plots of the cumulative incidence rate by treatment groups were used to depict failure in PFS. Percentage of observed subjects with outcome measure events during the trial are reported.

The analysis population consisted of the FAS which comprised all randomised and treated subjects (who received at least one dose of IMP) and was analysed based on the planned (randomised) treatment.

End point type	Secondary

End point timeframe:

From randomisation to end-of-trial for each subject (subjects not censored at Day 336)

End point values	Degarelix 240 mg/80 mg	Leuprolide 22.5 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	275	269		
Units: percentage of subjects				
number (not applicable)	8.7	10.0		

Statistical analyses

Statistical analysis title	Degarelix 240 mg/80 mg, Leuprolide 22.5 mg
Comparison groups	Degarelix 240 mg/80 mg v Leuprolide 22.5 mg

Number of subjects included in analysis	544
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.6701
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.887
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.512
upper limit	1.539

Secondary: Changes From Baseline in International Prostate Symptom Score (IPSS) Total and Quality of Life (QoL) Scores

End point title	Changes From Baseline in International Prostate Symptom Score (IPSS) Total and Quality of Life (QoL) Scores

End point description:

Lower urinary tract symptoms were measured with the IPSS Version 1 (IPSS-1). The IPSS is a subject-administered questionnaire containing seven items to evaluate symptoms of urinary obstruction (incomplete emptying, frequency, intermittency, urgency, weak stream, straining, nocturia) over the preceding week. Each urinary symptom question was assigned points from 0 to 5 indicating increasing severity of the particular symptom. The total IPSS-1 score was then calculated as summation over the responses for all 7 questions. The total IPSS-1 score was transformed to a scale from 0 (lowest score) to 100 (highest score). Higher scores reflect higher severity of symptoms. The IPSS-1 included an additional single question to assess a subject's QoL in relation to his urinary symptoms; response to this question was analysed separately and was not included in the total IPSS score. The score was similarly scaled from 0 to 100.

Change from baseline in IPSS Total and QoL scores are presented.

End point type	Secondary

End point timeframe:

Baseline to Days 168 and 336 (end-of-trial)

Degarelix: 240 mg/80 mg: Day 168 (n=234), Day 336 (n=195)
Leuprolide 22.5 mg: Day 168 (n=232), Day 336 (n=191)

End point values	Degarelix 240 mg/80 mg	Leuprolide 22.5 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	234	232		
Units: score on a scale				
least squares mean (confidence interval 95%)				
IPSS Total at Day 168	-0.000 (-0.804 to 0.804)	0.907 (0.098 to 1.715)		
IPSS, QoL at Day 168	-0.115 (-0.298 to 0.068)	0.098 (-0.086 to 0.282)		
IPSS Total at Day 336	-0.795 (-1.619 to 0.029)	0.121 (-0.712 to 0.953)		
IPSS, QoL at Day 336	-0.281 (-0.467 to -0.095)	-0.234 (-0.422 to -0.046)		

Statistical analyses

Statistical analysis title	Degarelix 240 mg/80 mg, Leuprolide 22.5 mg
Statistical analysis description: IPSS Total at Day 168	
Comparison groups	Degarelix 240 mg/80 mg v Leuprolide 22.5 mg
Number of subjects included in analysis	466
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.1193
Method	ANCOVA
Parameter estimate	Treatment difference
Point estimate	-0.907
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.048
upper limit	0.235

Statistical analysis title	Degarelix 240 mg/80 mg, Leuprolide 22.5 mg
Statistical analysis description: IPSS, QoL at Day 168	
Comparison groups	Leuprolide 22.5 mg v Degarelix 240 mg/80 mg
Number of subjects included in analysis	466
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.108
Method	ANCOVA
Parameter estimate	Treatment difference
Point estimate	-0.213
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.473
upper limit	0.047

Statistical analysis title	Degarelix 240 mg/80 mg, Leuprolide 22.5 mg

Statistical analysis description:
IPSS Total at Day 336

n=386

Comparison groups	Degarelix 240 mg/80 mg v Leuprolide 22.5 mg
Number of subjects included in analysis	466
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.1256
Method	ANCOVA
Parameter estimate	Treatment Difference
Point estimate	-0.916
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.089
upper limit	0.257

Statistical analysis title	Degarelix 240 mg/80 mg, Leuprolide 22.5 mg

Statistical analysis description:

IPSS, QoL at Day 336

n=386

Comparison groups	Degarelix 240 mg/80 mg v Leuprolide 22.5 mg
Number of subjects included in analysis	466
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.7261
Method	ANCOVA
Parameter estimate	Treatment Difference
Point estimate	-0.047
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.312
upper limit	0.218

Secondary: Total Number of CV-related Hospitalisation Events Over the Duration of the Trial

End point title	Total Number of CV-related Hospitalisation Events Over the Duration of the Trial

End point description:

The total number of CV-related hospitalisations over the duration of the trial was defined as the number of hospitalisations due to CV-related adverse events, observed from the first exposure to IMP up until Day 336 for each subject.

End point type	Secondary

End point timeframe:

First dose of IMP to Day 336 (end-of-trial)

End point values	Degarelix 240 mg/80 mg	Leuprolide 22.5 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	275	269		
Units: Number of events				
number (not applicable)				
Subjects with events	12	14		
Events	15	17		

Statistical analyses

No statistical analyses for this end point

Secondary: Total Number of Coronary Artery By-pass Grafting (CABG) or Percutaneous Coronary Intervention (PCI) Procedures Over the Duration of the Trial

End point title	Total Number of Coronary Artery By-pass Grafting (CABG) or Percutaneous Coronary Intervention (PCI) Procedures Over the Duration of the Trial

End point description:

The total number of CABG or PCI procedures observed for each subject over the duration of the trial

End point type	Secondary

End point timeframe:

First dose of IMP to Day 336 (end-of-trial)

End point values	Degarelix 240 mg/80 mg	Leuprolide 22.5 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	275	269		
Units: Number of events				
number (not applicable)				
Subjects with events	2	4		
Events	3	6		

Statistical analyses

No statistical analyses for this end point

Secondary: Total Number of CV-related Emergency Room (ER) Visit Events Over the Duration of the Trial

End point title	Total Number of CV-related Emergency Room (ER) Visit Events Over the Duration of the Trial

End point description:

CV-related ER visit events (that did not lead to hospitalisation) was observed from the first exposure to IMP up until Day 336 for each subject.

End point type	Secondary

End point timeframe:

First dose of IMP to Day 336 (end-of-trial)

End point values	Degarelix 240 mg/80 mg	Leuprolide 22.5 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	275	269		
Units: Number of events				
number (not applicable)				
Subjects with events	8	2		
Events	8	2		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Utility, Based on EuroQol Group 5 Dimensions 5 Levels Questionnaire (EQ-5D-5L)

End point title	Change in Utility, Based on EuroQol Group 5 Dimensions 5 Levels Questionnaire (EQ-5D-5L)

End point description:

The EQ-5D-5L essentially consists of 2 systems - the EQ-5D-5L descriptive system and the EQ visual analogue scale (EQ VAS). The EQ-5D-5L descriptive system comprises the following 5 dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. The EQ VAS is an overall estimation of the present health status. The results from the EQ-5D-5L questionnaire were converted into quality adjusted life year (QALY) units.

The analysis population consisted of the FAS which comprised all randomised and treated subjects (who received at least one dose of IMP) and was analysed based on the planned (randomised) treatment.

End point type	Secondary

End point timeframe:

Baseline to Day 336 (end-of-trial)

End point values	Degarelix 240 mg/80 mg	Leuprolide 22.5 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	243	239		
Units: QALY				
least squares mean (confidence interval 95%)	0.794 (0.770 to 0.818)	0.796 (0.772 to 0.820)		

Statistical analyses

Statistical analysis title	Degarelix 240 mg/80 mg, Leuprolide 22.5 mg
Comparison groups	Degarelix 240 mg/80 mg v Leuprolide 22.5 mg
Number of subjects included in analysis	482
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.911
Method	ANCOVA
Parameter estimate	Treatment difference
Point estimate	-0.002
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.036
upper limit	0.032

Secondary: Changes From Baseline in Duke Activity Status Index (DASI) Global Score

End point title	Changes From Baseline in Duke Activity Status Index (DASI) Global Score

End point description:

The DASI is a self-administered instrument developed to measure functional capacity in subjects with CVD. It contains 12 items referring to the present time, assessing the ability to perform physical tasks in five domains: personal care (1 item), ambulation (4 items), household tasks (4 items), sexual function (1 item) and recreation (2 items). Each question was answered by one of four options: 'yes with no difficulty' / 'yes, but with some difficulty' / 'no, I can't do this' / 'don't do this for other reasons'. A global score was calculated with a higher score indicating a higher functional capacity.

Change from baseline in DASI Global score is presented.

The analysis population consisted of the FAS which comprised all randomised and treated subjects (who received at least one dose of IMP) and was analysed based on the planned (randomised) treatment.

End point type	Secondary

End point timeframe:

Baseline to Days 168 and 336 (end-of-trial)

Degarelix 240 mg/80 mg: Day 168 (n=234), Day 336 (n=195)
Leuprolide 22.5 mg: Day 168 (n=232), Day 336 (n=191)

End point values	Degarelix 240 mg/80 mg	Leuprolide 22.5 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	234	232		
Units: score on a scale				
least squares mean (confidence interval 95%)				
Change in DASI to Day 168	-2.65 (-3.95 to -1.35)	-1.08 (-2.38 to 0.23)		
Change in DASI to Day 336	-2.18 (-3.54 to -0.81)	-3.01 (-4.39 to -1.63)		

Statistical analyses

Statistical analysis title	Degarelix 240 mg/80 mg, Leuprolide 22.5 mg Day 168
Statistical analysis description: DASI at Day 168	
Comparison groups	Degarelix 240 mg/80 mg v Leuprolide 22.5 mg
Number of subjects included in analysis	466
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0936
Method	ANCOVA
Parameter estimate	Treatment difference
Point estimate	-1.57
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.41
upper limit	0.27

Statistical analysis title	Degarelix 240 mg/80 mg, Leuprolide 22.5 mg Day 336
Statistical analysis description: DASI at Day 336 n=386	
Comparison groups	Degarelix 240 mg/80 mg v Leuprolide 22.5 mg
Number of subjects included in analysis	466
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.4
Method	ANCOVA
Parameter estimate	Treatment Difference
Point estimate	0.84
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.11
upper limit	2.78

Secondary: Changes From Baseline in Cardiac Anxiety Questionnaire (CAQ) Global Score and Score Per Domain

End point title	Changes From Baseline in Cardiac Anxiety Questionnaire (CAQ)

	Global Score and Score Per Domain

End point description:

The CAQ is a self-administered questionnaire developed to measure heart-focused anxiety in persons with or without heart disease. It contains 18 items referring to the present time assessing cardiac anxiety in three domains: fear (8 items), avoidance (5 items) and attention (5 items). Each question was assigned a score between 0 "never" to 4 "always". A global score and scores per domain was computed with higher score indicating greater cardiac anxiety.

Change from baseline in CAQ Global score and score per domain are presented.

The analysis population consisted of the FAS which comprised all randomised and treated subjects (who received at least one dose of IMP) and was analysed based on the planned (randomised) treatment.

End point type	Secondary

End point timeframe:

Baseline to Days 168 and 336 (end-of-trial)

Degarelix 240 mg/80 mg: Day 168 (n=234), Day 336 (n=195)
Leuprolide 22.5 mg: Day 168 (n=232), Day 336 (n=191)

End point values	Degarelix 240 mg/80 mg	Leuprolide 22.5 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	234	232		
Units: score on a scale				
least squares mean (confidence interval 95%)				
CAQ Global Score (Day 168)	0.034 (-0.021 to 0.088)	-0.011 (-0.066 to 0.044)		
CAQ domain score for Attention (Day 168)	0.030 (-0.034 to 0.094)	-0.006 (-0.070 to 0.059)		
CAQ domain score for Avoidance (Day 168)	0.155 (0.062 to 0.248)	0.039 (-0.054 to 0.133)		
CAQ domain score for Fear (Day 168)	-0.036 (-0.106 to 0.034)	-0.048 (-0.119 to 0.022)		
CAQ Global Score (Day 336)	0.102 (0.043 to 0.161)	0.051 (-0.009 to 0.110)		
CAQ domain score for Attention (Day 336)	0.023 (-0.046 to 0.092)	-0.015 (-0.085 to 0.054)		
CAQ domain score for Avoidance (Day 336)	0.228 (0.130 to 0.325)	0.220 (0.122 to 0.319)		
CAQ domain score for Fear (Day 336)	0.075 (-0.003 to 0.153)	-0.018 (-0.097 to 0.061)		

Statistical analyses

Statistical analysis title	Degarelix 240 mg/80 mg, Leuprolide 22.5 mg

Statistical analysis description:

CAQ global score at Day 168

Comparison groups	Degarelix 240 mg/80 mg v Leuprolide 22.5 mg

Number of subjects included in analysis	466
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.2535
Method	ANCOVA
Parameter estimate	Treatment difference
Point estimate	0.045
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.032
upper limit	0.122

Statistical analysis title	Degarelix 240 mg/80 mg, Leuprolide 22.5 mg
Statistical analysis description: CAQ domain score for Attention at Day 168	
Comparison groups	Degarelix 240 mg/80 mg v Leuprolide 22.5 mg
Number of subjects included in analysis	466
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.437
Method	ANCOVA
Parameter estimate	Treatment difference
Point estimate	0.036
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.055
upper limit	0.127

Statistical analysis title	Degarelix 240 mg/80 mg, Leuprolide 22.5 mg
Statistical analysis description: CAQ domain score for Avoidance at Day 168	
Comparison groups	Degarelix 240 mg/80 mg v Leuprolide 22.5 mg
Number of subjects included in analysis	466
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0852
Method	ANCOVA
Parameter estimate	Treatment difference
Point estimate	0.116
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.016
upper limit	0.248

Statistical analysis title	Degarelix 240 mg/80 mg, Leuprolide 22.5 mg
Statistical analysis description: CAQ domain score for Fear at Day 168	
Comparison groups	Degarelix 240 mg/80 mg v Leuprolide 22.5 mg
Number of subjects included in analysis	466
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.8156
Method	ANCOVA
Parameter estimate	Treatment difference
Point estimate	0.012
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.087
upper limit	0.111

Statistical analysis title	Degarelix 240 mg/80 mg, Leuprolide 22.5 mg
Statistical analysis description: CAQ Global Score at Day 336 n=386	
Comparison groups	Degarelix 240 mg/80 mg v Leuprolide 22.5 mg
Number of subjects included in analysis	466
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.2299
Method	ANCOVA
Parameter estimate	Treatment Difference
Point estimate	0.051
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.033
upper limit	0.135

Statistical analysis title	Degarelix 240 mg/80 mg, Leuprolide 22.5 mg
Statistical analysis description: CAQ domain score for Attention at Day 336 n=386	
Comparison groups	Degarelix 240 mg/80 mg v Leuprolide 22.5 mg

Number of subjects included in analysis	466
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.444
Method	ANCOVA
Parameter estimate	Treatment Difference
Point estimate	0.038
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.06
upper limit	0.136

Statistical analysis title	Degarelix 240 mg/80 mg, Leuprolide 22.5 mg

Statistical analysis description:

CAQ domain score for Avoidance at Day 336

n=386

Comparison groups	Degarelix 240 mg/80 mg v Leuprolide 22.5 mg
Number of subjects included in analysis	466
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.9172
Method	ANCOVA
Parameter estimate	Treatment Difference
Point estimate	0.007
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.131
upper limit	0.146

Statistical analysis title	Degarelix 240 mg/80 mg, Leuprolide 22.5 mg

Statistical analysis description:

CAQ domain score for Fear at Day 336

n=386

Comparison groups	Degarelix 240 mg/80 mg v Leuprolide 22.5 mg
Number of subjects included in analysis	466
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.1028
Method	ANCOVA
Parameter estimate	Treatment Difference
Point estimate	0.093

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.019
upper limit	0.204

Secondary: Number of Subjects With Adverse Events (AEs)

End point title	Number of Subjects With Adverse Events (AEs)

End point description:

Adverse events were recorded from signed informed consent until end-of-trial. Adverse events with onset after start of IMP treatment, and within 3 months after (1 month=28 days) last dosing of IMP, were considered 'treatment-emergent' and are presented for the safety analysis set.

The analysis population consisted of safety analysis set which comprised all treated subjects (who received at least one dose of IMP) and was analysed based on the actual treatment received.

End point type	Secondary

End point timeframe:

Start of IMP treatment until 3 months after last dosing of IMP

End point values	Degarelix 240 mg/80 mg	Leuprolide 22.5 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	275	269		
Units: subjects				
number (not applicable)				
AEs	250	228		
SAEs	47	44		
AE leading to death	11	9		

Statistical analyses

No statistical analyses for this end point

Secondary: Intensity of AEs

End point title	Intensity of AEs

End point description:

The intensity of AE was graded using the National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE) (version 4.02) 5-point scale and categorised as mild (grade 1), moderate (grade 2), and severe (grades 3, 4, and 5).

The analysis population consisted of the safety analysis set which comprised all treated subjects (who received at least one dose of IMP) and was analysed based on the actual treatment received.

End point type	Secondary

End point timeframe:

Start of IMP treatment until 3 months after last dosing of IMP

End point values	Degarelix 240 mg/80 mg	Leuprolide 22.5 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	275	269		
Units: subjects				
number (not applicable)				
Mild AE	224	200		
Moderate AE	160	135		
Severe AE	59	55		

Statistical analyses

No statistical analyses for this end point

Secondary: Changes in Vital Signs

End point title	Changes in Vital Signs

End point description:

Number of subjects shifting from normal value(s) in vital signs (pulse and blood pressure) at baseline to clinically significant abnormal value(s) at end-of-trial are presented.
Note: Only subjects with appropriate baseline and post-baseline data are included in the evaluation.

The analysis population consisted of the safety analysis set which comprised all treated subjects (who received at least one dose of IMP) and was analysed based on the actual treatment received.

End point type	Secondary

End point timeframe:

Baseline to Day 336 (end-of-trial)

End point values	Degarelix 240 mg/80 mg	Leuprolide 22.5 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	196	193		
Units: subjects				
number (not applicable)	0	1		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Start of IMP treatment until 3 months after last dosing of IMP

Adverse event reporting additional description:

Adverse events were recorded from signed informed consent until end-of-trial. Events with onset after start of IMP, and within 3 months (3x28 days) after last dosing, were 'treatment-emergent' and presented (safety analysis set). Reporting exceptions: non-fatal serious myocardial infarction, stroke, and unstable angina (6 degarelix; 10 leuprolide).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.0

Reporting groups

Reporting group title	Degarelix 240 mg/80 mg

Reporting group description:

Degarelix 240 mg/80 mg: Degarelix at a starting dose of 240 mg administered as two subcutaneous (SC) depot injections, each containing 120 mg of degarelix; followed by up to 11 maintenance doses of 80 mg degarelix administered as single SC depot injections at monthly (28-day) intervals.

Reporting group title	Leuprolide 22.5 mg

Reporting group description:

Leuprolide 22.5 mg: Leuprolide at dose of 22.5 mg administered as intramuscular depot injection every 3 months throughout the trial.

Serious adverse events	Degarelix 240 mg/80 mg	Leuprolide 22.5 mg	
Total subjects affected by serious adverse events			
subjects affected / exposed	47 / 275 (17.09%)	44 / 269 (16.36%)	
number of deaths (all causes)	11	9	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Brain neoplasm			
subjects affected / exposed	0 / 275 (0.00%)	1 / 269 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hodgkin's disease			
subjects affected / exposed	0 / 275 (0.00%)	1 / 269 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatic carcinoma			

subjects affected / exposed	0 / 275 (0.00%)	1 / 269 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Hypotension			
subjects affected / exposed	2 / 275 (0.73%)	1 / 269 (0.37%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Deep vein thrombosis			
subjects affected / exposed	0 / 275 (0.00%)	2 / 269 (0.74%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertension			
subjects affected / exposed	0 / 275 (0.00%)	1 / 269 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypovolaemic shock			
subjects affected / exposed	1 / 275 (0.36%)	0 / 269 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral artery thrombosis			
subjects affected / exposed	1 / 275 (0.36%)	0 / 269 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral ischaemia			
subjects affected / exposed	1 / 275 (0.36%)	0 / 269 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombosis			
subjects affected / exposed	1 / 275 (0.36%)	0 / 269 (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			

Death			
subjects affected / exposed	3 / 275 (1.09%)	1 / 269 (0.37%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 3	0 / 1	
Malaise			
subjects affected / exposed	1 / 275 (0.36%)	1 / 269 (0.37%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injection site swelling			
subjects affected / exposed	0 / 275 (0.00%)	1 / 269 (0.37%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Non-cardiac chest pain			
subjects affected / exposed	1 / 275 (0.36%)	0 / 269 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oedema peripheral			
subjects affected / exposed	1 / 275 (0.36%)	0 / 269 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	1 / 275 (0.36%)	0 / 269 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Prostatitis			
subjects affected / exposed	1 / 275 (0.36%)	0 / 269 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			

subjects affected / exposed	2 / 275 (0.73%)	1 / 269 (0.37%)	
occurrences causally related to treatment / all	1 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Acute respiratory failure			
subjects affected / exposed	1 / 275 (0.36%)	1 / 269 (0.37%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumothorax			
subjects affected / exposed	0 / 275 (0.00%)	2 / 269 (0.74%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	2 / 275 (0.73%)	0 / 269 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 2	0 / 0	
Acute respiratory distress syndrome			
subjects affected / exposed	1 / 275 (0.36%)	0 / 269 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 275 (0.00%)	1 / 269 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary oedema			
subjects affected / exposed	1 / 275 (0.36%)	0 / 269 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Psychiatric disorders			
Suicidal ideation			
subjects affected / exposed	1 / 275 (0.36%)	1 / 269 (0.37%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Completed suicide			

subjects affected / exposed	0 / 275 (0.00%)	1 / 269 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Investigations			
Heart rate irregular			
subjects affected / exposed	0 / 275 (0.00%)	1 / 269 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	2 / 275 (0.73%)	0 / 269 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anastomotic ulcer haemorrhage			
subjects affected / exposed	1 / 275 (0.36%)	0 / 269 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cervical vertebral fracture			
subjects affected / exposed	0 / 275 (0.00%)	1 / 269 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femoral neck fracture			
subjects affected / exposed	1 / 275 (0.36%)	0 / 269 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femur fracture			
subjects affected / exposed	0 / 275 (0.00%)	1 / 269 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hip fracture			
subjects affected / exposed	0 / 275 (0.00%)	1 / 269 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Lumbar vertebral fracture			
subjects affected / exposed	1 / 275 (0.36%)	0 / 269 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rib fracture			
subjects affected / exposed	1 / 275 (0.36%)	0 / 269 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin laceration			
subjects affected / exposed	0 / 275 (0.00%)	1 / 269 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal compression fracture			
subjects affected / exposed	0 / 275 (0.00%)	1 / 269 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subdural haematoma			
subjects affected / exposed	1 / 275 (0.36%)	0 / 269 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper limb fracture			
subjects affected / exposed	1 / 275 (0.36%)	0 / 269 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Cardiac failure chronic			
subjects affected / exposed	3 / 275 (1.09%)	1 / 269 (0.37%)	
occurrences causally related to treatment / all	1 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure			
subjects affected / exposed	1 / 275 (0.36%)	2 / 269 (0.74%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 1	
Atrial flutter			

subjects affected / exposed	2 / 275 (0.73%)	0 / 269 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrioventricular block complete			
subjects affected / exposed	2 / 275 (0.73%)	0 / 269 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bradycardia			
subjects affected / exposed	2 / 275 (0.73%)	0 / 269 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute myocardial infarction			
subjects affected / exposed	0 / 275 (0.00%)	1 / 269 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Angina pectoris			
subjects affected / exposed	1 / 275 (0.36%)	0 / 269 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arrhythmia			
subjects affected / exposed	0 / 275 (0.00%)	1 / 269 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Ischaemic cardiomyopathy			
subjects affected / exposed	1 / 275 (0.36%)	0 / 269 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinus node dysfunction			
subjects affected / exposed	1 / 275 (0.36%)	0 / 269 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Supraventricular tachycardia			

subjects affected / exposed	1 / 275 (0.36%)	0 / 269 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tachyarrhythmia			
subjects affected / exposed	1 / 275 (0.36%)	0 / 269 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular fibrillation			
subjects affected / exposed	0 / 275 (0.00%)	1 / 269 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Nervous system disorders			
Syncope			
subjects affected / exposed	0 / 275 (0.00%)	4 / 269 (1.49%)	
occurrences causally related to treatment / all	0 / 0	1 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular accident			
subjects affected / exposed	1 / 275 (0.36%)	1 / 269 (0.37%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Cerebral haemorrhage			
subjects affected / exposed	1 / 275 (0.36%)	0 / 269 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cognitive disorder			
subjects affected / exposed	0 / 275 (0.00%)	1 / 269 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sciatica			
subjects affected / exposed	1 / 275 (0.36%)	0 / 269 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Toxic encephalopathy			

subjects affected / exposed	1 / 275 (0.36%)	0 / 269 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tremor			
subjects affected / exposed	1 / 275 (0.36%)	0 / 269 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 275 (0.36%)	0 / 269 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric ulcer haemorrhage			
subjects affected / exposed	0 / 275 (0.00%)	1 / 269 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematochezia			
subjects affected / exposed	0 / 275 (0.00%)	1 / 269 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileus			
subjects affected / exposed	0 / 275 (0.00%)	1 / 269 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inguinal hernia			
subjects affected / exposed	1 / 275 (0.36%)	0 / 269 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal obstruction			
subjects affected / exposed	0 / 275 (0.00%)	1 / 269 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal haemorrhage			

subjects affected / exposed	1 / 275 (0.36%)	0 / 269 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Umbilical hernia			
subjects affected / exposed	0 / 275 (0.00%)	1 / 269 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	0 / 275 (0.00%)	1 / 269 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic failure			
subjects affected / exposed	1 / 275 (0.36%)	0 / 269 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 275 (0.00%)	3 / 269 (1.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary retention			
subjects affected / exposed	2 / 275 (0.73%)	1 / 269 (0.37%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephrolithiasis			
subjects affected / exposed	1 / 275 (0.36%)	0 / 269 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal failure			
subjects affected / exposed	1 / 275 (0.36%)	0 / 269 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract obstruction			

subjects affected / exposed	0 / 275 (0.00%)	1 / 269 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 275 (0.36%)	2 / 269 (0.74%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bone pain			
subjects affected / exposed	1 / 275 (0.36%)	0 / 269 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rhabdomyolysis			
subjects affected / exposed	0 / 275 (0.00%)	1 / 269 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Pneumonia			
subjects affected / exposed	5 / 275 (1.82%)	3 / 269 (1.12%)	
occurrences causally related to treatment / all	1 / 5	0 / 4	
deaths causally related to treatment / all	0 / 1	0 / 0	
Sepsis			
subjects affected / exposed	2 / 275 (0.73%)	3 / 269 (1.12%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 1	0 / 1	
COVID-19 pneumonia			
subjects affected / exposed	2 / 275 (0.73%)	0 / 269 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	1 / 275 (0.36%)	1 / 269 (0.37%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Bacteraemia			
subjects affected / exposed	1 / 275 (0.36%)	0 / 269 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cellulitis			
subjects affected / exposed	0 / 275 (0.00%)	1 / 269 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cystitis			
subjects affected / exposed	0 / 275 (0.00%)	1 / 269 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulitis intestinal haemorrhagic			
subjects affected / exposed	1 / 275 (0.36%)	0 / 269 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterococcal sepsis			
subjects affected / exposed	0 / 275 (0.00%)	1 / 269 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic echinococciasis			
subjects affected / exposed	0 / 275 (0.00%)	1 / 269 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral discitis			
subjects affected / exposed	1 / 275 (0.36%)	0 / 269 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Osteomyelitis			
subjects affected / exposed	1 / 275 (0.36%)	0 / 269 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pyelonephritis			

subjects affected / exposed	0 / 275 (0.00%)	1 / 269 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract infection			
subjects affected / exposed	0 / 275 (0.00%)	1 / 269 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hyperkalaemia			
subjects affected / exposed	0 / 275 (0.00%)	2 / 269 (0.74%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Failure to thrive			
subjects affected / exposed	0 / 275 (0.00%)	1 / 269 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypocalcaemia			
subjects affected / exposed	0 / 275 (0.00%)	1 / 269 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypokalaemia			
subjects affected / exposed	0 / 275 (0.00%)	1 / 269 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Degarelix 240 mg/80 mg	Leuprolide 22.5 mg	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	250 / 275 (90.91%)	228 / 269 (84.76%)	
Vascular disorders			
Hot flush			
subjects affected / exposed	107 / 275 (38.91%)	120 / 269 (44.61%)	
occurrences (all)	112	127	

Hypertension			
subjects affected / exposed	17 / 275 (6.18%)	23 / 269 (8.55%)	
occurrences (all)	27	31	
Nervous system disorders			
Dizziness			
subjects affected / exposed	20 / 275 (7.27%)	14 / 269 (5.20%)	
occurrences (all)	20	16	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	50 / 275 (18.18%)	34 / 269 (12.64%)	
occurrences (all)	57	35	
Injection site pain			
subjects affected / exposed	73 / 275 (26.55%)	6 / 269 (2.23%)	
occurrences (all)	232	7	
Injection site erythema			
subjects affected / exposed	58 / 275 (21.09%)	1 / 269 (0.37%)	
occurrences (all)	163	1	
Injection site swelling			
subjects affected / exposed	27 / 275 (9.82%)	3 / 269 (1.12%)	
occurrences (all)	62	3	
Asthenia			
subjects affected / exposed	15 / 275 (5.45%)	8 / 269 (2.97%)	
occurrences (all)	18	9	
Oedema peripheral			
subjects affected / exposed	8 / 275 (2.91%)	15 / 269 (5.58%)	
occurrences (all)	8	17	
Injection site induration			
subjects affected / exposed	19 / 275 (6.91%)	2 / 269 (0.74%)	
occurrences (all)	79	3	
Pyrexia			
subjects affected / exposed	16 / 275 (5.82%)	5 / 269 (1.86%)	
occurrences (all)	20	6	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	23 / 275 (8.36%)	26 / 269 (9.67%)	
occurrences (all)	26	28	

Constipation			
subjects affected / exposed	18 / 275 (6.55%)	20 / 269 (7.43%)	
occurrences (all)	21	20	
Nausea			
subjects affected / exposed	19 / 275 (6.91%)	11 / 269 (4.09%)	
occurrences (all)	21	12	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	12 / 275 (4.36%)	14 / 269 (5.20%)	
occurrences (all)	12	14	
Renal and urinary disorders			
Pollakiuria			
subjects affected / exposed	24 / 275 (8.73%)	28 / 269 (10.41%)	
occurrences (all)	25	31	
Dysuria			
subjects affected / exposed	25 / 275 (9.09%)	21 / 269 (7.81%)	
occurrences (all)	27	24	
Haematuria			
subjects affected / exposed	8 / 275 (2.91%)	15 / 269 (5.58%)	
occurrences (all)	17	17	
Nocturia			
subjects affected / exposed	8 / 275 (2.91%)	14 / 269 (5.20%)	
occurrences (all)	8	14	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	24 / 275 (8.73%)	16 / 269 (5.95%)	
occurrences (all)	29	17	
Back pain			
subjects affected / exposed	22 / 275 (8.00%)	19 / 269 (7.06%)	
occurrences (all)	25	22	
Pain in extremity			
subjects affected / exposed	15 / 275 (5.45%)	11 / 269 (4.09%)	
occurrences (all)	19	13	
Infections and infestations			
Urinary tract infection			

subjects affected / exposed occurrences (all)	20 / 275 (7.27%) 26	13 / 269 (4.83%) 14	

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

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

The trial was originally planned to include approximately 900 patients but was stopped prematurely for feasibility reasons. The decision was not based on any safety concerns, any knowledge of the results, or issues imposed by the COVID-19 pandemic.

Notes: