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Neoadjuvant Study Investigating Degarelix in Patients Suffering From Prostate Cancer

This study has been completed.

Sponsor:	Ferring Pharmaceuticals
Collaborators:	
Information provided by (Responsible Party):	Ferring Pharmaceuticals
ClinicalTrials.gov Identifier:	NCT00833248

Purpose

The purpose of this phase 3B trial was to see how well a new trial drug (degarelix) works in terms of reducing the size of the prostate volume in prostate cancer patients who were scheduled to undergo subsequent radiotherapy for treatment of their prostate cancer. Prior to receiving radiotherapy, it is recommended that patients with intermediate to high risk prostate cancer are pre-treated with hormone therapy (so-called neoadjuvant therapy) which is known to reduce the size of the prostate and thereby decrease the required radiation field and enable a more safe and effective treatment. In this trial, participants were randomly selected (like flipping a coin) to receive either degarelix given alone or a standard hormone therapy (combination of goserelin and bicalutamide. The treatment was given for three months and the prostate size was measured by ultra sound at the beginning and at the end of the trial. The participants were required to come to the clinic for 5 or 6 visits during the three months.

Condition	Intervention	Phase
Prostate Cancer	Drug: Degarelix Drug: Goserelin Drug: Bicalutamide	Phase 3

Study Type: Interventional
Study Design: Treatment, Parallel Assignment, Open Label, Randomized, Efficacy Study

Official Title: A Randomised, Parallel Arm, Open-label Trial Comparing Degarelix With Goserelin Plus Anti-androgen Flare Protection (Bicalutamide), in Terms of Prostate Size Reduction in Prostate Cancer Patients of Intermediate-to-high Risk, Who Require Neoadjuvant Hormone Therapy Prior to Radiotherapy (Curative Intent)

Further study details as provided by Ferring Pharmaceuticals:

Primary Outcome Measure:

- Change From Baseline in Prostate Size Based on Trans Rectal Ultra Sound (TRUS) at Week 12 (Full Analysis Set) [Time Frame: After treatment of 12 weeks compared to Baseline] [Designated as safety issue: No]
  TRUS is a method of measuring the size of the prostate.
- Change From Baseline in Prostate Size Based on Trans Rectal Ultra Sound (TRUS) at Week 12 (Per Protocol Analysis Set) [Time Frame: After treatment of 12 weeks compared to Baseline] [Designated as safety issue: No]
  TRUS is a method of measuring the size of the prostate.

Secondary Outcome Measures:

- Change From Baseline in Total International Prostate Symptom Score (IPSS) at Week 4, 8, and 12 [Time Frame: After treatment of 4, 8, and 12 weeks compared to Baseline] [Designated as safety issue: No]
  The IPSS is a tool commonly used to assess the severity of lower urinary tract symptoms (LUTS), and to monitor the progress of the disease once treatment has been initiated. The participant completes a questionnaire containing 7 questions regarding incomplete emptying, frequency, intermittency, urgency, weak stream, straining, and nocturia. Each question is assigned a score of 0-5. The total score is then classified according to the following scale: 0 to 7 = mildly symptomatic; 8 to 19 = moderately symptomatic; and 20 to 35 = severely symptomatic.
- Change From Baseline in Serum Testosterone Levels During the Study [Time Frame: After treatment of 4, 8, and 12 weeks compared to Baseline] [Designated as safety issue: No]
- Change From Baseline in Serum Prostate-Specific Antigen (PSA) Levels During the Study [Time Frame: After treatment of 4, 8, and 12 weeks compared to Baseline] [Designated as safety issue: No]
- Change From Baseline in Serum Oestradiol Levels During the Study [Time Frame: After treatment of 4, 8, and 12 weeks compared to Baseline] [Designated as safety issue: No]
- Change From Baseline in Quality of Life (QoL) Related to Urinary Symptoms at Each Visit [Time Frame: After treatment of 4, 8, and 12 weeks compared to Baseline] [Designated as safety issue: No]
  The IPSS questionnaire included an additional single question to assess the participant's QoL in relation to his urinary symptoms. The question was: 'If you were to spend the rest of your life with your urinary condition the way it is now, how would you feel about that?' The possible answers to this question ranged from 'delighted' (a score of '0') to 'terrible' (a score of '6').
- Number of Participants With Markedly Abnormal Values in Vital Signs and Body Weight [Time Frame: Baseline to 12 weeks of treatment] [Designated as safety issue: No]
  This outcome measure included incidence of markedly abnormal changes in blood pressure (systolic and diastolic), pulse, and body weight. The table presents the number of participants with normal baseline and at least one post-baseline markedly abnormal value.
- Number of Participants With Markedly Abnormal Values in Safety Laboratory Variables [Time Frame: Baseline to 12 weeks of treatment] [Designated as safety issue: No]
  The figures present the number of participants who had abnormal (defined as above upper limit of normal range (ULN)) levels of safety laboratory variables. Only the laboratory variables that had at least one percentage of participants in either group with abnormal value are presented, more variables were included in the study.

Enrollment: 246
Study Start Date: April 2009
Primary Completion Date: September 2011
Study Completion Date: September 2011

Arms	Assigned Interventions
Experimental: Degarelix 240 mg/80 mg The degarelix doses were administered into the abdominal wall every 28 days. A starting dose of 240 mg (40 mg/mL) degarelix was administered on Day 0 as two 3 mL subcutaneous (s.c.) injections. The second and third doses of 80 mg (20 mg/mL) degarelix were administered as single 4 mL s.c. injections on Days 28 and 56, respectively.	Drug: Degarelix The degarelix doses were administered into the abdominal wall every 28 days. A starting dose of 240 mg (40 mg/mL) degarelix was administered on Day 0 as two 3 mL subcutaneous (s.c.) injections. The second and third doses of 80 mg (20 mg/mL) degarelix were administered as single 4 mL s.c. injections on Days 28 and 56, respectively. Other Names: FE200486 Firmagon
Active Comparator: Goserelin (3.6 mg) + bicalutamide (50 mg) On Day 0, the participants began once-daily oral (p.o.) treatment with bicalutamide as anti-androgen flare protection. This treatment continued for 2 weeks after the first dose of goserelin (i.e. 17 days in total). On Day 3, the first goserelin implant was inserted s.c. into the abdominal wall. The second and third doses of goserelin were administered on Days 31 and 59, respectively.	Drug: Goserelin Goserelin implants (3.6 mg) were inserted s.c. into the abdominal wall every 28 days. The first dose was administered on Day 3. The second and third doses of goserelin were administered on Days 31 and 59, respectively. Other Names: Zoladex Drug: Bicalutamide On Day 0, participants began once-daily per-oral (p.o.) treatment with bicalutamide (50 mg) as anti-androgen flare protection; this treatment continued for 14 days after the first dose of goserelin. Other Names: Casodex

Eligibility

Ages Eligible for Study: 18 Years and older
Genders Eligible for Study: Male
Accepts Healthy Volunteers: No

Criteria

Inclusion Criteria:

- Patient has given written informed consent before any trial-related activity is performed.
- Has a confirmed prostate cancer in which this type of treatment is needed.

Exclusion Criteria:

- Previous treatment for prostate cancer
- Previous trans-urethral resection of the prostate
- Patients who are lymph node positive or have other metastatic disease
- Use of urethral catheter
- Current treatment with a 5-alpha reductase inhibitor or α-adrenoceptor antagonist.
- History of severe untreated asthma, anaphylactic reactions, or severe urticaria and/or angioedema.
- Hypersensitivity towards any component of the investigational product
- Other previous cancers within the last five years with the exception of prostate cancer and some types of skin cancer.
- Certain risk factors for abnormal heart rhythms/QT prolongation (corrected QT interval over 450 msec., Torsades de Pointes or use of certain medications with potential risk)
- Clinical disorders other than prostate cancer including but not limited to renal, haematological, gastrointestinal, endocrine, cardiac, neurological, psychiatric disease, alcohol or drug abuse or other conditionals as judged by the investigator.

Contacts and Locations

Locations

United States, Alabama

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Birmingham, Alabama, United States, 35209

Urology Centers of Alabama

Homewood, Alabama, United States, 35209

United States, Alaska

Alaska Urological Association

Anchorage, Alaska, United States, 99508

United States, Arizona

Arizona Urologic Specialists

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United States, California

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Tri-Valley Urology Medical Group

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United States, Connecticut

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United States, Florida

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Investigators

Study Director:	Clinical Development Support	Ferring Pharmaceuticals

More Information

Responsible Party:	Ferring Pharmaceuticals
Study ID Numbers:	FE200486 CS30 2008-005232-33 [EudraCT Number]
Health Authority:	United Kingdom: Medicines and Healthcare Products Regulatory Agency Germany: Federal Institute for Drugs and Medical Devices

Spain: Spanish Agency of Medicines
France: Afssaps - Agence française de sécurité sanitaire des produits de santé (Saint-Denis)
Greece: National Organization of Medicines
Netherlands: The Central Committee on Research Involving Human Subjects (CCMO)
United States: Food and Drug Administration

Study Results

Participant Flow

Recruitment Details	The participants were recruited by outpatient urologists, radiotherapists or oncologists. A total of 240 patients were to be randomised in a 3:1 ratio to one of two treatment groups (180 participants were to be treated with degarelix; 60 participants were to be treated with goserelin+bicalutamide). The recruitment period was April 2009 - June 2011.

Reporting Groups

	Description
Degarelix 240 mg/80 mg	The degarelix doses were administered into the abdominal wall every 28 days. A starting dose of 240 mg (40 mg/mL) degarelix was administered on Day 0 as two 3 mL subcutaneous (s.c.) injections. The second and third doses of 80 mg (20 mg/mL) degarelix were administered as single 4 mL s.c. injections on Days 28 and 56, respectively.
Goserelin (3.6 mg) + Bicalutamide (50 mg)	On Day 0, the participants began once-daily oral (p.o.) treatment with bicalutamide as anti-androgen flare protection. This treatment continued for 2 weeks after the first dose of goserelin (i.e. 17 days in total). On Day 3, the first goserelin implant was inserted s.c. into the abdominal wall. The second and third doses of goserelin were administered on Days 31 and 59, respectively.

Overall Study

	Degarelix 240 mg/80 mg	Goserelin (3.6 mg) + Bicalutamide (50 mg)
Started	181	65
Full Analysis Set (FAS)	180	64
Per Protocol (PP) Analysis Set	164	57
Safety Analysis Set	181	64
Completed	177	62
Not Completed	4	3

	Degarelix 240 mg/80 mg	Goserelin (3.6 mg) + Bicalutamide (50 mg)
Adverse Event	3	0
Protocol Violation	1	2
Withdrawal by Subject	0	1

Baseline Characteristics

Reporting Groups

	Description
Degarelix 240 mg/80 mg	The degarelix doses were administered into the abdominal wall every 28 days. A starting dose of 240 mg (40 mg/mL) degarelix was administered on Day 0 as two 3 mL subcutaneous (s.c.) injections. The second and third doses of 80 mg (20 mg/mL) degarelix were administered as single 4 mL s.c. injections on Days 28 and 56, respectively.
Goserelin (3.6 mg) + Bicalutamide (50 mg)	On Day 0, the participants began once-daily oral (p.o.) treatment with bicalutamide as anti-androgen flare protection. This treatment continued for 2 weeks after the first dose of goserelin (i.e. 17 days in total). On Day 3, the first goserelin implant was inserted s.c. into the abdominal wall. The second and third doses of goserelin were administered on Days 31 and 59, respectively.

Baseline Measures

	Degarelix 240 mg/80 mg	Goserelin (3.6 mg) + Bicalutamide (50 mg)	Total
Number of Participants	180	64	244
Age, Continuous [1] [units: years] Mean (Standard Deviation)	70.6 (6.37)	70.8 (5.96)	70.6 (6.25)
Gender, Male/Female [2] [units: participants]			
Female	0	0	0
Male	180	64	244
Race (NIH/OMB) [2] [units: participants]			
American Indian or Alaska Native	1	0	1
Asian	1	0	1

	Degarelix 240 mg/80 mg	Goserelin (3.6 mg) + Bicalutamide (50 mg)	Total
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	15	3	18
White	163	61	224
More than one race	0	0	0
Unknown or Not Reported	0	0	0
Region of Enrollment [2] [units: participants]			
United States	45	16	61
France	60	22	82
Greece	5	2	7
Spain	9	3	12
Netherlands	11	2	13
Germany	9	4	13
United Kingdom	41	15	56
Body Weight [2] [units: kilogram] Mean (Standard Deviation)	83.6 (14.2)	80.9 (12.4)	82.9 (13.8)
Body Mass Index [2] [units: kilogram per square meter] Mean (Standard Deviation)	27.8 (3.99)	26.8 (3.69)	27.5 (3.93)
Gleason Score [3] [units: participants]			
Gleason Score 2-6	41	12	53
Gleason Score 7	97	42	139
Gleason Score 8-10	42	10	52
Stage of Prostate Cancer [4] [units: participants]			
Localized	111	41	152
Locally Advanced	63	20	83

	Degarelix 240 mg/80 mg	Goserelin (3.6 mg) + Bicalutamide (50 mg)	Total
Metastatic	0	0	0
Not Classifiable	6	3	9
Serum Testosterone Levels [2] [units: nanograms per milliliter] Median (Full Range)	3.92 (0.557 to 11.2)	4.42 (0.188 to 8.16)	4.06 (0.188 to 11.2)
Serum Prostate-Specific Antigen (PSA) Levels [2] [units: nanograms per millilter] Median (Full Range)	10 (2.5 to 339)	9.75 (2.9 to 80)	9.95 (2.5 to 339)
Serum Oestradiol Levels [2] [units: nanograms per deciliter] Median (Full Range)	1.9 (0.74 to 4.4)	1.9 (1 to 3.6)	1.9 (0.74 to 4.4)
Prostate Volume [5] [units: milliliter] Mean (Standard Deviation)	50.9 (20.3)	52.5 (18.8)	51.3 (19.9)
Total International Prostate Symptom Score (IPSS) [6] [units: scores on a scale] Mean (Standard Deviation)	9.5 (6.71)	8.46 (6.3)	9.23 (6.61)
Quality of Life (QoL) Related to Urinary Symptoms [7] [units: scores on a scale] Mean (Standard Deviation)	2.27 (1.63)	1.94 (1.56)	2.19 (1.62)

[1] Full analysis set (FAS).

[2] FAS.

[3] FAS. The Gleason score is a system of grading the aggressiveness of the prostate cancer and how fast it is likely to grow and spread. Scale is 2-10, with low numbers being the least aggressive and 10 being the most aggressive.

[4] FAS. Prostate cancer stage was classified according to the Tumor, Nodes, and Metastatic (TNM) scale to describe the extent of cancer. Localized refers to tumors without involvement of lymph nodes or metastasis. Advanced localized can be larger tumors that may involve the lymph nodes but no metastasis. Metastatic are more advanced cancers that are spreading beyond the original tumor. Some participants did not have their prostate cancer classified for the complete TNM scale (9 participants).

[5] FAS. Prostate volume was measured with a Trans Rectal Ultrasound Scan (TRUS).

[6] FAS. The IPSS is a tool commonly used to assess the severity of lower urinary tract symptoms (LUTS), and to monitor the progress of the disease once treatment has been initiated. The participant completes a questionnaire containing 7 questions regarding incomplete

emptying, frequency, intermittency, urgency, weak stream, straining, and nocturia. Each question is assigned a score of 0-5. The total score is then classified according to the following scale: 0 to 7 = mildly symptomatic; 8 to 19 = moderately symptomatic; and 20 to 35 = severely symptomatic.

[7] FAS. The IPSS questionnaire included an additional single question to assess the participant's QoL in relation to his urinary symptoms. The question was: 'If you were to spend the rest of your life with your urinary condition the way it is now, how would you feel about that?' The possible answers to this question ranged from 'delighted' (a score of '0') to 'terrible' (a score of '6').

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Change From Baseline in Prostate Size Based on Trans Rectal Ultra Sound (TRUS) at Week 12 (Full Analysis Set)
Measure Description	TRUS is a method of measuring the size of the prostate.
Time Frame	After treatment of 12 weeks compared to Baseline
Safety Issue?	No

Analysis Population Description

FAS, Observed Case (OC) i.e. only participants with a reported value were included in the analysis.

Reporting Groups

	Description
Degarelix 240 mg/80 mg	The degarelix doses were administered into the abdominal wall every 28 days. A starting dose of 240 mg (40 mg/mL) degarelix was administered on Day 0 as two 3 mL subcutaneous (s.c.) injections. The second and third doses of 80 mg (20 mg/mL) degarelix were administered as single 4 mL s.c. injections on Days 28 and 56, respectively.
Goserelin (3.6 mg) + Bicalutamide (50 mg)	On Day 0, the participants began once-daily oral (p.o.) treatment with bicalutamide as anti-androgen flare protection. This treatment continued for 2 weeks after the first dose of goserelin (i.e. 17 days in total). On Day 3, the first goserelin implant was inserted s.c. into the abdominal wall. The second and third doses of goserelin were administered on Days 31 and 59, respectively.

Measured Values

	Degarelix 240 mg/80 mg	Goserelin (3.6 mg) + Bicalutamide (50 mg)
Number of Participants Analyzed	176	62
Change From Baseline in Prostate Size Based on Trans Rectal Ultra Sound (TRUS) at Week 12 (Full Analysis Set) [units: milliliter] Mean (Standard Deviation)	-36.0 (14.5)	-35.3 (16.7)

Statistical Analysis 1 for Change From Baseline in Prostate Size Based on Trans Rectal Ultra Sound (TRUS) at Week 12 (Full Analysis Set)

Statistical Analysis Overview	Comparison Groups	Degarelix 240 mg/80 mg, Goserelin (3.6 mg) + Bicalutamide (50 mg)
	Comments	FAS. Estimates from analysis of variance with treatment as factors and baseline IPSS and baseline Prostate volume as covariates.
	Non-Inferiority or Equivalence Analysis?	Yes
	Comments	Non-inferiority was to be established if the treatment difference in adjusted (for baseline volume, and baseline total IPSS) mean percentage reduction was significantly greater (two-sided at α=0.05 level) than Δ = 10 points (non-inferiority margin) in both the FAS and PP analyses sets.

Statistical Test of Hypothesis	P-Value	0.8942
	Comments	[Not specified]
	Method	ANCOVA
	Comments	The baseline IPSS and baseline Prostate volume were used as covariates and treatment was used as a factor in the analysis.

Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	-0.3
	Confidence Interval	(2-Sided) 95% -4.74 to 4.14
	Estimation Comments	[Not specified]

2. Primary Outcome Measure:

Measure Title	Change From Baseline in Prostate Size Based on Trans Rectal Ultra Sound (TRUS) at Week 12 (Per Protocol Analysis Set)
Measure Description	TRUS is a method of measuring the size of the prostate.
Time Frame	After treatment of 12 weeks compared to Baseline
Safety Issue?	No

Analysis Population Description

FAS, OC.

Reporting Groups

	Description
Degarelix 240 mg/80 mg	The degarelix doses were administered into the abdominal wall every 28 days. A starting dose of 240 mg (40 mg/mL) degarelix was administered on Day 0 as two 3 mL subcutaneous (s.c.) injections. The second and third doses of 80 mg (20 mg/mL) degarelix were administered as single 4 mL s.c. injections on Days 28 and 56, respectively.
Goserelin (3.6 mg) + Bicalutamide (50 mg)	On Day 0, the participants began once-daily oral (p.o.) treatment with bicalutamide as anti-androgen flare protection. This treatment continued for 2 weeks after the first dose of goserelin (i.e. 17 days in total). On Day 3, the first goserelin implant was inserted s.c. into the abdominal wall. The second and third doses of goserelin were administered on Days 31 and 59, respectively.

Measured Values

	Degarelix 240 mg/80 mg	Goserelin (3.6 mg) + Bicalutamide (50 mg)
Number of Participants Analyzed	154	54
Change From Baseline in Prostate Size Based on Trans Rectal Ultra Sound (TRUS) at Week 12 (Per Protocol Analysis Set) [units: milliliter] Mean (Standard Deviation)	-36.2 (14.5)	-35.4 (16.9)

Statistical Analysis 1 for Change From Baseline in Prostate Size Based on Trans Rectal Ultra Sound (TRUS) at Week 12 (Per Protocol Analysis Set)

Statistical Analysis Overview	Comparison Groups	Degarelix 240 mg/80 mg, Goserelin (3.6 mg) + Bicalutamide (50 mg)
	Comments	PP analysis set. Estimates from analysis of variance with treatment as factors and baseline IPSS and baseline Prostate volume as covariates.
	Non-Inferiority or Equivalence Analysis?	Yes
	Comments	Non-inferiority was to be established if the treatment difference in adjusted (for baseline volume, and baseline total IPSS) mean percentage reduction was significantly greater (two-sided at α=0.05 level) than Δ = 10 points (non-inferiority margin) in both the FAS and PP analyses sets.

Statistical Test of Hypothesis	P-Value	0.9123
	Comments	[Not specified]
	Method	ANCOVA

	Comments	The baseline IPSS and baseline Prostate volume were used as covariates and treatment was used as a factor in the analysis.

Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	-0.268
	Confidence Interval	(2-Sided) 95% -5.05 to 4.52
	Estimation Comments	[Not specified]

3. Secondary Outcome Measure:

Measure Title	Change From Baseline in Total International Prostate Symptom Score (IPSS) at Week 4, 8, and 12
Measure Description	The IPSS is a tool commonly used to assess the severity of lower urinary tract symptoms (LUTS), and to monitor the progress of the disease once treatment has been initiated. The participant completes a questionnaire containing 7 questions regarding incomplete emptying, frequency, intermittency, urgency, weak stream, straining, and nocturia. Each question is assigned a score of 0-5. The total score is then classified according to the following scale: 0 to 7 = mildly symptomatic; 8 to 19 = moderately symptomatic; and 20 to 35 = severely symptomatic.
Time Frame	After treatment of 4, 8, and 12 weeks compared to Baseline
Safety Issue?	No

Analysis Population Description
FAS, OC.

Reporting Groups

	Description
Degarelix 240 mg/80 mg	The degarelix doses were administered into the abdominal wall every 28 days. A starting dose of 240 mg (40 mg/mL) degarelix was administered on Day 0 as two 3 mL subcutaneous (s.c.) injections. The second and third doses of 80 mg (20 mg/mL) degarelix were administered as single 4 mL s.c. injections on Days 28 and 56, respectively.
Goserelin (3.6 mg) + Bicalutamide (50 mg)	On Day 0, the participants began once-daily oral (p.o.) treatment with bicalutamide as anti-androgen flare protection. This treatment continued for 2 weeks after the first dose of goserelin (i.e. 17 days in total). On Day 3, the first goserelin implant was inserted s.c. into the abdominal wall. The second and third doses of goserelin were administered on Days 31 and 59, respectively.

Measured Values

	Degarelix 240 mg/80 mg	Goserelin (3.6 mg) + Bicalutamide (50 mg)
Number of Participants Analyzed	177	63

	Degarelix 240 mg/80 mg	Goserelin (3.6 mg) + Bicalutamide (50 mg)
Change From Baseline in Total International Prostate Symptom Score (IPSS) at Week 4, 8, and 12 [units: scores on a scale] Mean (Standard Deviation)		
Week 4	-0.21 (5.05)	0.36 (4.83)
Week 8	-1.53 (5.43)	0.02 (5.41)
Week 12	-1.71 (5.54)	0.11 (5.13)

4. Secondary Outcome Measure:

Measure Title	Change From Baseline in Serum Testosterone Levels During the Study
Measure Description	
Time Frame	After treatment of 4, 8, and 12 weeks compared to Baseline
Safety Issue?	No

Analysis Population Description

FAS, OC.

Reporting Groups

	Description
Degarelix 240 mg/80 mg	The degarelix doses were administered into the abdominal wall every 28 days. A starting dose of 240 mg (40 mg/mL) degarelix was administered on Day 0 as two 3 mL subcutaneous (s.c.) injections. The second and third doses of 80 mg (20 mg/mL) degarelix were administered as single 4 mL s.c. injections on Days 28 and 56, respectively.
Goserelin (3.6 mg) + Bicalutamide (50 mg)	On Day 0, the participants began once-daily oral (p.o.) treatment with bicalutamide as anti-androgen flare protection. This treatment continued for 2 weeks after the first dose of goserelin (i.e. 17 days in total). On Day 3, the first goserelin implant was inserted s.c. into the abdominal wall. The second and third doses of goserelin were administered on Days 31 and 59, respectively.

Measured Values

	Degarelix 240 mg/80 mg	Goserelin (3.6 mg) + Bicalutamide (50 mg)
Number of Participants Analyzed	170	63
Change From Baseline in Serum Testosterone Levels During the Study		

	Degarelix 240 mg/80 mg	Goserelin (3.6 mg) + Bicalutamide (50 mg)
[units: nanograms per milliliter] Median (Full Range)		
Week 4	-3.8 (-11.06 to -0.51)	-4.22 (-8.06 to 0.52)
Week 8	-3.77 (-11.01 to -0.51)	-4.26 (-8.11 to -0.14)
Week 12	-3.81 (-11.09 to -0.51)	-4.3 (-8.11 to -0.14)

5. Secondary Outcome Measure:

Measure Title	Change From Baseline in Serum Prostate-Specific Antigen (PSA) Levels During the Study
Measure Description	
Time Frame	After treatment of 4, 8, and 12 weeks compared to Baseline
Safety Issue?	No

Analysis Population Description

FAS, OC.

Reporting Groups

	Description
Degarelix 240 mg/80 mg	The degarelix doses were administered into the abdominal wall every 28 days. A starting dose of 240 mg (40 mg/mL) degarelix was administered on Day 0 as two 3 mL subcutaneous (s.c.) injections. The second and third doses of 80 mg (20 mg/mL) degarelix were administered as single 4 mL s.c. injections on Days 28 and 56, respectively.
Goserelin (3.6 mg) + Bicalutamide (50 mg)	On Day 0, the participants began once-daily oral (p.o.) treatment with bicalutamide as anti-androgen flare protection. This treatment continued for 2 weeks after the first dose of goserelin (i.e. 17 days in total). On Day 3, the first goserelin implant was inserted s.c. into the abdominal wall. The second and third doses of goserelin were administered on Days 31 and 59, respectively.

Measured Values

	Degarelix 240 mg/80 mg	Goserelin (3.6 mg) + Bicalutamide (50 mg)
Number of Participants Analyzed	172	62
Change From Baseline in Serum Prostate-Specific Antigen (PSA) Levels During the Study [units: nanograms per milliliter] Median (Full Range)		

	Degarelix 240 mg/80 mg	Goserelin (3.6 mg) + Bicalutamide (50 mg)
Week 4	-6.3 (-333 to 4.5)	-5.9 (-76 to 4)
Week 8	-7.95 (-337 to -2)	-8.8 (-79.4 to -1.7)
Week 12	-8.35 (-338 to -2)	-9.05 (-78.8 to -1.8)

6. Secondary Outcome Measure:

Measure Title	Change From Baseline in Serum Oestradiol Levels During the Study
Measure Description	
Time Frame	After treatment of 4, 8, and 12 weeks compared to Baseline
Safety Issue?	No

Analysis Population Description
FAS, OC.

Reporting Groups

	Description
Degarelix 240 mg/80 mg	The degarelix doses were administered into the abdominal wall every 28 days. A starting dose of 240 mg (40 mg/mL) degarelix was administered on Day 0 as two 3 mL subcutaneous (s.c.) injections. The second and third doses of 80 mg (20 mg/mL) degarelix were administered as single 4 mL s.c. injections on Days 28 and 56, respectively.
Goserelin (3.6 mg) + Bicalutamide (50 mg)	On Day 0, the participants began once-daily oral (p.o.) treatment with bicalutamide as anti-androgen flare protection. This treatment continued for 2 weeks after the first dose of goserelin (i.e. 17 days in total). On Day 3, the first goserelin implant was inserted s.c. into the abdominal wall. The second and third doses of goserelin were administered on Days 31 and 59, respectively.

Measured Values

	Degarelix 240 mg/80 mg	Goserelin (3.6 mg) + Bicalutamide (50 mg)
Number of Participants Analyzed	124	36
Change From Baseline in Serum Oestradiol Levels During the Study [units: nanogram per deciliter] Median (Full Range)		
Week 4	-1.55 (-4.35 to -0.63)	-1.65 (-3.5 to -0.9)

	Degarelix 240 mg/80 mg	Goserelin (3.6 mg) + Bicalutamide (50 mg)
Week 8	-1.6 (-3.6 to -0.27)	-1.65 (-3.55 to -0.95)
Week 12	-1.55 (-4.35 to -0.48)	-1.6 (-3.55 to -0.8)

7. Secondary Outcome Measure:

Measure Title	Change From Baseline in Quality of Life (QoL) Related to Urinary Symptoms at Each Visit
Measure Description	The IPSS questionnaire included an additional single question to assess the participant's QoL in relation to his urinary symptoms. The question was: 'If you were to spend the rest of your life with your urinary condition the way it is now, how would you feel about that?' The possible answers to this question ranged from 'delighted' (a score of '0') to 'terrible' (a score of '6').
Time Frame	After treatment of 4, 8, and 12 weeks compared to Baseline
Safety Issue?	No

Analysis Population Description

FAS, OC.

Reporting Groups

	Description
Degarelix 240 mg/80 mg	The degarelix doses were administered into the abdominal wall every 28 days. A starting dose of 240 mg (40 mg/mL) degarelix was administered on Day 0 as two 3 mL subcutaneous (s.c.) injections. The second and third doses of 80 mg (20 mg/mL) degarelix were administered as single 4 mL s.c. injections on Days 28 and 56, respectively.
Goserelin (3.6 mg) + Bicalutamide (50 mg)	On Day 0, the participants began once-daily oral (p.o.) treatment with bicalutamide as anti-androgen flare protection. This treatment continued for 2 weeks after the first dose of goserelin (i.e. 17 days in total). On Day 3, the first goserelin implant was inserted s.c. into the abdominal wall. The second and third doses of goserelin were administered on Days 31 and 59, respectively.

Measured Values

	Degarelix 240 mg/80 mg	Goserelin (3.6 mg) + Bicalutamide (50 mg)
Number of Participants Analyzed	179	63
Change From Baseline in Quality of Life (QoL) Related to Urinary Symptoms at Each Visit [units: scores on a scale] Mean (Standard Deviation)		

	Degarelix 240 mg/80 mg	Goserelin (3.6 mg) + Bicalutamide (50 mg)
Week 4	-0.07 (1.31)	0.16 (0.92)
Week 8	-0.24 (1.34)	0.05 (1.11)
Week 12	-0.33 (1.46)	0.16 (1.4)

8. Secondary Outcome Measure:

Measure Title	Number of Participants With Markedly Abnormal Values in Vital Signs and Body Weight
Measure Description	This outcome measure included incidence of markedly abnormal changes in blood pressure (systolic and diastolic), pulse, and body weight. The table presents the number of participants with normal baseline and at least one post-baseline markedly abnormal value.
Time Frame	Baseline to 12 weeks of treatment
Safety Issue?	No

Analysis Population Description

Safety analysis set.

Reporting Groups

	Description
Degarelix 240 mg/80 mg	The degarelix doses were administered into the abdominal wall every 28 days. A starting dose of 240 mg (40 mg/mL) degarelix was administered on Day 0 as two 3 mL subcutaneous (s.c.) injections. The second and third doses of 80 mg (20 mg/mL) degarelix were administered as single 4 mL s.c. injections on Days 28 and 56, respectively.
Goserelin (3.6 mg) + Bicalutamide (50 mg)	On Day 0, the participants began once-daily oral (p.o.) treatment with bicalutamide as anti-androgen flare protection. This treatment continued for 2 weeks after the first dose of goserelin (i.e. 17 days in total). On Day 3, the first goserelin implant was inserted s.c. into the abdominal wall. The second and third doses of goserelin were administered on Days 31 and 59, respectively.

Measured Values

	Degarelix 240 mg/80 mg	Goserelin (3.6 mg) + Bicalutamide (50 mg)
Number of Participants Analyzed	181	64
Number of Participants With Markedly Abnormal Values in Vital Signs and Body Weight [units: participants]		

	Degarelix 240 mg/80 mg	Goserelin (3.6 mg) + Bicalutamide (50 mg)
Diastolic blood pressure <=50 and decrease >=15	0	0
Diastolic blood pressure >=105 and increase >=15	3	0
Systolic blood pressure <=90 and decrease >=20	0	0
Systolic blood pressure >=180 and increase >=20	1	1
Heart rate <=50 and decrease >=15	1	1
Heart rate >=120 and increase >=15	0	0
Body weight decrease of >=7 percent	3	2
Body weight increase of >=7 percent	5	0

9. Secondary Outcome Measure:

Measure Title	Number of Participants With Markedly Abnormal Values in Safety Laboratory Variables
Measure Description	The figures present the number of participants who had abnormal (defined as above upper limit of normal range (ULN)) levels of safety laboratory variables. Only the laboratory variables that had at least one percentage of participants in either group with abnormal value are presented, more variables were included in the study.
Time Frame	Baseline to 12 weeks of treatment
Safety Issue?	No

Analysis Population Description

Safety analysis set.

Reporting Groups

	Description
Degarelix 240 mg/80 mg	The degarelix doses were administered into the abdominal wall every 28 days. A starting dose of 240 mg (40 mg/mL) degarelix was administered on Day 0 as two 3 mL subcutaneous (s.c.) injections. The second and third doses of 80 mg (20 mg/mL) degarelix were administered as single 4 mL s.c. injections on Days 28 and 56, respectively.
Goserelin (3.6 mg) + Bicalutamide (50 mg)	On Day 0, the participants began once-daily oral (p.o.) treatment with bicalutamide as anti-androgen flare protection. This treatment continued for 2 weeks after the first dose of goserelin (i.e. 17 days in total). On Day 3, the first goserelin implant was inserted s.c. into the abdominal wall. The second and third doses of goserelin were administered on Days 31 and 59, respectively.

Measured Values

	Degarelix 240 mg/80 mg	Goserelin (3.6 mg) + Bicalutamide (50 mg)
Number of Participants Analyzed	181	64
Number of Participants With Markedly Abnormal Values in Safety Laboratory Variables [units: participants]		
B-Haematocrit (Ratio) <=0.37	31	8
B-Haemoglobin (g/L) <=115	4	1
S-Alanine aminotransferase (IU/L) >3 x ULN	1	1
S-Potassium (mmol/L) >=5.8	4	1
S-Urea nitrogen (mmol/L) >=10.7	10	3

Reported Adverse Events

Time Frame	12 weeks.
Additional Description	Each participant's condition was monitored throughout the trial from the time of signing the informed consent until the end of the follow-up period. The investigator was to record all adverse events (AEs) in the AE log of the participant's Case Report Form.

Reporting Groups

	Description
Degarelix 240 mg/80 mg	The degarelix doses were administered into the abdominal wall every 28 days. A starting dose of 240 mg (40 mg/mL) degarelix was administered on Day 0 as two 3 mL subcutaneous (s.c.) injections. The second and third doses of 80 mg (20 mg/mL) degarelix were administered as single 4 mL s.c. injections on Days 28 and 56, respectively.
Goserelin (3.6 mg) + Bicalutamide (50 mg)	On Day 0, the participants began once-daily oral (p.o.) treatment with bicalutamide as anti-androgen flare protection. This treatment continued for 2 weeks after the first dose of goserelin (i.e. 17 days in total). On Day 3, the first goserelin implant was inserted s.c. into the abdominal wall. The second and third doses of goserelin were administered on Days 31 and 59, respectively.

Serious Adverse Events

	Degarelix 240 mg/80 mg		Goserelin (3.6 mg) + Bicalutamide (50 mg)	
	Affected/At Risk (%)	# Events	Affected/At Risk (%)	# Events
Total	7/181 (3.87%)		0/64 (0%)	
Cardiac disorders				
Atrial fibrillation [A] †	1/181 (0.55%)	1	0/64 (0%)	0
Eye disorders				
Retinal detachment [A] †	1/181 (0.55%)	1	0/64 (0%)	0
Investigations				
Alanine aminotransferase increased [A] †	1/181 (0.55%)	1	0/64 (0%)	0
Aspartate aminotransferase increased [A] †	1/181 (0.55%)	1	0/64 (0%)	0
Blood alkaline phosphatase increased [A] †	1/181 (0.55%)	1	0/64 (0%)	0
Gamma-glutamyltransferase increased [A] †	1/181 (0.55%)	1	0/64 (0%)	0
Musculoskeletal and connective tissue disorders				
Musculoskeletal chest pain [A] †	1/181 (0.55%)	1	0/64 (0%)	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)				
Gastric cancer [A] †	1/181 (0.55%)	1	0/64 (0%)	0
Lung neoplasm malignant [A] †	1/181 (0.55%)	1	0/64 (0%)	0
Renal and urinary disorders				
Urinary retention [A] †	1/181 (0.55%)	1	0/64 (0%)	0

† Indicates events were collected by systematic assessment.
A Term from vocabulary, MedDRA 12.0

Other Adverse Events

Frequency Threshold Above Which Other Adverse Events are Reported: 5%

	Degarelix 240 mg/80 mg		Goserelin (3.6 mg) + Bicalutamide (50 mg)	
	Affected/At Risk (%)	# Events	Affected/At Risk (%)	# Events
Total	158/181 (87.29%)		53/64 (82.81%)	

	Degarelix 240 mg/80 mg		Goserelin (3.6 mg) + Bicalutamide (50 mg)	
	Affected/At Risk (%)	# Events	Affected/At Risk (%)	# Events
General disorders				
Asthenia [A] †	13/181 (7.18%)	15	6/64 (9.38%)	6
Fatigue [A] †	11/181 (6.08%)	13	6/64 (9.38%)	6
Injection site erythema [A] †	45/181 (24.86%)	73	0/64 (0%)	0
Injection site pain [A] †	60/181 (33.15%)	93	1/64 (1.56%)	1
Injection site pruritus [A] †	13/181 (7.18%)	19	0/64 (0%)	0
Injection site swelling [A] †	11/181 (6.08%)	17	0/64 (0%)	0
Psychiatric disorders				
Libido decreased [A] †	12/181 (6.63%)	12	4/64 (6.25%)	4
Renal and urinary disorders				
Pollakiuria [A] †	11/181 (6.08%)	13	4/64 (6.25%)	4
Reproductive system and breast disorders				
Erectile dysfunction [A] †	14/181 (7.73%)	15	7/64 (10.94%)	7
Vascular disorders				
Hot flush [A] †	108/181 (59.67%)	132	40/64 (62.5%)	46

† Indicates events were collected by systematic assessment.
A Term from vocabulary, MedDRA 12.0

Limitations and Caveats

[Not specified]

More Information

Certain Agreements:
Principal Investigators are NOT employed by the organization sponsoring the study.

There IS an agreement between the Principal Investigator and the Sponsor (or its agents) that restricts the PI's rights to discuss or publish trial results after the trial is completed.

The only disclosure restriction on the PI is that the sponsor can review the draft manuscript prior to publication and can request delay of publication where any contents are deemed patentable by the sponsor or confidential to the sponsor. Comments will be given within four weeks from receipt of the draft manuscript. Additional time may be required to allow Ferring to seek patent protection of the invention.

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