ClinicalTrials.gov Protocol and Results Registration System (PRS) Receipt
Release Date: 10/21/2013

Investigation of the Effect of Degarelix in Terms of Prostate Volume Reduction in Prostate Cancer Patients

This study has been completed.

Sponsor:	Ferring Pharmaceuticals
Collaborators:	
Information provided by (Responsible Party):	Ferring Pharmaceuticals
ClinicalTrials.gov Identifier:	NCT00884273

Purpose

This was a Phase 3b clinical study in prostate cancer patients which aimed to compare the current standard therapy of a gonadotrophin releasing hormone (GnRH) agonist, goserelin (3.6 mg; plus anti-androgen flare protection, bicalutamide), to a novel GnRH antagonist, degarelix (240 mg starting dose/80 mg maintenance dose) with respect to mean percentage reduction in prostate volume.

The hypothesis was that degarelix could decrease prostate size at least as effectively as the combination of a GnRH agonist with an anti-androgen for flare protection.

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 Volume Reduction of the Prostate in Patients With Prostate Cancer Being Candidates for Medical Castration

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 Prostate Size Based on TRUS at Week 4 and 8 [Time Frame: After treatment of 4 and 8 weeks compared to Baseline] [Designated as safety issue: No]
  TRUS is a method of measuring the size of the prostate.
- 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 in Serum Testosterone Levels During the Study [Time Frame: At 4, 8, and 12 weeks compared to baseline.] [Designated as safety issue: No]
- Change in Serum Prostate-Specific Antigen (PSA) Levels During the Study [Time Frame: At 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').
- Change From Baseline in Burden of Urinary Symptoms Based on the Benign Prostatic Hyperplasia Impact Index (BPHII) [Time Frame: After treatment of 4, 8, and 12 weeks compared to Baseline] [Designated as safety issue: No]
  The Benign Prostatic Hyperplasia Impact Index (BPHII) is a self-administered questionnaire to measure how much urinary problems affect various domains of health. The higher value the worse are the urinary problems. The minimum possible total value is 0 and the maximum possible total value is 16.
- 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: 182
Study Start Date: August 2009
Primary Completion Date: March 2011
Study Completion Date: March 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) Goserelin implants (3.6 mg) were inserted s.c. into the abdominal wall every 28 days. The first dose was administered on Day 0. The second and third doses of goserelin were administered on Days 28 and 56, respectively. 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 28 days after the first dose of goserelin.	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 0. The second and third doses of goserelin were administered on Days 28 and 56, 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 28 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:

1. Patient has given written informed consent
2. Patient is 18 years or older
3. Patient has histologically confirmed prostate cancer
4. Patient has a serum prostate-specific antigen (PSA) level at screening >2 ng/mL

5. The prostate size is >30 cubic centimetres (cc), measured by TRUS
6. Patient has had a bone-scan within 12 weeks before inclusion
7. Patient must be able to undergo transrectal examinations
8. Patient has an estimated life expectancy of at least 12 months

Exclusion Criteria:

1. Any previous treatments for prostate cancer
2. Previous trans-urethral resection of the prostate (TURP)
3. Is not considered a candidate for medical castration
4. Use of urethral catheter
5. Is currently treated with a 5-alpha reductase inhibitor
6. Is currently treated with an alpha-adrenoceptor antagonist
7. Treatment with botulinum toxin A (Botox)
8. Require radiotherapy during the trial
9. History of severe untreated asthma, anaphylactic reactions, or severe urticaria and/or angioedema
10. Hypersensitivity towards any component of the investigational products or excipients
11. Previous history or presence of another malignancy
12. A clinically significant disorder
13. A corrected QT interval over 450 msec
14. Mental incapacity or language barrier precluding adequate understanding or co-operation
15. Receipt of an investigational drug within the last 28 days proceeding screening
16. Previous participation in any degarelix trial

Contacts and Locations

Locations

Belgium

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University Hospitals Leuven
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Denmark

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Aalborg, Denmark

Herlev Hospital
Ballerup, Denmark

Regionhospitalet Holstebro
Holstebro, Denmark

Sygehus Syd, Næstved Sygehus
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Investigators

Study Director:	Clinical Development Support	Ferring Pharmaceuticals

More Information

Results Publications:

Axcrona K, Aaltomaa S, da Silva CM, Ozen H, Damber JE, Tankó LB, Colli E, Klarskov P. Androgen deprivation therapy for volume reduction, lower urinary tract symptom relief and quality of life improvement in patients with prostate cancer: degarelix vs goserelin plus bicalutamide. BJU Int. 2012 Dec;110(11):1721-8. doi: 10.1111/j.1464-410X.2012.11107.x. Epub 2012 Apr 13.

Responsible Party: Ferring Pharmaceuticals
Study ID Numbers: FE200486 CS31
2008-008604-40 [EudraCT Number]
Health Authority: Denmark: Danish Medicines Agency
Sweden: Medical Products Agency
Finland: Finnish Medicines Agency
Norway: Norwegian Medicines Agency
Portugal: National Pharmacy and Medicines Institute
Italy: The Italian Medicines Agency
Belgium: Federal Agency for Medicinal Products and Health Products
Turkey: Ministry of Health

Study Results

Participant Flow

Recruitment Details	The participants were recruited by outpatient urologists. 180 participants were to be randomised in a 1:1 ratio to one of two treatment groups (90 participants were to be treated with degarelix; 90 participants were to be treated with goserelin plus bicalutamide). The recruitment period was August 2009 - December 2010.
Pre-Assignment Details	The apparent skewed number of actual participants in the two groups is due to the fact that randomisation was done in blocks per site rather than per study.

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)	Goserelin implants (3.6 mg) were inserted s.c. into the abdominal wall every 28 days. The first dose was administered on Day 0. The second and third doses of goserelin were administered on Days 28 and 56, respectively. 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 28 days after the first dose of goserelin.

Overall Study

	Degarelix 240 mg/80 mg	Goserelin (3.6 mg) + Bicalutamide (50 mg)
Started	84 [1]	98 [2]
Full Analysis Set (FAS)	82 [3]	97 [4]
Per Protocol (PP) Analysis Set	81	92
Safety Analysis Set	84	98
Completed	82	93
Not Completed	2	5
Adverse Event	0	2
Protocol Violation	1	3
Practical reasons	1	0

[1] Intention-to-treat (ITT) population.
[2] ITT population.
[3] Two participants did not have any post-dose efficacy assessment and were excluded from the FAS.
[4] One participant did not have any post-dose efficacy assessment and was excluded from the FAS.

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)	Goserelin implants (3.6 mg) were inserted s.c. into the abdominal wall every 28 days. The first dose was administered on Day 0. The second and third doses of goserelin were administered on Days 28 and 56, respectively. 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 28 days after the first dose of goserelin.

Baseline Measures

	Degarelix 240 mg/80 mg	Goserelin (3.6 mg) + Bicalutamide (50 mg)	Total
Number of Participants	82	97	179

	Degarelix 240 mg/80 mg	Goserelin (3.6 mg) + Bicalutamide (50 mg)	Total
Age, Continuous [1] [units: years] Mean (Standard Deviation)	71.9 (7.71)	73.0 (7.10)	72.5 (7.39)
Gender, Male/Female [2] [units: participants]			
Female	0	0	0
Male	82	97	179
Race (NIH/OMB) [3] [units: participants]			
American Indian or Alaska Native	0	0	0
Asian	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	82	97	179
More than one race	0	0	0
Unknown or Not Reported	0	0	0
Region of Enrollment [2] [units: participants]			
Portugal	4	7	11
Finland	14	17	31
Belgium	2	2	4
Turkey	14	14	28
Denmark	13	15	28
Norway	4	8	12
Italy	20	22	42
Sweden	11	12	23
Body Weight [2] [units: kilogram]	79.7 (12.4)	79.7 (12.2)	79.7 (12.2)

	Degarelix 240 mg/80 mg	Goserelin (3.6 mg) + Bicalutamide (50 mg)	Total
Mean (Standard Deviation)			
Body Mass Index [2] [units: kilogram per square meter] Mean (Standard Deviation)	26.8 (4.07)	26.5 (3.72)	26.6 (3.88)
Gleason Score [4] [units: participants]			
Gleason Score 2-4	1	1	2
Gleason Score 5-6	16	15	31
Gleason Score 7-10	65	81	146
Stage of Prostate Cancer [5] [units: participants]			
Localized	24	32	56
Locally Advanced	30	23	53
Metastatic	22	31	53
Not Classifiable	6	11	17
Serum Testosterone Levels [units: nanograms per milliliter] Median (Full Range)	4.08 (0.32 to 10.8)	4.33 (0.13 to 9.6)	4.23 (0.13 to 10.8)
Serum Protsate-Specific Antigen (PSA) Levels [units: nanograms per milliliter] Median (Full Range)	27.8 (1.9 to 6206)	15.6 (3.0 to 2829)	20.2 (1.9 to 6206)
Prostate Volume [6] [units: milliliter] Mean (Standard Deviation)	54.8 (26.0)	49.9 (15.5)	52.1 (21.1)
Total International Prostate Symptom Score (IPSS) [7] [units: scores on a scale] Mean (Standard Deviation)	14.3 (6.91)	13.4 (7.36)	13.8 (7.15)
Quality of Life (QoL) Related to Urinary Symptoms [8] [units: scores on a scale] Mean (Standard Deviation)	2.85 (1.62)	2.73 (1.66)	2.79 (1.64)

	Degarelix 240 mg/80 mg	Goserelin (3.6 mg) + Bicalutamide (50 mg)	Total
Benign Prostatic Hyperplasia Impact Index (BPHII) [9] [units: scores on a scale] Mean (Standard Deviation)	5.06 (3.39)	4.58 (3.58)	4.80 (3.49)

[1] Full Analysis Set (FAS).

[2] FAS.

[3] FAS

[4] 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.

[5] 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 (17 participants).

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

[7] 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.

[8] 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'). The figures in the tables present the change (ie decrease) in IPSS QoL score, i.e. the bigger the decrease the better QoL.

[9] The Benign Prostatic Hyperplasia Impact Index (BPHII) is a self-administered questionnaire to measure how much urinary problems affect various domains of health. The higher value the worse are the urinary problems. The minimum possible total value is 0 and the maximum possible total value is 16.

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

Full Analysis Set (FAS), Last Observation Carried Forward (LOCF).

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)	Goserelin implants (3.6 mg) were inserted s.c. into the abdominal wall every 28 days. The first dose was administered on Day 0. The second and third doses of goserelin were administered on Days 28 and 56, respectively. 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 28 days after the first dose of goserelin.

Measured Values

	Degarelix 240 mg/80 mg	Goserelin (3.6 mg) + Bicalutamide (50 mg)
Number of Participants Analyzed	82	97
Change From Baseline in Prostate Size Based on Trans Rectal Ultra Sound (TRUS) at Week 12 (Full Analysis Set) [units: milliliter] Mean (Standard Deviation)	-37.2 (16.8)	-39.0 (17.7)

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	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. If the Week 12 treatment assessment of prostate volume was missing the LOCF approach was used, i.e., the prostate volume value closest to and before Week 12 was used.

Statistical Test of Hypothesis	P-Value	0.36
	Comments	FAS.
	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	2.37
	Confidence Interval	(2-Sided) 95% -2.78 to 7.52
	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

Per Protocol (PP) Analysis Set, Last Observation Carried Forward (LOCF).

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)	Goserelin implants (3.6 mg) were inserted s.c. into the abdominal wall every 28 days. The first dose was administered on Day 0. The second and third doses of goserelin were administered on Days 28 and 56, respectively. 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 28 days after the first dose of goserelin.

Measured Values

	Degarelix 240 mg/80 mg	Goserelin (3.6 mg) + Bicalutamide (50 mg)
Number of Participants Analyzed	81	92
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)	-37.3 (16.8)	-39.0 (18.4)

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	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. If the Week 12 treatment assessment of prostate volume was missing the LOCF approach was used, i.e., the prostate volume value closest to and before Week 12 was used.

Statistical Test of Hypothesis	P-Value	0.41
	Comments	PP.
	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 (Net)
	Estimated Value	2.24
	Confidence Interval	(2-Sided) 95% -3.10 to 7.58
	Estimation Comments	[Not specified]

3. Secondary Outcome Measure:

Measure Title	Change From Baseline in Prostate Size Based on TRUS at Week 4 and 8
Measure Description	TRUS is a method of measuring the size of the prostate.
Time Frame	After treatment of 4 and 8 weeks compared to Baseline
Safety Issue?	No

Analysis Population Description

FAS, Last Observation Carried Forward (LOCF).

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)	Goserelin implants (3.6 mg) were inserted s.c. into the abdominal wall every 28 days. The first dose was administered on Day 0. The second and third doses of goserelin were administered on Days 28 and 56, respectively. 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 28 days after the first dose of goserelin.

Measured Values

	Degarelix 240 mg/80 mg	Goserelin (3.6 mg) + Bicalutamide (50 mg)
Number of Participants Analyzed	82	97
Change From Baseline in Prostate Size Based on TRUS at Week 4 and 8 [units: milliliter] Mean (Standard Deviation)		
Week 4	-19.2 (15.2)	-21.2 (17.7)
Week 8	-33.1 (14.8)	-33.2 (20.6)

4. 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, Last Observation Carried Forward (LOCF).

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)	Goserelin implants (3.6 mg) were inserted s.c. into the abdominal wall every 28 days. The first dose was administered on Day 0. The second and third doses of goserelin were administered on Days 28 and 56, respectively. 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 28 days after the first dose of goserelin.

Measured Values

	Degarelix 240 mg/80 mg	Goserelin (3.6 mg) + Bicalutamide (50 mg)
Number of Participants Analyzed	82	97
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	-2.09 (4.36)	-1.36 (5.86)
Week 8	-3.55 (5.95)	-3.13 (6.06)
Week 12	-4.39 (6.66)	-2.74 (6.37)

5. Secondary Outcome Measure:

Measure Title	Change in Serum Testosterone Levels During the Study
Measure Description	
Time Frame	At 4, 8, and 12 weeks compared to baseline.
Safety Issue?	No

Analysis Population Description
FAS.

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)	Goserelin implants (3.6 mg) were inserted s.c. into the abdominal wall every 28 days. The first dose was administered on Day 0. The second and third doses of goserelin were administered on Days 28 and 56, respectively. 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 28 days after the first dose of goserelin.

Measured Values

	Degarelix 240 mg/80 mg	Goserelin (3.6 mg) + Bicalutamide (50 mg)
Number of Participants Analyzed	82	97
Change in Serum Testosterone Levels During the Study [units: nanograms per milliliter] Median (Full Range)		
Week 4	-3.91 (-10.62 to -0.20)	-4.17 (-9.30 to 0.03)
Week 8	-3.97 (-10.61 to -0.12)	-4.24 (-9.44 to -0.08)
Week 12	-4.09 (-10.58 to 0.00)	-4.23 (-9.31 to -0.03)

6. Secondary Outcome Measure:

Measure Title	Change in Serum Prostate-Specific Antigen (PSA) Levels During the Study

Measure Description	
Time Frame	At 4, 8, and 12 weeks compared to baseline.
Safety Issue?	No

Analysis Population Description
FAS.

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)	Goserelin implants (3.6 mg) were inserted s.c. into the abdominal wall every 28 days. The first dose was administered on Day 0. The second and third doses of goserelin were administered on Days 28 and 56, respectively. 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 28 days after the first dose of goserelin.

Measured Values

	Degarelix 240 mg/80 mg	Goserelin (3.6 mg) + Bicalutamide (50 mg)
Number of Participants Analyzed	82	97
Change in Serum Prostate-Specific Antigen (PSA) Levels During the Study [units: nanograms per milliliter] Median (Full Range)		
Week 4	-20.25 (-4205 to 4.5)	-12.10 (-2823 to 3.3)
Week 8	-22.5 (-6192 to 4.3)	-14.6 (-2828 to -2)
Week 12	-25.15 (-6195 to 4.7)	-13.1 (-2815 to -1.2)

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.

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)	Goserelin implants (3.6 mg) were inserted s.c. into the abdominal wall every 28 days. The first dose was administered on Day 0. The second and third doses of goserelin were administered on Days 28 and 56, respectively. 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 28 days after the first dose of goserelin.

Measured Values

	Degarelix 240 mg/80 mg	Goserelin (3.6 mg) + Bicalutamide (50 mg)
Number of Participants Analyzed	82	97
Change From Baseline in Quality of Life (QoL) Related to Urinary Symptoms at Each Visit [units: scores on a scale] Mean (Standard Deviation)		
Week 4	-0.46 (1.43)	-0.56 (1.30)
Week 8	-0.83 (1.62)	-0.79 (1.37)
Week 12	-0.99 (1.64)	-1.01 (1.38)

8. Secondary Outcome Measure:

Measure Title	Change From Baseline in Burden of Urinary Symptoms Based on the Benign Prostatic Hyperplasia Impact Index (BPHII)
Measure Description	The Benign Prostatic Hyperplasia Impact Index (BPHII) is a self-administered questionnaire to measure how much urinary problems affect various domains of health. The higher value the worse are the urinary problems. The minimum possible total value is 0 and the maximum possible total value is 16.
Time Frame	After treatment of 4, 8, and 12 weeks compared to Baseline
Safety Issue?	No

Analysis Population Description

FAS.

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)	Goserelin implants (3.6 mg) were inserted s.c. into the abdominal wall every 28 days. The first dose was administered on Day 0. The second and third doses of goserelin were administered on Days 28 and 56, respectively. 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 28 days after the first dose of goserelin.

Measured Values

	Degarelix 240 mg/80 mg	Goserelin (3.6 mg) + Bicalutamide (50 mg)
Number of Participants Analyzed	82	97
Change From Baseline in Burden of Urinary Symptoms Based on the Benign Prostatic Hyperplasia Impact Index (BPHII) [units: scores on a scale] Mean (Standard Deviation)		
Week 4	-0.78 (2.03)	-0.70 (2.34)
Week 8	-0.88 (2.73)	-1.09 (2.48)
Week 12	-1.28 (2.62)	-1.16 (2.67)

9. 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)	Goserelin implants (3.6 mg) were inserted s.c. into the abdominal wall every 28 days. The first dose was administered on Day 0. The second and third doses of goserelin were administered on Days 28 and 56, respectively. 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 28 days after the first dose of goserelin.

Measured Values

	Degarelix 240 mg/80 mg	Goserelin (3.6 mg) + Bicalutamide (50 mg)
Number of Participants Analyzed	84	98
Number of Participants With Markedly Abnormal Values in Vital Signs and Body Weight [units: participants]		
Diastolic blood pressure <=50 and decrease >=15	0	0
Diastolic blood pressure >=105 and increase >=15	0	1
Systolic blood pressure <=90 and decrease >=20	0	0
Systolic blood pressure >=180 and increase >=20	2	4
Heart rate <=50 and decrease >=15	1	0

	Degarelix 240 mg/80 mg	Goserelin (3.6 mg) + Bicalutamide (50 mg)
Heart rate >=120 and increase >=15	0	0
Body weight decrease of >=7 percent	0	5
Body weight increase of >=7 percent	2	3

10. 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)	Goserelin implants (3.6 mg) were inserted s.c. into the abdominal wall every 28 days. The first dose was administered on Day 0. The second and third doses of goserelin were administered on Days 28 and 56, respectively. 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 28 days after the first dose of goserelin.

Measured Values

	Degarelix 240 mg/80 mg	Goserelin (3.6 mg) + Bicalutamide (50 mg)
Number of Participants Analyzed	84	98
Number of Participants With Markedly Abnormal Values in Safety Laboratory Variables [units: participants]		

	Degarelix 240 mg/80 mg	Goserelin (3.6 mg) + Bicalutamide (50 mg)
B-Haematocrit (Ratio) <=0.37	13	16
B-Haemoglobin (g/L) <=115	2	1
B-Red blood cell count (10^12/L) <=3.5	1	0
B-White blood cell count (10^9/L) <=2.8	3	1
S-Alanine aminotransferase (IU/L) >3xULN	1	2
S-Alkaline phosphatase (IU/L) >3xULN+25% increase	0	1
S-Aspartate aminotransferase (IU/L) >3xULN	0	2
S-Cholesterol (mmol/L) >=8.0	2	0
S-Glutamyltransferase (IU/L) >3xULN	1	0
S-Potassium (mmol/L) >=5.8	3	3
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.

	Description
Goserelin (3.6 mg) + Bicalutamide (50 mg)	Goserelin implants (3.6 mg) were inserted s.c. into the abdominal wall every 28 days. The first dose was administered on Day 0. The second and third doses of goserelin were administered on Days 28 and 56, respectively. 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 28 days after the first dose of goserelin.

Serious Adverse Events

	Degarelix 240 mg/80 mg		Goserelin (3.6 mg) + Bicalutamide (50 mg)	
	Affected/At Risk (%)	# Events	Affected/At Risk (%)	# Events
Total	1/84 (1.19%)		7/98 (7.14%)	
Cardiac disorders				
Cardiac failure [A] †	0/84 (0%)	0	2/98 (2.04%)	2
Gastrointestinal disorders				
Gastric ulcer [A] †	0/84 (0%)	0	1/98 (1.02%)	1
General disorders				
Catheter related complication [A] †	1/84 (1.19%)	1	0/98 (0%)	0
Infections and infestations				
Pneumonia [A] †	0/84 (0%)	0	2/98 (2.04%)	2
Staphylococcal sepsis [A] †	0/84 (0%)	0	1/98 (1.02%)	1
Investigations				
Haemoglobin decreased [A] †	0/84 (0%)	0	1/98 (1.02%)	1
Metabolism and nutrition disorders				
Gout [A] †	0/84 (0%)	0	1/98 (1.02%)	1
Neoplasms benign, malignant and unspecified (incl cysts and polyps)				
Bladder cancer [A] †	0/84 (0%)	0	1/98 (1.02%)	1
Rectosigmoid cancer [A] †	0/84 (0%)	0	1/98 (1.02%)	1
Nervous system disorders				

	Degarelix 240 mg/80 mg		Goserelin (3.6 mg) + Bicalutamide (50 mg)	
	Affected/At Risk (%)	# Events	Affected/At Risk (%)	# Events
Transient ischaemic attack [A] †	0/84 (0%)	0	1/98 (1.02%)	1
Renal and urinary disorders				
Ureteric obstruction [A] †	1/84 (1.19%)	1	0/98 (0%)	0
Respiratory, thoracic and mediastinal disorders				
Dyspnoea [A] †	0/84 (0%)	0	1/98 (1.02%)	1

† 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: 2%

	Degarelix 240 mg/80 mg		Goserelin (3.6 mg) + Bicalutamide (50 mg)	
	Affected/At Risk (%)	# Events	Affected/At Risk (%)	# Events
Total	33/84 (39.29%)		47/98 (47.96%)	
Blood and lymphatic system disorders				
Anaemia [A] †	0/84 (0%)	0	2/98 (2.04%)	2
Cardiac disorders				
Atrial fibrillation [A] †	0/84 (0%)	0	2/98 (2.04%)	2
Cardiac failure [A] †	0/84 (0%)	0	2/98 (2.04%)	2
Gastrointestinal disorders				
Gastric ulcer [A] †	0/84 (0%)	0	2/98 (2.04%)	2
General disorders				
Asthenia [A] †	2/84 (2.38%)	2	1/98 (1.02%)	1
Injection site erythema [A] †	3/84 (3.57%)	4	0/98 (0%)	0
Injection site induration [A] †	2/84 (2.38%)	4	0/98 (0%)	0
Injection site inflammation [A] †	2/84 (2.38%)	2	0/98 (0%)	0

	Degarelix 240 mg/80 mg		Goserelin (3.6 mg) + Bicalutamide (50 mg)	
	Affected/At Risk (%)	# Events	Affected/At Risk (%)	# Events
Injection site pain [A] †	12/84 (14.29%)	20	0/98 (0%)	0
Injection site pruritus [A] †	2/84 (2.38%)	2	0/98 (0%)	0
Injection site swelling [A] †	3/84 (3.57%)	4	0/98 (0%)	0
Infections and infestations				
Pneumonia [A] †	0/84 (0%)	0	3/98 (3.06%)	3
Urinary tract infection [A] †	0/84 (0%)	0	2/98 (2.04%)	2
Investigations				
Blood alkaline phosphatase increased [A] †	0/84 (0%)	0	2/98 (2.04%)	2
Weight decreased [A] †	1/84 (1.19%)	1	3/98 (3.06%)	3
Weight increased [A] †	0/84 (0%)	0	2/98 (2.04%)	2
Musculoskeletal and connective tissue disorders				
Back pain [A] †	2/84 (2.38%)	2	2/98 (2.04%)	2
Myalgia [A] †	1/84 (1.19%)	1	2/98 (2.04%)	2
Nervous system disorders				
Headache [A] †	3/84 (3.57%)	3	0/98 (0%)	0
Renal and urinary disorders				
Urinary retention [A] †	0/84 (0%)	0	2/98 (2.04%)	2
Reproductive system and breast disorders				
Erectile dysfunction [A] †	4/84 (4.76%)	5	4/98 (4.08%)	4
Skin and subcutaneous tissue disorders				
Hyperhidrosis [A] †	4/84 (4.76%)	4	5/98 (5.1%)	5
Vascular disorders				
Flushing [A] †	1/84 (1.19%)	1	2/98 (2.04%)	2

	Degarelix 240 mg/80 mg		Goserelin (3.6 mg) + Bicalutamide (50 mg)	
	Affected/At Risk (%)	# Events	Affected/At Risk (%)	# Events
Hot flush [A] †	8/84 (9.52%)	8	17/98 (17.35%)	17
Hypertension [A] †	2/84 (2.38%)	2	1/98 (1.02%)	1

† 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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