ClinicalTrials.gov Protocol and Results Registration System (PRS) Receipt
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Grantor: CDER IND/IDE Number: 104367 Serial Number:

A Trial of Degarelix in Men With Lower Urinary Tract Symptoms (LUTS) Associated With Benign Prostatic Hyperplasia (BPH) (DELUTS)

This study has been completed.

Sponsor:	Ferring Pharmaceuticals
Collaborators:	
Information provided by (Responsible Party):	Ferring Pharmaceuticals
ClinicalTrials.gov Identifier:	NCT00947882

Purpose

A dose-finding, multi-centre, double-blind, randomised, parallel, placebo-controlled trial to investigate efficacy and safety of degarelix in men with lower urinary tract symptoms (LUTS) associated with benign prostatic hyperplasia (BPH)

Condition	Intervention	Phase
Lower Urinary Tract Symptoms (LUTS)	Drug: Placebo Drug: Degarelix 10 mg Drug: Degarelix 20 mg Drug: Degarelix 30 mg	Phase 2

Study Type: Interventional
Study Design: Treatment, Parallel Assignment, Double Blind (Subject, Investigator, Outcomes Assessor), Randomized, Safety/Efficacy Study
Official Title: A Dose-Finding, Multi-Centre, Double-Blind, Randomised, Parallel, Placebo-Controlled Trial to Investigate Efficacy and Safety of Degarelix in Men With Lower Urinary Tract Symptoms (LUTS) Associated With Benign Prostatic Hyperplasia (BPH)

Further study details as provided by Ferring Pharmaceuticals:

Primary Outcome Measure:

- Mean Change in International Prostate Symptom Score (IPSS) [Time Frame: From Baseline to Month 3 after Dosing] [Designated as safety issue: No]
  This outcome measure was used to assess the dose-response of the 3 degarelix dose groups in terms of severity of lower urinary tract symptoms (LUTS) and progress of the disease process, versus the placebo group. One treatment month equals 28 days. The IPSS questionnaire is a tool commonly used to assess the severity of LUTS, and to monitor the progress of the symptoms during treatment. It contains 7 questions regarding incomplete emptying, frequency, intermittency, urgency, weak stream, straining, and nocturia. Each question is assigned a score of 0-5 (i.e. minimum total score is 0 and the maximum score is 35), where "0" corresponds to a response of "not at all" for the first six symptoms and "none" for nocturia, and "5" corresponds to a response of "almost always" for the first six symptoms and "5 times or more" for nocturia. The IPSS also includes a question to evaluate a patient's quality of life in relation to his urinary symptoms, which is not included in the total IPSS score.

Secondary Outcome Measures:

- Mean Change in IPSS [Time Frame: From Baseline to Month 4, Month 5 and Month 6 after Dosing] [Designated as safety issue: No]
  This secondary outcome measure was used to assess the maintained dose-response of the 3 degarelix dose groups in terms of severity of LUTS and progress of the disease process, versus the placebo group.
- Odds Ratio (as Compared to Placebo) of Treatment Response in IPSS [Time Frame: At Month 3, Month 4, Month 5 and Month 6 after Dosing] [Designated as safety issue: No]
  A 3-point reduction in IPSS score compared to baseline is defined as a clinically meaningful treatment response. Percentage of participants who met criteria for a clinically meaningful treatment response and odds ratios of treatment responses between each degarelix dose group and the placebo group are presented.
- Mean Percentage Change in Total Prostate Volume (TPV) [Time Frame: From Baseline to Month 3 and Month 6 after Dosing] [Designated as safety issue: No]
  TPV was measured directly by standardised trans-rectal ultrasound (TRUS).
- Mean Change in Maximum Urinary Flow (Qmax) [Time Frame: From Baseline to Month 3 and Month 6 after Dosing] [Designated as safety issue: No]
  Urinary flow rate (mL/second) was measured using uroflowmetry performed according to the recommendation from the International Continence Society (ICS).

Enrollment: 404
Study Start Date: August 2009
Primary Completion Date: March 2011
Study Completion Date: June 2011

Arms	Assigned Interventions
Placebo Comparator: Placebo	Drug: Placebo Mannitol 50 mg/mL solution
Experimental: Degarelix 10 mg	Drug: Degarelix 10 mg 10 mg degarelix, 40 mg/mL solution Other Names: FE200486 Firmagon
Experimental: Degarelix 20 mg	Drug: Degarelix 20 mg 20 mg degarelix, 40 mg/mL solution Other Names: FE200486

Arms	Assigned Interventions
	Firmagon
Experimental: Degarelix 30 mg	Drug: Degarelix 30 mg 30 mg degarelix, 40 mg/mL solution Other Names: FE200486 Firmagon

Eligibility

Ages Eligible for Study: 50 Years and older
Genders Eligible for Study: Male
Accepts Healthy Volunteers: No

Criteria

Inclusion Criteria:

- Signed informed consent obtained before any trial-related activity is performed
- Men, aged 50 or older
- Clinical signs and symptoms of BPH for ≥6 months
- Moderate to severe LUTS at screening, as defined by International Prostate Symptom Score (IPSS) ≥13
- An IPSS QoL score of ≥3 at screening
- Prostate specific antigen (PSA) at screening ≤10 ng/mL (responsibility of the Investigator to rule out prostate cancer when PSA is >4 ng/mL, except in the USA where patients with a PSA >4 and ≤10 ng/mL should undergo a prostatic biopsy or have a negative prostatic biopsy within 12 months prior to participation in the trial)
- Maximum urinary flow (Qmax) ranging between 5 to 15 mL/second with a minimum voided volume >125 mL at screening

Exclusion Criteria:

- Post void residual volume (PVR) >250 mL
- Stone in the bladder or urethra causing symptoms
- Acute or chronic prostatitis
- Interstitial cystitis / painful bladder syndrome
- Acute or recurrent urinary tract infections
- History of acute urinary retention (AUR)
- Lower urinary tract instrumentation (including prostate biopsy) within 30 days of dosing at Visit 2
- Clinical evidence of any of the following urinary tract conditions:
    a. Mullerian duct cysts
    b. Atonic, decompensated, or hypocontractile bladder
    c. Detrusor-sphincter dyssynergia (contraction of the detrusor without sphincter relaxation)
- History of any of the following pelvic conditions:

a. Pelvic surgery or any other pelvic procedure, including radical prostatectomy, pelvic surgery for removal of malignancy, or open lower colonic or rectal surgery
b. Pelvic radiotherapy
c. Any prior surgical procedure of the urinary tract, including minimally invasive LUTS/BPH therapies
d. Lower tract malignancy or trauma

- Clinically significant microscopic haematuria at screening
- History of significant renal insufficiency, defined as receiving renal dialysis or having an estimated creatinine clearance <30 mL/minute at screening
- Systolic blood pressure >180 or <90 mmHg or diastolic blood pressure >110 or <50 mmHg at screening or malignant hypertension
- Any causes other than BPH, which may affect evaluation of symptoms of urine flow (e.g. neurogenic bladder, bladder neck contracture, urethral stricture, and bladder malignancy) as judged by the Investigator
- Use of any prohibited therapies
- Elevated liver function tests at screening:

a. Aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP) >2 times the upper limit of normal
b. Total bilirubin >1.5 times the upper limit of normal

- QTc interval on the screening ECG >450 ms, or a family history of long QT syndrome
- Any clinically significant disorder (other than BPH) including, but not limited to, renal, haematological, gastrointestinal, endocrine, cardiac, neurological, or psychiatric disease, or any other condition, which may affect the patient's health or the outcome of the trial as judged by the Investigator
- Diagnosed cancer within the last 5 years except for adequately managed basal cell carcinoma and squamous cell carcinoma of the skin
- History of severe untreated asthma, anaphylactic reactions, or severe urticaria and/or angioedema
- Mental incapacity or language barrier precluding adequate understanding or co-operation
- History or current evidence of drug, alcohol, or substance abuse within 6 months prior to screening
- Hypersensitivity towards any component of the investigational medicinal product (IMP)
- Previous participation in any degarelix trial

Contacts and Locations

Locations

United States, Alabama

Urology Centers of Alabama, PC
Homewood, Alabama, United States

Coastal Clinical Research Inc
Mobile, Alabama, United States

United States, California

California Professional Research
Newport Beach, California, United States

United States, Colorado

The Urology Center of Colorado
Denver, Colorado, United States

Genitourinary Surgical Consultants
Denver, Colorado, United States

Urology Associates , PC
Englewood, Colorado, United States

United States, Florida

South Florida Medical Research
Aventura, Florida, United States
Winter Park Urology Associates
Orlando, Florida, United States
Pinellas Urology Inc
St Petersburg, Florida, United States
Florida Urology Partners
Tampa, Florida, United States
United States, Illinois
Northwestern University
Chicago, Illinois, United States
United States, Maryland
University of Maryland
Baltimore, Maryland, United States
United States, New York
Weill Cornell Medical College New York Presbyterian
New York, New York, United States
Hudson Valley Urology, PC
Poughkeepsie, New York, United States
United States, North Carolina
Duke University Medical Center
Durham, North Carolina, United States
United States, North Dakota
St Alexius Medical Center
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United States, Ohio
Patient Priority Clinical Sites, LLC
Cincinnati, Ohio, United States
United States, Rhode Island
Omega Medical Research
Warwick, Rhode Island, United States
United States, South Carolina
Medical University of South Carolina
Charleston, South Carolina, United States
Carolina Urologic Research Center
Myrtle Beach, South Carolina, United States
United States, Texas
The UT Southwestern Medical Center at Dallas
Dallas, Texas, United States
United States, Virginia
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Brampton, Ontario, Canada
Brandford Urology Research
Brantford, Ontario, Canada
Kenneth Jansz Professional Corporation
Burlington, Ontario, Canada
Guelp Urology
Guelph, Ontario, Canada
Centre for Applied Urological Research
Kingston, Ontario, Canada
Mor Urology Inc
Newmarket, Ontario, Canada
Investigational Site
North Bay, Ontario, Canada
Female/Male Health Centres
Oakville, Ontario, Canada
Mahoney Medicine Professional Corporation
Ottawa, Ontario, Canada
Todd Webster Ontario Inc
Owen Sound, Ontario, Canada
Anthony Skehan Medicine Professional Corporation
Thunder Bay, Ontario, Canada
The Male Health Centre
Toronto, Ontario, Canada
Canada, Quebec
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Montreal, Quebec, Canada
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Brno, Czech Republic
Prvni privatni chirurgicke centrum SANUS, Labská kotlina I/1220
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Litomerice, Czech Republic
Slezska nemocnice, prospevkova organizace, Urologicke oddeleni
Opava, Czech Republic
Androgeos - soukrome urologicke a andrologicke cen, Na valech 4/289
Praha, Czech Republic
Urocentrum, Karlovo namesti 3
Praha, Czech Republic
Urologica ambulance, Praha 10
Praha, Czech Republic
Ústecké urocentrum, Ústi nad Labem (Liehne)
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Investigators

Study Director:	Clinical Development Support	Ferring Pharmaceuticals

More Information

Responsible Party:	Ferring Pharmaceuticals
Study ID Numbers:	FE200486 CS36 2009-012325-11 [EudraCT Number] 104367 [IND Number]
Health Authority:	United States: Food and Drug Administration United States: Institutional Review Board Canada: Health Canada Canada: Ethics Review Committee Italy: The Italian Medicines Agency Italy: Ministry of Health Italy: National Bioethics Committee Czech Republic: State Institute for Drug Control Czech Republic: Ethics Committee Poland: Ministry of Health Poland: Office for Registration of Medicinal Products, Medical Devices and Biocidal Products Belgium: Federal Agency for Medicinal Products and Health Products Belgium: Institutional Review Board United Kingdom: Medicines and Healthcare Products Regulatory Agency United Kingdom: Research Ethics Committee Denmark: Danish Medicines Agency Denmark: The Danish National Committee on Biomedical Research Ethics

Study Results

Participant Flow

Recruitment Details	Patients who met the eligibility criteria were randomised in a 1:1:1:1 manner to 1 of the 4 treatment groups in this trial. The randomisation was stratified by region (North America and Europe) and prostate volume (<30 mL and ≥30 mL). 404 patients were randomised and received a single dose of placebo, 10 mg, 20 mg, or 30 mg degarelix.

Reporting Groups

	Description
Placebo	Placebo: Mannitol 50 mg/mL solution. The dose was administered as a subcutaneous (s.c.) injection in the abdominal region.
Degarelix 10 mg	Degarelix 10 mg: 10 mg degarelix, 40 mg/mL solution. The dose was administered as a s.c. injection in the abdominal region.
Degarelix 20 mg	Degarelix 20 mg: 20 mg degarelix, 40 mg/mL solution. The dose was administered as a s.c. injection in the abdominal region.
Degarelix 30 mg	Degarelix 30 mg: 30 mg degarelix, 40 mg/mL solution. The dose was administered as a s.c. injection in the abdominal region.

Overall Study

	Placebo	Degarelix 10 mg	Degarelix 20 mg	Degarelix 30 mg
Started	100 [1]	101	101	102
Full Analysis Set (FAS)	100 [2]	101	100 [3]	102
Actual Treatment	98 [4]	101	100 [5]	105
Safety Analysis Set	98 [6]	101	100	105
Visit 12, Month 6	93 [7]	91	90	95
Completed	26 [8]	24	22	20
Not Completed	74	77	79	82
Adverse Event	0	1	4	4
Withdrawal by Subject	2	0	8	2
Protocol Violation	0	0	1	0

	Placebo	Degarelix 10 mg	Degarelix 20 mg	Degarelix 30 mg
Lost to Follow-up	0	2	1	0
Other/Unknown	10	13	3	6
Trial Terminated by Sponsor	62	61	62	70

[1] Started: Randomised.
[2] FAS: Received a dose of IMP and completed at least one post-baseline IPSS questionnaire.
[3] 1 patient received 20 mg degarelix but had no post-baseline IPSS value and was excluded from the FAS
[4] 2 placebo patients received 30 mg degarelix
[5] 1 patient randomised to 20 mg degarelix received 30 mg degarelix
[6] Safety Analysis Set: Received a dose of Investigational Medicinal Product (IMP).
[7] The trial was stopped when all patients had completed Visit 12, scheduled 6 months after the dosing.
[8] End of Trial, Month 12: Patients who had completed the 12-month period when the trial was stopped.

Baseline Characteristics

Analysis Population Description

FAS. The efficacy analyses were based on the “as planned” treatment. Three patients deviated from the planned dosing and were included in the planned treatment groups in the FAS (i.e. not in the actual treatment groups as for the Safety Analysis Set).

Reporting Groups

	Description
Placebo	Placebo: Mannitol 50 mg/mL solution. The dose was administered as a s.c. injection in the abdominal region.
Degarelix 10 mg	Degarelix 10 mg: 10 mg degarelix, 40 mg/mL solution. The dose was administered as a s.c. injection in the abdominal region.
Degarelix 20 mg	Degarelix 20 mg: 20 mg degarelix, 40 mg/mL solution. The dose was administered as a s.c. injection in the abdominal region.
Degarelix 30 mg	Degarelix 30 mg: 30 mg degarelix, 40 mg/mL solution. The dose was administered as a s.c. injection in the abdominal region.

Baseline Measures

	Placebo	Degarelix 10 mg	Degarelix 20 mg	Degarelix 30 mg	Total
Number of Participants	100	101	100	102	403
Age, Continuous [units: years] Mean (Standard Deviation)	65.2 (7.86)	64.9 (7.89)	65.7 (7.12)	65.4 (7.56)	65.3 (7.59)
Gender, Male/Female					

	Placebo	Degarelix 10 mg	Degarelix 20 mg	Degarelix 30 mg	Total
[units: participants]					
Female	0	0	0	0	0
Male	100	101	100	102	403
Ethnicity (NIH/OMB) [units: participants]					
Hispanic or Latino	1	4	0	4	9
Not Hispanic or Latino	99	97	100	98	394
Unknown or Not Reported	0	0	0	0	0
Race (NIH/OMB) [units: participants]					
American Indian or Alaska Native	0	1	0	1	2
Asian	0	1	1	2	4
Native Hawaiian or Other Pacific Islander	0	0	0	0	0
Black or African American	4	3	3	3	13
White	96	96	96	96	384
More than one race	0	0	0	0	0
Unknown or Not Reported	0	0	0	0	0
Region of Enrollment [units: participants]					
North America	59	60	61	60	240
Europe	41	41	39	42	163
Baseline Body Mass Index (BMI) [units: (kg/m^2)] Mean (Standard Deviation)	28.5 (3.66)	28.4 (3.93)	27.9 (3.84)	28.2 (4.81)	28.2 (4.08)
Baseline International Prostate Symptom Scores (IPSS) [1] [units: units on a scale] Mean (Standard Deviation)	19.1 (4.38)	19.9 (5.21)	19.6 (4.42)	19.8 (4.88)	19.6 (4.73)
Baseline Total Prostate Volume (TPV) [2] [units: mL]	41.6 (17.8)	42.9 (18.8)	42.3 (20.2)	42.1 (20.2)	42.2 (19.2)

	Placebo	Degarelix 10 mg	Degarelix 20 mg	Degarelix 30 mg	Total
Mean (Standard Deviation)					
Baseline Maximum Urinary Flow (Qmax) [3] [units: mL/sec] Mean (Standard Deviation)	10.2 (2.51)	10.3 (2.65)	10.6 (4.58)	10.2 (2.44)	10.3 (3.05)

[1] The IPSS questionnaire was used to assess the severity of Lower Urinary Tract Symptoms (LUTS). A detailed description of the questionnaire is provided in the Primary Outcome Measure section.

[2] TPV was measured directly by Trans-Rectal Ultrasound (TRUS).

[3] Uroflowmetry was used according to International Continence Society (ICS) recommendation.

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Mean Change in International Prostate Symptom Score (IPSS)
Measure Description	This outcome measure was used to assess the dose-response of the 3 degarelix dose groups in terms of severity of lower urinary tract symptoms (LUTS) and progress of the disease process, versus the placebo group. One treatment month equals 28 days. The IPSS questionnaire is a tool commonly used to assess the severity of LUTS, and to monitor the progress of the symptoms during treatment. It contains 7 questions regarding incomplete emptying, frequency, intermittency, urgency, weak stream, straining, and nocturia. Each question is assigned a score of 0-5 (i.e. minimum total score is 0 and the maximum score is 35), where "0" corresponds to a response of "not at all" for the first six symptoms and "none" for nocturia, and "5" corresponds to a response of "almost always" for the first six symptoms and "5 times or more" for nocturia. The IPSS also includes a question to evaluate a patient's quality of life in relation to his urinary symptoms, which is not included in the total IPSS score.
Time Frame	From Baseline to Month 3 after Dosing
Safety Issue?	No

Analysis Population Description

FAS. The "as planned" patient allocation for treatment groups was used in the efficacy analyses (please refer to the Baseline Characteristics section).

Reporting Groups

	Description
Placebo	Mannitol 50 mg/mL solution. The dose was administered as a subcutaneous (s.c.) injection in the abdominal region.

	Description
Degarelix 10 mg	Degarelix 10 mg: 10 mg degarelix, 40 mg/mL solution. The dose was administered as a subcutaneous (s.c.) injection in the abdominal region.
Degarelix 20 mg	Degarelix 20 mg: 20 mg degarelix, 40 mg/mL solution. The dose was administered as a s.c. injection in the abdominal region.
Degarelix 30 mg	Degarelix 30 mg: 30 mg degarelix, 40 mg/mL solution. The dose was administered as a s.c. injection in the abdominal region.

Measured Values

	Placebo	Degarelix 10 mg	Degarelix 20 mg	Degarelix 30 mg
Number of Participants Analyzed	100	101	100	102
Mean Change in International Prostate Symptom Score (IPSS) [units: percentage change from baseline] Mean (Standard Deviation)	-4.46 (5.34)	-5.65 (6.03)	-6.11 (5.7)	-5.88 (5.97)

Statistical Analysis 1 for Mean Change in International Prostate Symptom Score (IPSS)

Statistical Analysis Overview	Comparison Groups	Placebo, Degarelix 30 mg
	Comments	Analysis of Covariance (ANCOVA) of the change from baseline in IPSS at Month 3 in the FAS population using the Last Observation Carried Forward (LOCF) method, including the baseline IPSS as adjusting covariate and treatment group, prostate volume stratum (<30 mL and ≥30 mL), and region (North America and Europe) as factors.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.0911
	Comments	P-value based on Williams' extended trend test of comparison vs. placebo at Month 3. No adjustment for multiple comparisons was made.
	Method	Other [Step-down, Williams' extended trend test]
	Comments	Step-down procedure (starting with 30 mg vs. placebo) to identify the minimum effective dose. The step-down testing protects the type I error rate.

Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	-1.30

	Estimation Comments	Treatment difference between "Degarelix 30 mg" and "Placebo" at Month 3.

Statistical Analysis 2 for Mean Change in International Prostate Symptom Score (IPSS)

Statistical Analysis Overview	Comparison Groups	Placebo, Degarelix 20 mg
	Comments	Analysis of Covariance (ANCOVA) of the change from baseline in IPSS at Month 3 in the FAS population using the Last Observation Carried Forward (LOCF) method, including the baseline IPSS as adjusting covariate and treatment group, prostate volume stratum (<30 mL and ≥30 mL), and region (North America and Europe) as factors.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.0865
	Comments	P-value based on Williams' extended trend test of comparison vs. placebo at Month 3. No adjustment for multiple comparisons was made.
	Method	Other [Step-down, Williams' extended trend test]
	Comments	Step-down procedure (starting with 30 mg vs. placebo) to identify the minimum effective dose. The step-down testing protects the type I error rate.

Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	-1.44
	Estimation Comments	Treatment difference between "Degarelix 20 mg" and "Placebo" at Month 3.

Statistical Analysis 3 for Mean Change in International Prostate Symptom Score (IPSS)

Statistical Analysis Overview	Comparison Groups	Placebo, Degarelix 10 mg
	Comments	Analysis of Covariance (ANCOVA) of the change from baseline in IPSS at Month 3 in the FAS population using the Last Observation Carried Forward (LOCF) method, including the baseline IPSS as adjusting covariate and treatment group, prostate volume stratum (<30 mL and ≥30 mL), and region (North America and Europe) as factors.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.2342
	Comments	P-value based on Williams' extended trend test of comparison vs. placebo at Month 3. No adjustment for multiple comparisons was made.

	Method	Other [Step-down, Williams' extended trend test]
	Comments	Step-down procedure (starting with 30 mg vs. placebo) to identify the minimum effective dose. The step-down testing protects the type I error rate.

Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	-0.92
	Estimation Comments	Treatment difference between "Degarelix 10 mg" and "Placebo" at Month 3.

2. Secondary Outcome Measure:

Measure Title	Mean Change in IPSS
Measure Description	This secondary outcome measure was used to assess the maintained dose-response of the 3 degarelix dose groups in terms of severity of LUTS and progress of the disease process, versus the placebo group.
Time Frame	From Baseline to Month 4, Month 5 and Month 6 after Dosing
Safety Issue?	No

Analysis Population Description

FAS. The "as planned" patient allocation for treatment groups was used (please refer to the Baseline Characteristics section).

Reporting Groups

	Description
Placebo	Mannitol 50 mg/mL solution. The dose was administered as a subcutaneous (s.c.) injection in the abdominal region.
Degarelix 10 mg	Degarelix 10 mg: 10 mg degarelix, 40 mg/mL solution. The dose was administered as a s.c. injection in the abdominal region.
Degarelix 20 mg	Degarelix 20 mg: 20 mg degarelix, 40 mg/mL solution. The dose was administered as a s.c. injection in the abdominal region.
Degarelix 30 mg	Degarelix 30 mg: 30 mg degarelix, 40 mg/mL solution. The dose was administered as a s.c. injection in the abdominal region.

Measured Values

	Placebo	Degarelix 10 mg	Degarelix 20 mg	Degarelix 30 mg
Number of Participants Analyzed	100	101	100	102
Mean Change in IPSS [units: percentage change from baseline] Mean (Standard Deviation)				

	Placebo	Degarelix 10 mg	Degarelix 20 mg	Degarelix 30 mg
Mean Percentage Change at Month 4	-4.12 (5.65)	-5.52 (6.18)	-6.3 (6.38)	-5.64 (5.6)
Mean Percentage Change at Month 5	-4.34 (5.94)	-5.59 (6.89)	-6.1 (6.46)	-5.37 (5.97)
Mean Percentage Change at Month 6	-4.3 (5.47)	-5.42 (6.7)	-5.72 (5.59)	-5.62 (5.69)

Statistical Analysis 1 for Mean Change in IPSS

Statistical Analysis Overview	Comparison Groups	Placebo, Degarelix 30 mg
	Comments	ANCOVA of the change from baseline in IPSS at Months 4 in the FAS population using the LOCF method, including the baseline IPSS as adjusting covariate and treatment group, prostate volume stratum (<30 mL and ≥30 mL), and region (North America and Europe) as factors.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.0367
	Comments	P-values based on Williams' extended trend test of comparison vs. placebo at Month 4. No adjustment for multiple comparisons was made.
	Method	Other [Step-down, Williams' extended trend test]
	Comments	Step-down procedure (starting with 30 mg vs. placebo) to identify the minimum effective dose. The step-down testing protects the type I error rate.

Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	-1.62
	Estimation Comments	Treatment difference between "Degarelix 30 mg" and "Placebo" at Month 4.

Statistical Analysis 2 for Mean Change in IPSS

Statistical Analysis Overview	Comparison Groups	Placebo, Degarelix 20 mg
	Comments	ANCOVA of the change from baseline in IPSS at Month 4 in the FAS population using the LOCF method, including the baseline IPSS as adjusting covariate and treatment group, prostate volume stratum (<30 mL and ≥30 mL), and region (North America and Europe) as factors.
	Non-Inferiority or Equivalence Analysis?	No

	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.0231
	Comments	P-value based on Williams' extended trend test of comparison vs. placebo at Month 4. No adjustment for multiple comparisons was made.
	Method	Other [Step-down, Williams' extended trend test]
	Comments	Step-down procedure (starting with 30 mg vs. placebo) to identify the minimum effective dose. The step-down testing protects the type I error rate.

Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	-1.97
	Estimation Comments	Treatment difference between "Degarelix 20 mg" and "Placebo" at Month 4.

Statistical Analysis 3 for Mean Change in IPSS

Statistical Analysis Overview	Comparison Groups	Placebo, Degarelix 10 mg
	Comments	ANCOVA of the change from baseline in IPSS at Month 4 in the FAS population using the LOCF method, including the baseline IPSS as adjusting covariate and treatment group, prostate volume stratum (<30 mL and ≥30 mL), and region (North America and Europe) as factors.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.1638
	Comments	P-value based on Williams' extended trend test of comparison vs. placebo at Month 4. No adjustment for multiple comparisons was made.
	Method	Other [Step-down, Williams' extended trend test]
	Comments	Step-down procedure (starting with 30 mg vs. placebo) to identify the minimum effective dose. The step-down testing protects the type I error rate.

Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	-1.11
	Estimation Comments	Treatment difference between "Degarelix 10 mg" and "Placebo" at Month 4.

Statistical Analysis 4 for Mean Change in IPSS

Statistical Analysis Overview	Comparison Groups	Placebo, Degarelix 30 mg
	Comments	ANCOVA of the change from baseline in IPSS at Month 5 in the FAS population using the LOCF method, including the baseline IPSS as adjusting covariate and treatment group, prostate volume stratum (<30 mL and ≥30 mL), and region (North America and Europe) as factors.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.1941
	Comments	P-values based on Williams' extended trend test of comparisons vs. placebo at Month 5. No adjustment for multiple comparison was made.
	Method	Other [Step-down, Williams' extended trend test]
	Comments	Step-down procedure (starting with 30 mg vs. placebo) to identify the minimum effective dose. The step-down testing protects the type I error rate.

Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	-1.14
	Estimation Comments	Treatment difference between "Degarelix 30 mg" and "Placebo" at Month 5.

Statistical Analysis 5 for Mean Change in IPSS

Statistical Analysis Overview	Comparison Groups	Placebo, Degarelix 20 mg
	Comments	ANCOVA of the change from baseline in IPSS at Month 5 in the FAS population using the LOCF method, including the baseline IPSS as adjusting covariate and treatment group, prostate volume stratum (<30 mL and ≥30 mL), and region (North America and Europe) as factors.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.1083
	Comments	P-value based on Williams' extended trend test of comparison vs. placebo at Month 5. No adjustment for multiple comparisons was made.
	Method	Other [Step-down, Williams' extended trend test]

	Comments	Step-down procedure (starting with 30 mg vs. placebo) to identify the minimum effective dose. The step-down testing protects the type I error rate.

Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	-1.54
	Estimation Comments	Treatment difference between "Degarelix 20 mg" and "Placebo" at Month 5.

Statistical Analysis 6 for Mean Change in IPSS

Statistical Analysis Overview	Comparison Groups	Placebo, Degarelix 10 mg
	Comments	ANCOVA of the change from baseline in IPSS at Month 5 in the FAS population using the LOCF method, including the baseline IPSS as adjusting covariate and treatment group, prostate volume stratum (<30 mL and ≥30 mL), and region (North America and Europe) as factors.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.2782
	Comments	P-value based on Williams' extended trend test of comparison vs. placebo at Month 5. No adjustment for multiple comparisons was made.
	Method	Other [Step-down, Williams' extended trend test]
	Comments	Step-down procedure (starting with 30 mg vs. placebo) to identify the minimum effective dose. The step-down testing protects the type I error rate.

Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	-0.95
	Estimation Comments	Treatment difference between "Degarelix 10 mg" and "Placebo" at Month 5.

Statistical Analysis 7 for Mean Change in IPSS

Statistical Analysis Overview	Comparison Groups	Placebo, Degarelix 30 mg
	Comments	ANCOVA of the change from baseline in IPSS at Month 6 in the FAS population using the LOCF method, including the baseline IPSS as adjusting covariate and treatment group, prostate volume stratum (<30 mL and ≥30 mL), and region (North America and Europe) as factors.
	Non-Inferiority or Equivalence Analysis?	No

	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.1562
	Comments	P-values based on Williams' extended trend test of comparison vs. placebo at Month 6. No adjustment for multiple comparisons was made.
	Method	Other [Step-down, Williams' extended trend test]
	Comments	Step-down procedure (starting with 30 mg vs. placebo) to identify the minimum effective dose. The step-down testing protects the type I error rate.

Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	-1.15
	Estimation Comments	Treatment difference between "Degarelix 30 mg" and "Placebo" at Month 6.

Statistical Analysis 8 for Mean Change in IPSS

Statistical Analysis Overview	Comparison Groups	Placebo, Degarelix 20 mg
	Comments	ANCOVA of the change from baseline in IPSS at Month 6 in the FAS population using the LOCF method, including the baseline IPSS as adjusting covariate and treatment group, prostate volume stratum (<30 mL and ≥30 mL), and region (North America and Europe) as factors.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.1736
	Comments	P-value based on Williams' extended trend test of comparison vs. placebo at Month 6. No adjustment for multiple comparisons was made.
	Method	Other [Step-down, Williams' extended trend test]
	Comments	Step-down procedure (starting with 30 mg vs. placebo) to identify the minimum effective dose. The step-down testing protects the type I error rate.

Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	-1.24
	Estimation Comments	Treatment difference between "Degarelix 20 mg" and "Placebo" at Month 6.

Statistical Analysis 9 for Mean Change in IPSS

Statistical Analysis Overview	Comparison Groups	Placebo, Degarelix 10 mg
	Comments	ANCOVA of the change from baseline in IPSS at Month 6 in the FAS population using the LOCF method, including the baseline IPSS as adjusting covariate and treatment group, prostate volume stratum (<30 mL and ≥30 mL), and region (North America and Europe) as factors.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.3132
	Comments	P-value based on Williams' extended trend test of comparison vs. placebo at Month 6. No adjustment for multiple comparisons was made.
	Method	Other [Step-down, Williams' extended trend test]
	Comments	Step-down procedure (starting with 30 mg vs. placebo) to identify the minimum effective dose. The step-down testing protects the type I error rate.

Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	-0.84
	Estimation Comments	Treatment difference between "Degarelix 10 mg" and "Placebo" at Month 6.

3. Secondary Outcome Measure:

Measure Title	Odds Ratio (as Compared to Placebo) of Treatment Response in IPSS
Measure Description	A 3-point reduction in IPSS score compared to baseline is defined as a clinically meaningful treatment response. Percentage of participants who met criteria for a clinically meaningful treatment response and odds ratios of treatment responses between each degarelix dose group and the placebo group are presented.
Time Frame	At Month 3, Month 4, Month 5 and Month 6 after Dosing
Safety Issue?	No

Analysis Population Description

FAS. The "as planned" patient allocation for treatment groups was used (please refer to the Baseline Characteristics section).

Reporting Groups

	Description
Placebo	Mannitol 50 mg/mL solution. The dose was administered as a subcutaneous (s.c.) injection in the abdominal region.
Degarelix 10 mg	Degarelix 10 mg: 10 mg degarelix, 40 mg/mL solution. The dose was administered as a s.c. injection in the abdominal region.
Degarelix 20 mg	Degarelix 20 mg: 20 mg degarelix, 40 mg/mL solution. The dose was administered as a s.c. injection in the abdominal region.
Degarelix 30 mg	Degarelix 30 mg: 30 mg degarelix, 40 mg/mL solution. The dose was administered as a s.c. injection in the abdominal region.

Measured Values

	Placebo	Degarelix 10 mg	Degarelix 20 mg	Degarelix 30 mg
Number of Participants Analyzed	100	101	100	102
Odds Ratio (as Compared to Placebo) of Treatment Response in IPSS [units: percentage of participants]				
3-point reduction in IPSS vs. baseline (Month 3)	59.0	72.3	69.0	68.6
3-point reduction in IPSS vs. baseline (Month 4)	57.0	65.3	71.0	70.6
3-point reduction in IPSS vs. baseline (Month 5)	61.0	64.4	66.0	67.6
3-point reduction in IPSS vs. baseline (Month 6)	62.0	68.3	67.0	71.6

Statistical Analysis 1 for Odds Ratio (as Compared to Placebo) of Treatment Response in IPSS

Statistical Analysis Overview	Comparison Groups	Placebo, Degarelix 30 mg
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.2034
	Comments	Adjustments were made for treatment group, baseline IPSS, graphical region (North America and Europe) and baseline prostate size (<30 mL and ≥30 mL). Unadjusted p-value of comparison vs. placebo at Month 3.

	Method	Regression, Logistic
	Comments	No adjustment for multiple comparisons was made. LOCF.

Method of Estimation	Estimation Parameter	Odds Ratio (OR)
	Estimated Value	1.46
	Confidence Interval	(2-Sided) 95% 0.814 to 2.628
	Estimation Comments	Odds ratio of treatment response between "Degarelix 30 mg" and "Placebo" at Month 3.

Statistical Analysis 2 for Odds Ratio (as Compared to Placebo) of Treatment Response in IPSS

Statistical Analysis Overview	Comparison Groups	Placebo, Degarelix 20 mg
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.1748
	Comments	Adjustments were made for treatment group, baseline IPSS, graphical region (North America and Europe) and baseline prostate size (<30 mL and ≥30 mL). Unadjusted p-value of comparison vs. placebo at Month 3.
	Method	Regression, Logistic
	Comments	No adjustment for multiple comparisons was made. LOCF.

Method of Estimation	Estimation Parameter	Odds Ratio (OR)
	Estimated Value	1.50
	Confidence Interval	(2-Sided) 95% 0.834 to 2.710
	Estimation Comments	Odds ratio of treatment response between "Degarelix 20 mg" and "Placebo" at Month 3.

Statistical Analysis 3 for Odds Ratio (as Compared to Placebo) of Treatment Response in IPSS

Statistical Analysis Overview	Comparison Groups	Placebo, Degarelix 10 mg
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No

	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.0658
	Comments	Adjustments were made for treatment group, baseline IPSS, graphical region (North America and Europe) and baseline prostate size (<30 mL and ≥30 mL). Unadjusted p-value of comparison vs. placebo at Month 3.
	Method	Regression, Logistic
	Comments	No adjustment for multiple comparisons was made. LOCF.

Method of Estimation	Estimation Parameter	Odds Ratio (OR)
	Estimated Value	1.75
	Confidence Interval	(2-Sided) 95% 0.964 to 3.195
	Estimation Comments	Odds ratio of treatment response between "Degarelix 10 mg" and "Placebo" at Month 3.

Statistical Analysis 4 for Odds Ratio (as Compared to Placebo) of Treatment Response in IPSS

Statistical Analysis Overview	Comparison Groups	Placebo, Degarelix 30 mg
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.0587
	Comments	Adjustments were made for treatment group, baseline IPSS, graphical region (North America and Europe) and baseline prostate size (<30 mL and ≥30 mL). Unadjusted p-value of comparison vs. placebo at Month 4.
	Method	Regression, Logistic
	Comments	No adjustment for multiple comparisons was made. LOCF.

Method of Estimation	Estimation Parameter	Odds Ratio (OR)
	Estimated Value	1.77
	Confidence Interval	(2-Sided) 95% 0.979 to 3.184
	Estimation Comments	Odds ratio of treatment response between "Degarelix 30 mg" and "Placebo" at Month 4.

Statistical Analysis 5 for Odds Ratio (as Compared to Placebo) of Treatment Response in IPSS

Statistical Analysis Overview	Comparison Groups	Placebo, Degarelix 20 mg
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0490
	Comments	Adjustments were made for treatment group, baseline IPSS, graphical region (North America and Europe) and baseline prostate size (<30 mL and ≥30 mL). Unadjusted p-value of comparison vs. placebo at Month 4.
	Method	Regression, Logistic
	Comments	No adjustment for multiple comparisons was made. LOCF.
Method of Estimation	Estimation Parameter	Odds Ratio (OR)
	Estimated Value	1.81
	Confidence Interval	(2-Sided) 95% 1.003 to 3.283
	Estimation Comments	Odds ratio of treatment response between "Degarelix 20 mg" and "Placebo" at Month 4.

Statistical Analysis 6 for Odds Ratio (as Compared to Placebo) of Treatment Response in IPSS

Statistical Analysis Overview	Comparison Groups	Placebo, Degarelix 10 mg
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.2742
	Comments	Adjustments were made for treatment group, baseline IPSS, graphical region (North America and Europe) and baseline prostate size (<30 mL and ≥30 mL). Unadjusted p-value of comparison vs. placebo at Month 4.
	Method	Regression, Logistic
	Comments	No adjustment for multiple comparisons was made. LOCF.

Method of Estimation	Estimation Parameter	Odds Ratio (OR)
	Estimated Value	1.38
	Confidence Interval	(2-Sided) 95% 0.774 to 2.464
	Estimation Comments	Odds ratio of treatment response between "Degarelix 10 mg" and "Placebo" at Month 4.

Statistical Analysis 7 for Odds Ratio (as Compared to Placebo) of Treatment Response in IPSS

Statistical Analysis Overview	Comparison Groups	Placebo, Degarelix 30 mg
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.4206
	Comments	Adjustments were made for treatment group, baseline IPSS, graphical region (North America and Europe) and baseline prostate size (<30 mL and ≥30 mL). Unadjusted p-value of comparison vs. placebo at Month 5.
	Method	Regression, Logistic
	Comments	No adjustment for multiple comparisons was made. LOCF.

Method of Estimation	Estimation Parameter	Odds Ratio (OR)
	Estimated Value	1.28
	Confidence Interval	(2-Sided) 95% 0.706 to 2.304
	Estimation Comments	Odds ratio of treatment response between "Degarelix 30 mg" and "Placebo" at Month 5.

Statistical Analysis 8 for Odds Ratio (as Compared to Placebo) of Treatment Response in IPSS

Statistical Analysis Overview	Comparison Groups	Placebo, Degarelix 20 mg
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.5494
	Comments	Adjustments were made for treatment group, baseline IPSS, graphical region (North America and Europe) and baseline prostate size (<30 mL and ≥30 mL). Unadjusted p-value of comparison vs. placebo at Month 5.
	Method	Regression, Logistic
	Comments	No adjustment for multiple comparisons was made. LOCF.

Method of Estimation	Estimation Parameter	Odds Ratio (OR)
	Estimated Value	1.20
	Confidence Interval	(2-Sided) 95% 0.664 to 2.160
	Estimation Comments	Odds ratio of treatment response between "Degarelix 20 mg" and "Placebo" at Month 5.

Statistical Analysis 9 for Odds Ratio (as Compared to Placebo) of Treatment Response in IPSS

Statistical Analysis Overview	Comparison Groups	Placebo, Degarelix 10 mg
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.7586
	Comments	Adjustments were made for treatment group, baseline IPSS, graphical region (North America and Europe) and baseline prostate size (<30 mL and ≥30 mL). Unadjusted p-value of comparison vs. placebo at Month 5.
	Method	Regression, Logistic
	Comments	No adjustment for multiple comparisons was made. LOCF.

Method of Estimation	Estimation Parameter	Odds Ratio (OR)
	Estimated Value	1.10
	Confidence Interval	(2-Sided) 95% 0.609 to 1.975
	Estimation Comments	Odds ratio of treatment response between "Degarelix 10 mg" and "Placebo" at Month 5.

Statistical Analysis 10 for Odds Ratio (as Compared to Placebo) of Treatment Response in IPSS

Statistical Analysis Overview	Comparison Groups	Placebo, Degarelix 30 mg
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.1946
	Comments	Adjustments were made for treatment group, baseline IPSS, graphical region (North America and Europe) and baseline prostate size (<30 mL and ≥30 mL). Unadjusted p-value of comparison vs. placebo at Month 6.
	Method	Regression, Logistic
	Comments	No adjustment for multiple comparisons was made. LOCF.
Method of Estimation	Estimation Parameter	Odds Ratio (OR)
	Estimated Value	1.49
	Confidence Interval	(2-Sided) 95% 0.816 to 2.717
	Estimation Comments	Odds ratio of treatment response between "Degarelix 30 mg" and "Placebo" at Month 6.

Statistical Analysis 11 for Odds Ratio (as Compared to Placebo) of Treatment Response in IPSS

Statistical Analysis Overview	Comparison Groups	Placebo, Degarelix 20 mg
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.5380
	Comments	Adjustments were made for treatment group, baseline IPSS, graphical region (North America and Europe) and baseline prostate size (<30 mL and ≥30 mL). Unadjusted p-value of comparison vs. placebo at Month 6.
	Method	Regression, Logistic
	Comments	No adjustment for multiple comparisons was made. LOCF.

Method of Estimation	Estimation Parameter	Odds Ratio (OR)
	Estimated Value	1.20
	Confidence Interval	(2-Sided) 95% 0.667 to 2.174
	Estimation Comments	Odds ratio of treatment response between "Degarelix 20 mg" and "Placebo" at Month 6.

Statistical Analysis 12 for Odds Ratio (as Compared to Placebo) of Treatment Response in IPSS

Statistical Analysis Overview	Comparison Groups	Placebo, Degarelix 10 mg
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.4263
	Comments	Adjustments were made for treatment group, baseline IPSS, graphical region (North America and Europe) and baseline prostate size (<30 mL and ≥30 mL). Unadjusted p-value of comparison vs. placebo at Month 6.
	Method	Regression, Logistic
	Comments	No adjustment for multiple comparisons was made. LOCF.

Method of Estimation	Estimation Parameter	Odds Ratio (OR)
	Estimated Value	1.27
	Confidence Interval	(2-Sided) 95% 0.702 to 2.308
	Estimation Comments	Odds ratio of treatment response between "Degarelix 10 mg" and "Placebo" at Month 6.

4. Secondary Outcome Measure:

Measure Title	Mean Percentage Change in Total Prostate Volume (TPV)
Measure Description	TPV was measured directly by standardised trans-rectal ultrasound (TRUS).
Time Frame	From Baseline to Month 3 and Month 6 after Dosing
Safety Issue?	No

Analysis Population Description

FAS. The "as planned" patient allocation for treatment groups was used (please refer to the Baseline Characteristics section).

Reporting Groups

	Description
Placebo	Mannitol 50 mg/mL solution. The dose was administered as a subcutaneous (s.c.) injection in the abdominal region.
Degarelix 10 mg	Degarelix 10 mg: 10 mg degarelix, 40 mg/mL solution. The dose was administered as a s.c. injection in the abdominal region.
Degarelix 20 mg	Degarelix 20 mg: 20 mg degarelix, 40 mg/mL solution. The dose was administered as a s.c. injection in the abdominal region.
Degarelix 30 mg	Degarelix 30 mg: 30 mg degarelix, 40 mg/mL solution. The dose was administered as a s.c. injection in the abdominal region.

Measured Values

	Placebo	Degarelix 10 mg	Degarelix 20 mg	Degarelix 30 mg
Number of Participants Analyzed	100	101	100	102
Mean Percentage Change in Total Prostate Volume (TPV) [units: percentage change from baseline] Mean (Standard Deviation)				
Mean Percentage Change at Month 3	3.15 (23.3)	-1.46 (32.7)	-0.252 (24.5)	0.188 (24.4)
Mean Percentage Change at Month 6	3.96 (29.3)	1.57 (31)	2.35 (26.5)	-0.0112 (20.9)

Statistical Analysis 1 for Mean Percentage Change in Total Prostate Volume (TPV)

Statistical Analysis Overview	Comparison Groups	Placebo, Degarelix 30 mg
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.4607
	Comments	No adjustment for multiple comparisons was made. Unadjusted p-value of comparison vs. placebo at Month 3.

	Method	ANCOVA
	Comments	ANCOVA with baseline TPV as covariate and treatment group, region (North America,Europe) and prostate volume stratum (<30 mL,≥30 mL) as factors. LOCF.

Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	-2.76
	Confidence Interval	(2-Sided) 95% -10.113 to 4.590
	Estimation Comments	Treatment difference between "Degarelix 30 mg" and "Placebo" at Month 3.

Statistical Analysis 2 for Mean Percentage Change in Total Prostate Volume (TPV)

Statistical Analysis Overview	Comparison Groups	Placebo, Degarelix 20 mg
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.3876
	Comments	No adjustment for multiple comparisons was made. Unadjusted p-value of comparison vs. placebo at Month 3.
	Method	ANCOVA
	Comments	ANCOVA with baseline TPV as covariate and treatment group, region (North America,Europe) and prostate volume stratum (<30 mL,≥30 mL) as factors. LOCF.

Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	-3.24
	Confidence Interval	(2-Sided) 95% -10.614 to 4.128
	Estimation Comments	Treatment difference between "Degarelix 20 mg" and "Placebo" at Month 3.

Statistical Analysis 3 for Mean Percentage Change in Total Prostate Volume (TPV)

Statistical Analysis Overview	Comparison Groups	Placebo, Degarelix 10 mg
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No

	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.2548
	Comments	No adjustment for multiple comparisons was made. Unadjusted p-value of comparison vs. placebo at Month 3.
	Method	ANCOVA
	Comments	ANCOVA with baseline TPV as covariate and treatment group, region (North America,Europe) and prostate volume stratum (<30 mL,≥30 mL) as factors. LOCF.

Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	-4.28
	Confidence Interval	(2-Sided) 95% -11.650 to 3.096
	Estimation Comments	Treatment difference between "Degarelix 10 mg" and "Placebo" at Month 3.

Statistical Analysis 4 for Mean Percentage Change in Total Prostate Volume (TPV)

Statistical Analysis Overview	Comparison Groups	Placebo, Degarelix 30 mg
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.5652
	Comments	No adjustment for multiple comparisons was made. Unadjusted p-value of comparison vs. placebo at Month 6.
	Method	ANCOVA
	Comments	ANCOVA with baseline TPV as covariate and treatment group, region (North America,Europe) and prostate volume stratum (<30 mL,≥30 mL) as factors. LOCF.

Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	-2.20
	Confidence Interval	(2-Sided) 95% -9.729 to 5.322
	Estimation Comments	Treatment difference between "Degarelix 30 mg" and "Placebo" at Month 6.

Statistical Analysis 5 for Mean Percentage Change in Total Prostate Volume (TPV)

Statistical Analysis Overview	Comparison Groups	Placebo, Degarelix 20 mg
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.7502
	Comments	No adjustment for multiple comparisons was made. Unadjusted p-value of comparison vs. placebo at Month 6.
	Method	ANCOVA
	Comments	ANCOVA with baseline TPV as covariate and treatment group, region (North America,Europe) and prostate volume stratum (<30 mL,≥30 mL) as factors. LOCF.
Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	-1.22
	Confidence Interval	(2-Sided) 95% -8.768 to 6.322
	Estimation Comments	Treatment difference between "Degarelix 20 mg" and "Placebo" at Month 6.

Statistical Analysis 6 for Mean Percentage Change in Total Prostate Volume (TPV)

Statistical Analysis Overview	Comparison Groups	Placebo, Degarelix 10 mg
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.6089
	Comments	No adjustment for multiple comparisons was made. Unadjusted p-value of comparison vs. placebo at Month 6.
	Method	ANCOVA
	Comments	ANCOVA with baseline TPV as covariate and treatment group, region (North America,Europe) and prostate volume stratum (<30 mL,≥30 mL) as factors. LOCF.

Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	-1.97
	Confidence Interval	(2-Sided) 95% -9.513 to 5.581
	Estimation Comments	Treatment difference between "Degarelix 10 mg" and "Placebo" at Month 6.

5. Secondary Outcome Measure:

Measure Title	Mean Change in Maximum Urinary Flow (Qmax)
Measure Description	Urinary flow rate (mL/second) was measured using uroflowmetry performed according to the recommendation from the International Continence Society (ICS).
Time Frame	From Baseline to Month 3 and Month 6 after Dosing
Safety Issue?	No

Analysis Population Description

FAS. The "as planned" patient allocation for treatment groups was used (please refer to the Baseline Characteristics section).

Reporting Groups

	Description
Placebo	Mannitol 50 mg/mL solution. The dose was administered as a subcutaneous (s.c.) injection in the abdominal region.
Degarelix 10 mg	Degarelix 10 mg: 10 mg degarelix, 40 mg/mL solution. The dose was administered as a s.c. injection in the abdominal region.
Degarelix 20 mg	Degarelix 20 mg: 20 mg degarelix, 40 mg/mL solution. The dose was administered as a s.c. injection in the abdominal region.
Degarelix 30 mg	Degarelix 30 mg: 30 mg degarelix, 40 mg/mL solution. The dose was administered as a s.c. injection in the abdominal region.

Measured Values

	Placebo	Degarelix 10 mg	Degarelix 20 mg	Degarelix 30 mg
Number of Participants Analyzed	100	101	100	102
Mean Change in Maximum Urinary Flow (Qmax) [units: percentage change from baseline] Mean (Standard Deviation)				
Mean Percentage Change at Month 3	0.652 (3.8)	0.564 (5.08)	0.626 (5.68)	0.723 (3.91)

	Placebo	Degarelix 10 mg	Degarelix 20 mg	Degarelix 30 mg
Mean Percentage Change at Month 6	1.04 (5.34)	0.516 (4.85)	0.582 (5.43)	1.43 (5.29)

Statistical Analysis 1 for Mean Change in Maximum Urinary Flow (Qmax)

Statistical Analysis Overview	Comparison Groups	Placebo, Degarelix 30 mg
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.8511
	Comments	No adjustment for multiple comparisons was made. Unadjusted p-value of comparison vs. placebo at Month 3.
	Method	ANCOVA
	Comments	ANCOVA with baseline Qmax as covariate and treatment group, region (North America,Europe) and prostate volume stratum (<30 mL,≥30 mL) as factors.LOCF.

Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	0.11
	Confidence Interval	(2-Sided) 95% -1.068 to 1.294
	Estimation Comments	Treatment difference between "Degarelix 30 mg" and "Placebo" at Month 3.

Statistical Analysis 2 for Mean Change in Maximum Urinary Flow (Qmax)

Statistical Analysis Overview	Comparison Groups	Placebo, Degarelix 20 mg
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.6331
	Comments	No adjustment for multiple comparisons was made. Unadjusted p-value of comparison vs. placebo at Month 3.

	Method	ANCOVA
	Comments	ANCOVA with baseline Qmax as covariate and treatment group, region (North America,Europe) and prostate volume stratum (<30 mL,≥30 mL) as factors.LOCF.

Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	0.29
	Confidence Interval	(2-Sided) 95% -0.900 to 1.477
	Estimation Comments	Treatment difference between "Degarelix 20 mg" and "Placebo" at Month 3.

Statistical Analysis 3 for Mean Change in Maximum Urinary Flow (Qmax)

Statistical Analysis Overview	Comparison Groups	Placebo, Degarelix 10 mg
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.9090
	Comments	No adjustment for multiple comparisons was made. Unadjusted p-value of comparison vs. placebo at Month 3.
	Method	ANCOVA
	Comments	ANCOVA with baseline Qmax as covariate and treatment group, region (North America,Europe) and prostate volume stratum (<30 mL,≥30 mL) as factors.LOCF.

Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	0.07
	Confidence Interval	(2-Sided) 95% -1.113 to 1.250
	Estimation Comments	Treatment difference between "Degarelix 10 mg" and "Placebo" at Month 3.

Statistical Analysis 4 for Mean Change in Maximum Urinary Flow (Qmax)

Statistical Analysis Overview	Comparison Groups	Placebo, Degarelix 30 mg
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No

	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.5469
	Comments	No adjustment for multiple comparisons was made. Unadjusted p-value of comparison vs. placebo at Month 6.
	Method	ANCOVA
	Comments	ANCOVA with baseline Qmax as covariate and treatment group, region (North America,Europe) and prostate volume stratum (<30 mL,≥30 mL) as factors.LOCF.

Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	0.42
	Confidence Interval	(2-Sided) 95% -0.956 to 1.802
	Estimation Comments	Treatment difference between "Degarelix 30 mg" and "Placebo" at Month 6.

Statistical Analysis 5 for Mean Change in Maximum Urinary Flow (Qmax)

Statistical Analysis Overview	Comparison Groups	Placebo, Degarelix 20 mg
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.7906
	Comments	No adjustment for multiple comparisons was made. Unadjusted p-value of comparison vs. placebo at Month 6.
	Method	ANCOVA
	Comments	ANCOVA with baseline Qmax as covariate and treatment group, region (North America,Europe) and prostate volume stratum (<30 mL,≥30 mL) as factors.LOCF.

Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	-0.19
	Confidence Interval	(2-Sided) 95% -1.576 to 1.200
	Estimation Comments	Treatment difference between "Degarelix 20 mg" and "Placebo" at Month 6.

Statistical Analysis 6 for Mean Change in Maximum Urinary Flow (Qmax)

Statistical Analysis Overview	Comparison Groups	Placebo, Degarelix 10 mg
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.5757
	Comments	No adjustment for multiple comparisons was made. Unadjusted p-value of comparison vs. placebo at Month 6.
	Method	ANCOVA
	Comments	ANCOVA with baseline Qmax as covariate and treatment group, region (North America,Europe) and prostate volume stratum (<30 mL,≥30 mL) as factors.LOCF.
Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	-0.39
	Confidence Interval	(2-Sided) 95% -1.773 to 0.987
	Estimation Comments	Treatment difference between "Degarelix 10 mg" and "Placebo" at Month 6.

Reported Adverse Events

Time Frame	This was a single dose trial and adverse events were recorded from signed informed consent up to a maximum of 12 months after the dose. However, the trial was stopped when all patients had completed the visit scheduled 6 months after the dosing.
Additional Description	Adverse events were evaluated at each visit. The safety analyses were based on the actual treatment. Three patients did not receive their randomised treatment: 2 patients randomised to placebo received 30 mg, and 1 patient randomised to 20 mg received 30 mg degarelix. They were included in the actual treatment group in the safety analysis set.

Reporting Groups

	Description
Placebo	Placebo: Mannitol 50 mg/mL solution. The dose was administered as a s.c. injection in the abdominal region.

	Description
Degarelix 10 mg	Degarelix 10 mg: 10 mg degarelix, 40 mg/mL solution. The dose was administered as a s.c. injection in the abdominal region.
Degarelix 20 mg	Degarelix 20 mg: 20 mg degarelix, 40 mg/mL solution. The dose was administered as a s.c. injection in the abdominal region.
Degarelix 30 mg	Degarelix 30 mg: 30 mg degarelix, 40 mg/mL solution. The dose was administered as a s.c. injection in the abdominal region.

Serious Adverse Events

	Placebo		Degarelix 10 mg		Degarelix 20 mg		Degarelix 30 mg	
	Affected/ At Risk (%)	# Events	Affected/ At Risk (%)	# Events	Affected/ At Risk (%)	# Events	Affected/ At Risk (%)	# Events
Total	2/98 (2.04%)		8/101 (7.92%)		2/100 (2%)		7/105 (6.67%)	
Cardiac disorders								
Angina pectoris [A] †	1/98 (1.02%)	1	0/101 (0%)	0	0/100 (0%)	0	0/105 (0%)	0
Atrioventricular block complete [A] †	0/98 (0%)	0	0/101 (0%)	0	0/100 (0%)	0	1/105 (0.95%)	1
Sick sinus syndrome [A] †	0/98 (0%)	0	1/101 (0.99%)	1	0/100 (0%)	0	0/105 (0%)	0
Gastrointestinal disorders								
Abdominal pain upper [A] †	1/98 (1.02%)	1	0/101 (0%)	0	0/100 (0%)	0	0/105 (0%)	0
Ileus [A] †	0/98 (0%)	0	1/101 (0.99%)	1	0/100 (0%)	0	0/105 (0%)	0
Subileus [A] †	0/98 (0%)	0	1/101 (0.99%)	1	0/100 (0%)	0	0/105 (0%)	0
Infections and infestations								
Abscess intestinal [A] †	0/98 (0%)	0	1/101 (0.99%)	1	0/100 (0%)	0	0/105 (0%)	0
Clostridium difficile colitis [A] †	0/98 (0%)	0	0/101 (0%)	0	1/100 (1%)	1	0/105 (0%)	0

	Placebo		Degarelix 10 mg		Degarelix 20 mg		Degarelix 30 mg	
	Affected/ At Risk (%)	# Events	Affected/ At Risk (%)	# Events	Affected/ At Risk (%)	# Events	Affected/ At Risk (%)	# Events
Injury, poisoning and procedural complications								
Contusion [A] †	0/98 (0%)	0	1/101 (0.99%)	1	0/100 (0%)	0	0/105 (0%)	0
Investigations								
Coagulation time prolonged [A] †	1/98 (1.02%)	1	0/101 (0%)	0	0/100 (0%)	0	0/105 (0%)	0
Musculoskeletal and connective tissue disorders								
Intervertebral disc protrusion [A] †	0/98 (0%)	0	0/101 (0%)	0	1/100 (1%)	1	1/105 (0.95%)	1
Osteoarthritis [A] †	0/98 (0%)	0	1/101 (0.99%)	1	0/100 (0%)	0	1/105 (0.95%)	1
Neoplasms benign, malignant and unspecified (incl cysts and polyps)								
Adenosquamous cell carcinoma [A] †	0/98 (0%)	0	1/101 (0.99%)	1	0/100 (0%)	0	0/105 (0%)	0
Colon cancer metastatic [A] †	0/98 (0%)	0	0/101 (0%)	0	0/100 (0%)	0	1/105 (0.95%)	1
Prostate cancer [A] †	0/98 (0%)	0	1/101 (0.99%)	1	0/100 (0%)	0	0/105 (0%)	0
Nervous system disorders								
Carotid sinus syndrome [A] †	0/98 (0%)	0	1/101 (0.99%)	1	0/100 (0%)	0	0/105 (0%)	0
Cerebrovascular accident [A] †	0/98 (0%)	0	1/101 (0.99%)	1	0/100 (0%)	0	0/105 (0%)	0
Psychiatric disorders								
Depression [A] †	0/98 (0%)	0	0/101 (0%)	0	0/100 (0%)	0	1/105 (0.95%)	1
Respiratory, thoracic and mediastinal disorders								
Chronic obstructive pulmonary disease [A] †	0/98 (0%)	0	0/101 (0%)	0	0/100 (0%)	0	1/105 (0.95%)	1

	Placebo		Degarelix 10 mg		Degarelix 20 mg		Degarelix 30 mg	
	Affected/ At Risk (%)	# Events	Affected/ At Risk (%)	# Events	Affected/ At Risk (%)	# Events	Affected/ At Risk (%)	# Events
Nasal septum deviation [A] †	1/98 (1.02%)	1	0/101 (0%)	0	0/100 (0%)	0	0/105 (0%)	0
Pulmonary embolism [A] †	0/98 (0%)	0	1/101 (0.99%)	1	0/100 (0%)	0	0/105 (0%)	0
Respiratory failure [A] †	0/98 (0%)	0	1/101 (0.99%)	1	0/100 (0%)	0	0/105 (0%)	0
Vascular disorders								
Deep vein thrombosis [A] †	0/98 (0%)	0	1/101 (0.99%)	1	0/100 (0%)	0	0/105 (0%)	0
Hypertension [A] †	0/98 (0%)	0	0/101 (0%)	0	0/100 (0%)	0	1/105 (0.95%)	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: 5%

	Placebo		Degarelix 10 mg		Degarelix 20 mg		Degarelix 30 mg	
	Affected/ At Risk (%)	# Events	Affected/ At Risk (%)	# Events	Affected/ At Risk (%)	# Events	Affected/ At Risk (%)	# Events
Total	31/98 (31.63%)		35/101 (34.65%)		39/100 (39%)		56/105 (53.33%)	
General disorders								
Injection site erythema [A] †	0/98 (0%)	0	11/101 (10.89%)	11	14/100 (14%)	14	18/105 (17.14%)	18
Injection site induration [A] †	0/98 (0%)	0	6/101 (5.94%)	6	7/100 (7%)	7	11/105 (10.48%)	11
Injection site pain [A] †	0/98 (0%)	0	2/101 (1.98%)	2	10/100 (10%)	10	18/105 (17.14%)	19
Infections and infestations								

	Placebo		Degarelix 10 mg		Degarelix 20 mg		Degarelix 30 mg	
	Affected/ At Risk (%)	# Events	Affected/ At Risk (%)	# Events	Affected/ At Risk (%)	# Events	Affected/ At Risk (%)	# Events
Influenza [A] †	5/98 (5.1%)	5	5/101 (4.95%)	5	3/100 (3%)	3	5/105 (4.76%)	5
Nasopharyngitis [A] †	5/98 (5.1%)	5	7/101 (6.93%)	8	2/100 (2%)	2	5/105 (4.76%)	5
Investigations								
Prostatic specific antigen increased [A] †	6/98 (6.12%)	6	4/101 (3.96%)	4	5/100 (5%)	6	6/105 (5.71%)	6
Musculoskeletal and connective tissue disorders								
Back pain [A] †	9/98 (9.18%)	9	5/101 (4.95%)	5	5/100 (5%)	5	5/105 (4.76%)	6
Nervous system disorders								
Headache [A] †	5/98 (5.1%)	5	3/101 (2.97%)	3	3/100 (3%)	3	3/105 (2.86%)	3
Respiratory, thoracic and mediastinal disorders								
Cough [A] †	5/98 (5.1%)	5	3/101 (2.97%)	3	1/100 (1%)	1	2/105 (1.9%)	2
Vascular disorders								
Hot flush [A] †	1/98 (1.02%)	2	1/101 (0.99%)	1	4/100 (4%)	4	8/105 (7.62%)	10
Hypertension [A] †	7/98 (7.14%)	8	6/101 (5.94%)	6	4/100 (4%)	5	9/105 (8.57%)	10

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

Limitations and Caveats

Following the planned 6-month interim analysis when all patients had completed the visit scheduled 6 months after dosing, a decision was taken to stop the trial since the primary efficacy endpoint was not met.

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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