ClinicalTrials.gov Protocol and Results Registration System (PRS) Receipt
Release Date: 10/18/2013

# Symptomatic Study Investigating Degarelix in Patients Suffering From Prostate Cancer

This study has been terminated.
(Poor recruitment due to rare targeted population)

| | |
|---|---|
| Sponsor: | Ferring Pharmaceuticals |
| Collaborators: | |
| Information provided by: | Ferring Pharmaceuticals |
| ClinicalTrials.gov Identifier: | NCT00831233 |

## Purpose

The purpose of this trial was to see how well a new trial drug (degarelix) worked on lower urinary tract symptoms (also known as LUTS) in prostate cancer patients as compared to how a standard drug hormonal treatment worked on the same symptoms. The advancement/worsening of prostate cancer may be associated with LUTS and the symptoms may impact the ability to urinate normally and thereby the quality of life for these patients.

Patients were randomly selected (like flipping a coin) to receive either degarelix or standard hormone therapy (combination of goserelin and bicalutamide) for a 3 month treatment period. During this period the relief of urinary symptoms was evaluated via a questionnaire filled in by patients and addressing the severity and frequency of their symptoms.

| Condition | Intervention | Phase |
|---|---|---|
| Prostate Cancer | Drug: Degarelix<br>Drug: Goserelin<br>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 Reduction in International Prostate Symptom Score (IPSS), in Patients With Lower Urinary Tract Symptoms (LUTS) Secondary to Locally Advanced Prostate Cancer

Further study details as provided by Ferring Pharmaceuticals:

Primary Outcome Measure:

- Change From Baseline in Total International Prostate Symptom Score (IPSS) at Week 12 [Time Frame: After treatment of 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.

Secondary Outcome Measures:

- Change From Baseline in Total IPSS at Weeks 4 and 8 [Time Frame: After treatment of 4 and 8 weeks compared to Baseline] [Designated as safety issue: No]

  The IPSS is a tool commonly used to assess the severity of lower urinary tract symptoms (LUTS), and to monitor the progress of the disease once treatment has been initiated. The participant completes a questionnaire containing 7 questions regarding incomplete emptying, frequency, intermittency, urgency, weak stream, straining, and nocturia. Each question is assigned a score of 0-5. The total score is then classified according to the following scale: 0 to 7 = mildly symptomatic; 8 to 19 = moderately symptomatic; and 20 to 35 = severely symptomatic.
- Change From Baseline in Maximum Urine Flow (Qmax) at Each Visit [Time Frame: After treatment of 4, 8 and 12 weeks compared to Baseline] [Designated as safety issue: No]

  Uroflowmetry was used to quantify the maximum urine flow (Qmax; mL/sec)
- Change From Baseline in Residual Volume (Vresidual) at Each Visit [Time Frame: After treatment of 4, 8 and 12 weeks compared to Baseline] [Designated as safety issue: No]

  Uroflowmetry was used to quantify the residual volume (Vresidual; mL)
- Change From Baseline in Prostate Size Based on Trans Rectal Ultra Sound (TRUS) at Week 12 [Time Frame: After 12 weeks treatment compared to Baseline] [Designated as safety issue: No]

  TRUS is a method of measuring the size of the prostate.
- Number of Participants With Testosterone <=0.5 Nanograms/Milliliter at Each Visit [Time Frame: After treatment of 4, 8 and 12 weeks compared to Baseline] [Designated as safety issue: No]
- Percentage Change From Baseline in Prostate-specific Antigen (PSA) Concentration at Each Visit [Time Frame: After treatment of 4, 8 and 12 weeks compared to Baseline] [Designated as safety issue: No]
- Change From Baseline in Quality of Life (QoL) Related to Urinary Symptoms at Each Visit [Time Frame: After treatment of 4, 8 and 12 weeks compared to Baseline] [Designated as safety issue: No]

  The IPSS questionnaire included an additional single question to assess the participant's QoL in relation to his urinary symptoms. The question was: 'If you were to spend the rest of your life with your urinary condition the way it is now, how would you feel about that?' The possible answers to this question ranged from 'delighted' (a score of '0') to 'terrible' (a score of '6'). The figures in the tables present the change (ie decrease) in IPSS QoL score, i.e. the bigger the decrease the better QoL.
- 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 on participant with one abnormal value are presented, many more variables were included in the trial.

Enrollment: 42
Study Start Date: April 2009
Primary Completion Date: June 2010
Study Completion Date: July 2010

| Arms | Assigned Interventions |
|---|---|
| Experimental: Degarelix 240 mg/80 mg<br>Degarelix 240 mg (40 mg/mL) + 80 mg (20 mg/mL) | Drug: Degarelix<br>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.<br>Other Names:<br>FE200486 |
| Active Comparator: Goserelin (3.6 mg) + bicalutamide (50 mg)<br>Goserelin (3.6 mg) + bicalutamide (50 mg) | Drug: Goserelin<br>Goserelin implants (3.6 mg) were inserted s.c. into the abdominal wall every 28 days. The second and third doses of goserelin were administered on Days 31 and 59, respectively.<br>Other Names:<br>Zoladex<br>Drug: Bicalutamide<br>On Day 0, three days before the first dose of goserelin on Day 3, patients began once-daily per-oral (p.o.) treatment with bicalutamide (50 mg) as anti-androgen flare protection; this treatment continued for 14 days after the first dose of goserelin.<br>Other Names:<br>Casodex |

## Eligibility

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

### Criteria

Inclusion Criteria:

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

Exclusion Criteria:

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

## Contacts and Locations

Locations

Germany

Facharztpraxis für Urologie
Bamberg, Germany, 96047

Gemeinschaftspraxis
Borken, Germany, 46325

Universitätsklinikum Dresden
Dresden, Germany, 01307

Euromed Clinic
Fürth, Germany, 90763

Urologische Gemeinschaftspraxis
Hamburg, Germany, 22399

Gemeinschaftspraxis
Köln, Germany, 50667

VITURO Gesellschaft für Klinische Studien
Leipzig, Germany, 04109

Klinikum Offenbach GmbH
Offenbach, Germany, 63069

Urologische Klinik Planegg
Planegg, Germany, 82152

Wuppertaler Gemeinschaftspraxis
Wuppertal, Germany, 42103

Spain

Hospital Universitario Principe de Asturias
Alcalá de Henares-Madrid, Spain, 28805

Fundacion Hospital Alcorcón

Alcorcon, Spain, 28922
Fundación Puigvert
Barcelona, Spain, 08025
Hospital de Basurto
Bilbao (Bizkaia), Spain, 48013
Complejo Hospitalario Universitario A Coruña
Coruña, Spain
Hospital universitario Ramón y Cajal
Madrid, Spain, 28034
Hospital Clinico Universitario S. Carlos
Madrid, Spain, 28040
Hospital Universitario Puerta de Hierro
Majadahonda, Madrid, Spain, 28222
Hospital Manacor
Manacor, Spain, 07500
Hospital Universitario Central de Asturias
Oviedo, Spain, 33006
Hospital Santiago de Compostela
Santiago de Compostela, Spain, 15706
Hospital Virgen Macarena
Sevilla, Spain, 41014
Hospital Xeral de Vigo
Vigo, Spain, 36204
United Kingdom
United Bristol Healthcare NHSTrust Bristol Royal Infirmary
Bristol, United Kingdom, BS2 8HW
Falkirk and District Royal Infirmary
Falkirk, United Kingdom, FK1 5QE
Southern General Hospital
Glasgow, United Kingdom, G51 4TF
Castle Hill Hospital
Hull, United Kingdom, HU16 5JQ
The Royal Free Hospital
London, United Kingdom, NW3 2QG
King's College Hospital
London, United Kingdom, SE5 9RS
Whipps Cross University Hospital
London, United Kingdom, E11 1NR
Derriford Hospital
Plymouth, United Kingdom, PL6 8DH
Royal Hallamshire Hospital, Sheffield South
Sheffield, United Kingdom, S10 2JF
Sunderland Royal Hospital
Sunderland, United Kingdom, SR4 7TP

Investigators

| | | |
|---|---|---|
| Study Director: | Clinical Development Support | Ferring Pharmaceuticals |

## More Information

Results Publications:

Anderson J, Al-Ali G, Wirth M, Gual JB, Gomez Veiga F, Colli E, van der Meulen E, Persson BE. Degarelix versus goserelin (+ antiandrogen flare protection) in the relief of lower urinary tract symptoms secondary to prostate cancer: results from a phase IIIb study (NCT00831233). Urol Int. 2013;90(3):321-8. doi: 10.1159/000345423. Epub 2012 Dec 15.

| | |
|---|---|
| Responsible Party: | Ferring Pharmaceuticals (Clinical Development Support) |
| Study ID Numbers: | FE200486 CS28<br>2008-004338-26 [EudraCT Number] |
| Health Authority: | United Kingdom: Medicines and Healthcare Products Regulatory Agency<br>Germany: Federal Institute for Drugs and Medical Devices<br>Spain: Spanish Agency of Medicines |

# Study Results

## Participant Flow

| | |
|---|---|
| Recruitment Details | The participants were recruited by outpatient urologists. 280 participants were to be randomised in a 3:1 ratio to one of two treatment groups (210 patients were to be treated with degarelix; 70 patients were to be treated with goserelin plus bicalutamide). The trial was stopped early due to poor recruitment. |

Reporting Groups

| | Description |
|---|---|
| Degarelix 240 mg/80 mg | Degarelix 240 mg (40 mg/mL) + 80 mg (20 mg/mL) |
| Goserelin (3.6 mg) + Bicalutamide (50 mg) | Goserelin (3.6 mg) + bicalutamide (50 mg) |

Overall Study

| | Degarelix 240 mg/80 mg | Goserelin (3.6 mg) + Bicalutamide (50 mg) |
|---|---|---|
| Started | 29 [1] | 13 [2] |
| Full Analysis Set (FAS) | 27 [3] | 13 |
| Per Protocol (PP) Analysis Set | 26 | 11 |

| | Degarelix 240 mg/80 mg | Goserelin (3.6 mg) + Bicalutamide (50 mg) |
|---|---|---|
| Completed | 26 | 12 |
| Not Completed | 3 | 1 |
| Adverse Event | 0 | 1 |
| Protocol Violation | 1 | 0 |
| Selection Criteria Not Met | 2 | 0 |

[1] Intention-to-treat (ITT) population.
[2] ITT population.
[3] 2 participants were randomised but never treated.

## Baseline Characteristics

Reporting Groups

| | Description |
|---|---|
| Degarelix 240 mg/80 mg | Degarelix 240 mg (40 mg/mL) + 80 mg (20 mg/mL) |
| Goserelin (3.6 mg) + Bicalutamide (50 mg) | Goserelin (3.6 mg) + bicalutamide (50 mg) |

Baseline Measures

| | Degarelix 240 mg/80 mg | Goserelin (3.6 mg) + Bicalutamide (50 mg) | Total |
|---|---|---|---|
| Number of Participants | 27 | 13 | 40 |
| Age, Continuous [1]<br>[units: years]<br>Mean (Standard Deviation) | 69.9 (8.68) | 71.0 (8.39) | 70.3 (8.49) |
| Gender, Male/Female [2]<br>[units: participants] | | | |
| Female | 0 | 0 | 0 |
| Male | 27 | 13 | 40 |
| Race (NIH/OMB) [2]<br>[units: participants] | | | |
| American Indian or Alaska Native | 0 | 0 | 0 |

| | Degarelix 240 mg/80 mg | Goserelin (3.6 mg) + Bicalutamide (50 mg) | Total |
|---|---|---|---|
| Asian | 0 | 0 | 0 |
| Native Hawaiian or Other Pacific Islander | 0 | 0 | 0 |
| Black or African American | 0 | 1 | 1 |
| White | 27 | 12 | 39 |
| More than one race | 0 | 0 | 0 |
| Unknown or Not Reported | 0 | 0 | 0 |
| Region of Enrollment [2] [units: participants] | | | |
| Spain | 4 | 4 | 8 |
| Germany | 13 | 7 | 20 |
| United Kingdom | 10 | 2 | 12 |
| Body weight [2] [units: kilogram] Mean (Standard Deviation) | 81.4 (14.0) | 78.2 (8.5) | 80.3 (12.5) |
| Body mass index [2] [units: kilogram per square meter] Mean (Standard Deviation) | 26.7 (4.06) | 26.8 (3.75) | 26.7 (3.91) |
| Gleason Score [3] [units: participants] | | | |
| 2-4 | 0 | 0 | 0 |
| 5-6 | 2 | 0 | 2 |
| 7-10 | 25 | 13 | 38 |
| Stage of Prostate Cancer [4] [units: participants] | | | |
| Localized | 4 | 0 | 4 |
| Locally Advanced | 4 | 1 | 5 |
| Metastatic | 10 | 4 | 14 |
| Not Classifiable | 9 | 8 | 17 |

[1] Full Analysis Set (FAS).

[2] FAS.

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

[4] FAS. Prostate cancer stage was classified according to the Tumor, Nodes, and Metastatic (TNM) scale to describe the extent of cancer. Localized refers to tumors without involvement of lymph nodes or metastasis. Advanced localized can be larger tumors that may involve the lymph nodes but no metastasis. Metastatic are more advanced cancers that are spreading beyond the original tumor. The majority of participants did not have their prostate cancer classified for the complete TNM scale (17 participants) or were known for having metastatic prostate cancer (14 participants).

## Outcome Measures

1. Primary Outcome Measure:

| | |
|---|---|
| Measure Title | Change From Baseline in Total International Prostate Symptom Score (IPSS) at Week 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 12 weeks compared to Baseline |
| Safety Issue? | No |

Analysis Population Description

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

Reporting Groups

| | Description |
|---|---|
| Degarelix 240 mg/80 mg | Degarelix 240 mg (40 mg/mL) + 80 mg (20 mg/mL) |
| Goserelin (3.6 mg) + Bicalutamide (50 mg) | Goserelin (3.6 mg) + bicalutamide (50 mg) |

Measured Values

| | Degarelix 240 mg/80 mg | Goserelin (3.6 mg) + Bicalutamide (50 mg) |
|---|---|---|
| Number of Participants Analyzed | 27 | 13 |
| Change From Baseline in Total International Prostate Symptom Score (IPSS) at Week 12<br>[units: score on scale] | -11.2 (8.29) | -7.69 (7.61) |

| | Degarelix 240 mg/80 mg | Goserelin (3.6 mg) + Bicalutamide (50 mg) |
|---|---|---|
| Mean (Standard Deviation) | | |

Statistical Analysis 1 for Change From Baseline in Total International Prostate Symptom Score (IPSS) at Week 12

| | | |
|---|---|---|
| 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 and country as factors and age and baseline value as covariates. |
| | Non-Inferiority or Equivalence Analysis? | Yes |
| | Comments | The trial was positive if the treatment contrast of degarelix versus goserelin plus bicalutamide in adjusted (for baseline total IPSS, age, and country) mean change from baseline in total IPSS was statistically significantly smaller (two-sided at α=0.05 level) than Δ=3 points in both the FAS and the PP analysis set.<br><br>If the Week 12 treatment assessment of IPSS was missing the LOCF approach was used, i.e., the IPSS closest to and before Week 12 was used. |

| | | |
|---|---|---|
| Statistical Test of Hypothesis | P-Value | 0.1973 |
| | Comments | FAS. |
| | Method | ANCOVA |
| | Comments | The baseline score, age, and country 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 | -2.95 |
| | Confidence Interval | (2-Sided) 95%<br>-7.51 to 1.61 |
| | Estimation Comments | [Not specified] |

Statistical Analysis 2 for Change From Baseline in Total International Prostate Symptom Score (IPSS) at Week 12

| | | |
|---|---|---|
| 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 and country as factors and age and baseline value as covariates. |
| | Non-Inferiority or Equivalence Analysis? | Yes |

| | | |
|---|---|---|
| | Comments | The trial was positive if the treatment contrast of degarelix versus goserelin plus bicalutamide in adjusted (for baseline total IPSS, age, and country) mean change from baseline in total IPSS was statistically significantly smaller (two-sided at α=0.05 level) than Δ=3 points in both the FAS and the PP analysis set.<br><br>If the Week 12 treatment assessment of IPSS was missing the LOCF approach was used, i.e., the IPSS closest to and before Week 12 was used. |

| | | |
|---|---|---|
| Statistical Test of Hypothesis | P-Value | 0.0398 |
| | Comments | PP analysis set. |
| | Method | ANCOVA |
| | Comments | The baseline score, age, and country 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 | -5.88 |
| | Confidence Interval | (2-Sided) 95%<br>-11.5 to -0.291 |
| | Estimation Comments | [Not specified] |

2. Secondary Outcome Measure:

| | |
|---|---|
| Measure Title | Change From Baseline in Total IPSS at Weeks 4 and 8 |
| 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 and 8 weeks compared to Baseline |
| Safety Issue? | No |

Analysis Population Description
FAS, LOCF.

Reporting Groups

| | Description |
|---|---|
| Degarelix 240 mg/80 mg | Degarelix 240 mg (40 mg/mL) + 80 mg (20 mg/mL) |

| | Description |
|---|---|
| Goserelin (3.6 mg) + Bicalutamide (50 mg) | Goserelin (3.6 mg) + bicalutamide (50 mg) |

Measured Values

| | Degarelix 240 mg/80 mg | Goserelin (3.6 mg) + Bicalutamide (50 mg) |
|---|---|---|
| Number of Participants Analyzed | 26 | 13 |
| Change From Baseline in Total IPSS at Weeks 4 and 8<br>[units: score on scale]<br>Mean (Standard Deviation) | | |
| Week 4 | -7.31 (5.83) | -4.62 (5.49) |
| Week 8 | -9.46 (6.94) | -8.08 (9.00) |

Statistical Analysis 1 for Change From Baseline in Total IPSS at Weeks 4 and 8

| | | |
|---|---|---|
| Statistical Analysis Overview | Comparison Groups | Degarelix 240 mg/80 mg, Goserelin (3.6 mg) + Bicalutamide (50 mg) |
| | Comments | Week 4. Estimates from analysis of variance with treatment and country as factors and age and baseline value as covariates. |
| | Non-Inferiority or Equivalence Analysis? | No |
| | Comments | [Not specified] |

| | | |
|---|---|---|
| Statistical Test of Hypothesis | P-Value | 0.2298 |
| | Comments | [Not specified] |
| | Method | ANCOVA |
| | Comments | The baseline score, age, and country were used as covariates and treatment was used as a factor in the analysis for the FAS. |

| | | |
|---|---|---|
| Method of Estimation | Estimation Parameter | Mean Difference (Final Values) |
| | Estimated Value | -2.47 |
| | Confidence Interval | (2-Sided) 95%<br>-6.58 to 1.64 |
| | Estimation Comments | [Not specified] |

Statistical Analysis 2 for Change From Baseline in Total IPSS at Weeks 4 and 8

| | | |
|---|---|---|
| Statistical Analysis Overview | Comparison Groups | Degarelix 240 mg/80 mg, Goserelin (3.6 mg) + Bicalutamide (50 mg) |
| | Comments | Week 8. Estimates from analysis of variance with treatment and country as factors and age and baseline value as covariates. |
| | Non-Inferiority or Equivalence Analysis? | No |
| | Comments | [Not specified] |

| | | |
|---|---|---|
| Statistical Test of Hypothesis | P-Value | 0.6917 |
| | Comments | [Not specified] |
| | Method | ANCOVA |
| | Comments | The baseline score, age, and country were used as covariates and treatment was used as a factor in the analysis for the FAS. |

| | | |
|---|---|---|
| Method of Estimation | Estimation Parameter | Mean Difference (Final Values) |
| | Estimated Value | -0.983 |
| | Confidence Interval | (2-Sided) 95%<br>-5.98 to 4.02 |
| | Estimation Comments | [Not specified] |

3. Secondary Outcome Measure:

| | |
|---|---|
| Measure Title | Change From Baseline in Maximum Urine Flow (Qmax) at Each Visit |
| Measure Description | Uroflowmetry was used to quantify the maximum urine flow (Qmax; mL/sec) |
| Time Frame | After treatment of 4, 8 and 12 weeks compared to Baseline |
| Safety Issue? | No |

Analysis Population Description

FAS, LOCF.

Reporting Groups

| | Description |
|---|---|
| Degarelix 240 mg/80 mg | Degarelix 240 mg (40 mg/mL) + 80 mg (20 mg/mL) |
| Goserelin (3.6 mg) + Bicalutamide (50 mg) | Goserelin (3.6 mg) + bicalutamide (50 mg) |

Measured Values

| | Degarelix 240 mg/80 mg | Goserelin (3.6 mg) + Bicalutamide (50 mg) |
|---|---|---|
| Number of Participants Analyzed | 27 | 13 |
| Change From Baseline in Maximum Urine Flow (Qmax) at Each Visit<br>[units: mL/sec]<br>Mean (Standard Deviation) | | |
| Week 4 | 3.63 (7.82) | 3.55 (3.80) |
| Week 8 | 4.74 (6.60) | 3.52 (3.58) |
| Week 12 | 3.62 (7.37) | 2.07 (4.57) |

Statistical Analysis 1 for Change From Baseline in Maximum Urine Flow (Qmax) at Each Visit

| | | |
|---|---|---|
| Statistical Analysis Overview | Comparison Groups | Degarelix 240 mg/80 mg, Goserelin (3.6 mg) + Bicalutamide (50 mg) |
| | Comments | Week 4. Estimates from analysis of variance with treatment and country as factors and age and baseline value as covariates. |
| | Non-Inferiority or Equivalence Analysis? | No |
| | Comments | [Not specified] |

| | | |
|---|---|---|
| Statistical Test of Hypothesis | P-Value | 0.8151 |
| | Comments | [Not specified] |
| | Method | ANCOVA |
| | Comments | The baseline score, age, and country were used as covariates and treatment was used as a factor in the analysis for the FAS. |

| | | |
|---|---|---|
| Method of Estimation | Estimation Parameter | Mean Difference (Final Values) |
| | Estimated Value | -0.553 |
| | Confidence Interval | (2-Sided) 95%<br>-5.33 to 4.22 |
| | Estimation Comments | [Not specified] |

Statistical Analysis 2 for Change From Baseline in Maximum Urine Flow (Qmax) at Each Visit

| | | |
|---|---|---|
| Statistical Analysis Overview | Comparison Groups | Degarelix 240 mg/80 mg, Goserelin (3.6 mg) + Bicalutamide (50 mg) |
| | Comments | Week 8. Estimates from analysis of variance with treatment and country as factors and age and baseline value as covariates. |
| | Non-Inferiority or Equivalence Analysis? | No |
| | Comments | [Not specified] |
| Statistical Test of Hypothesis | P-Value | 0.455 |
| | Comments | [Not specified] |
| | Method | ANCOVA |
| | Comments | The baseline score, age, and country were used as covariates and treatment was used as a factor in the analysis for the FAS. |
| Method of Estimation | Estimation Parameter | Mean Difference (Final Values) |
| | Estimated Value | 1.46 |
| | Confidence Interval | (2-Sided) 95%<br>-2.46 to 5.38 |
| | Estimation Comments | [Not specified] |

Statistical Analysis 3 for Change From Baseline in Maximum Urine Flow (Qmax) at Each Visit

| | | |
|---|---|---|
| Statistical Analysis Overview | Comparison Groups | Degarelix 240 mg/80 mg, Goserelin (3.6 mg) + Bicalutamide (50 mg) |
| | Comments | Week 12. Estimates from analysis of variance with treatment and country as factors and age and baseline value as covariates. |
| | Non-Inferiority or Equivalence Analysis? | No |
| | Comments | [Not specified] |
| Statistical Test of Hypothesis | P-Value | 0.3186 |
| | Comments | [Not specified] |
| | Method | ANCOVA |
| | Comments | The baseline score, age, and country were used as covariates and treatment was used as a factor in the analysis for the FAS. |

| | | |
|---|---|---|
| Method of Estimation | Estimation Parameter | Mean Difference (Final Values) |
| | Estimated Value | 2.02 |
| | Confidence Interval | (2-Sided) 95%<br>-2.04 to 6.08 |
| | Estimation Comments | [Not specified] |

4. Secondary Outcome Measure:

| | |
|---|---|
| Measure Title | Change From Baseline in Residual Volume (Vresidual) at Each Visit |
| Measure Description | Uroflowmetry was used to quantify the residual volume (Vresidual; mL) |
| Time Frame | After treatment of 4, 8 and 12 weeks compared to Baseline |
| Safety Issue? | No |

Analysis Population Description

FAS, LOCF.

Reporting Groups

| | Description |
|---|---|
| Degarelix 240 mg/80 mg | Degarelix 240 mg (40 mg/mL) + 80 mg (20 mg/mL) |
| Goserelin (3.6 mg) + Bicalutamide (50 mg) | Goserelin (3.6 mg) + bicalutamide (50 mg) |

Measured Values

| | Degarelix 240 mg/80 mg | Goserelin (3.6 mg) + Bicalutamide (50 mg) |
|---|---|---|
| Number of Participants Analyzed | 27 | 13 |
| Change From Baseline in Residual Volume (Vresidual) at Each Visit<br>[units: mL]<br>Mean (Standard Deviation) | | |
| Week 4 | -36.2 (148) | -19.8 (63.5) |
| Week 8 | -43.8 (133) | -19.6 (85.4) |
| Week 12 | -50.7 (135) | -13.4 (85.8) |

Statistical Analysis 1 for Change From Baseline in Residual Volume (Vresidual) at Each Visit

| | | |
|---|---|---|
| Statistical Analysis Overview | Comparison Groups | Degarelix 240 mg/80 mg, Goserelin (3.6 mg) + Bicalutamide (50 mg) |
| | Comments | Week 4. Estimates from analysis of variance with treatment and country as factors and age and baseline value as covariates. |
| | Non-Inferiority or Equivalence Analysis? | No |
| | Comments | [Not specified] |

| | | |
|---|---|---|
| Statistical Test of Hypothesis | P-Value | 0.5627 |
| | Comments | [Not specified] |
| | Method | ANCOVA |
| | Comments | The baseline score, age, and country were used as covariates and treatment was used as a factor in the analysis for the FAS. |

| | | |
|---|---|---|
| Method of Estimation | Estimation Parameter | Mean Difference (Final Values) |
| | Estimated Value | 15.2 |
| | Confidence Interval | (2-Sided) 95%<br>-37.8 to 68.2 |
| | Estimation Comments | [Not specified] |

Statistical Analysis 2 for Change From Baseline in Residual Volume (Vresidual) at Each Visit

| | | |
|---|---|---|
| Statistical Analysis Overview | Comparison Groups | Degarelix 240 mg/80 mg, Goserelin (3.6 mg) + Bicalutamide (50 mg) |
| | Comments | Week 8. Estimates from analysis of variance with treatment and country as factors and age and baseline value as covariates. |
| | Non-Inferiority or Equivalence Analysis? | No |
| | Comments | [Not specified] |

| | | |
|---|---|---|
| Statistical Test of Hypothesis | P-Value | 0.8284 |
| | Comments | [Not specified] |
| | Method | ANCOVA |
| | Comments | The baseline score, age, and country were used as covariates and treatment was used as a factor in the analysis for the FAS. |

| | | |
|---|---|---|
| Method of Estimation | Estimation Parameter | Mean Difference (Final Values) |
| | Estimated Value | 5.91 |
| | Confidence Interval | (2-Sided) 95%<br>-49.1 to 60.9 |
| | Estimation Comments | [Not specified] |

Statistical Analysis 3 for Change From Baseline in Residual Volume (Vresidual) at Each Visit

| | | |
|---|---|---|
| Statistical Analysis Overview | Comparison Groups | Degarelix 240 mg/80 mg, Goserelin (3.6 mg) + Bicalutamide (50 mg) |
| | Comments | Week 12. Estimates from analysis of variance with treatment and country as factors and age and baseline value as covariates. |
| | Non-Inferiority or Equivalence Analysis? | No |
| | Comments | [Not specified] |

| | | |
|---|---|---|
| Statistical Test of Hypothesis | P-Value | 0.5984 |
| | Comments | [Not specified] |
| | Method | ANCOVA |
| | Comments | The baseline score, age, and country were used as covariates and treatment was used as a factor in the analysis for the FAS. |

| | | |
|---|---|---|
| Method of Estimation | Estimation Parameter | Mean Difference (Final Values) |
| | Estimated Value | 12.2 |
| | Confidence Interval | (2-Sided) 95%<br>-34.4 to 58.8 |
| | Estimation Comments | [Not specified] |

5. Secondary Outcome Measure:

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

Analysis Population Description

FAS, Observed Cases (OC).

Reporting Groups

| | Description |
|---|---|
| Degarelix 240 mg/80 mg | Degarelix 240 mg (40 mg/mL) + 80 mg (20 mg/mL) |
| Goserelin (3.6 mg) + Bicalutamide (50 mg) | Goserelin (3.6 mg) + bicalutamide (50 mg) |

Measured Values

| | Degarelix 240 mg/80 mg | Goserelin (3.6 mg) + Bicalutamide (50 mg) |
|---|---|---|
| Number of Participants Analyzed | 26 | 11 |
| Change From Baseline in Prostate Size Based on Trans Rectal Ultra Sound (TRUS) at Week 12<br>[units: mL]<br>Mean (Standard Deviation) | -22.4 (14.8) | -13.4 (10.0) |

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

| | | |
|---|---|---|
| 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 and country as factors and age and baseline value as covariates. |
| | Non-Inferiority or Equivalence Analysis? | No |
| | Comments | [Not specified] |

| | | |
|---|---|---|
| Statistical Test of Hypothesis | P-Value | 0.1018 |
| | Comments | [Not specified] |
| | Method | ANCOVA |
| | Comments | The baseline score, age, and country were used as covariates and treatment was used as a factor in the analysis for the FAS. |

| | | |
|---|---|---|
| Method of Estimation | Estimation Parameter | Mean Difference (Final Values) |
| | Estimated Value | -7.83 |
| | Confidence Interval | (2-Sided) 95%<br>-17.3 to 1.64 |
| | Estimation Comments | [Not specified] |

6. Secondary Outcome Measure:

| | |
|---|---|
| Measure Title | Number of Participants With Testosterone <=0.5 Nanograms/Milliliter at Each Visit |
| Measure Description | |
| Time Frame | After treatment of 4, 8 and 12 weeks compared to Baseline |
| Safety Issue? | No |

Analysis Population Description
FAS, OC.

Reporting Groups

| | Description |
|---|---|
| Degarelix 240 mg/80 mg | Degarelix 240 mg (40 mg/mL) + 80 mg (20 mg/mL) |
| Goserelin (3.6 mg) + Bicalutamide (50 mg) | Goserelin (3.6 mg) + bicalutamide (50 mg) |

Measured Values

| | Degarelix 240 mg/80 mg | Goserelin (3.6 mg) + Bicalutamide (50 mg) |
|---|---|---|
| Number of Participants Analyzed | 27 | 13 |
| Number of Participants With Testosterone <=0.5 Nanograms/Milliliter at Each Visit [units: participants] | | |
| Week 4 | 26 | 12 |
| Week 8 | 25 | 12 |
| Week 12 | 27 | 12 |

7. Secondary Outcome Measure:

| | |
|---|---|
| Measure Title | Percentage Change From Baseline in Prostate-specific Antigen (PSA) Concentration at Each Visit |
| Measure Description | |
| Time Frame | After treatment of 4, 8 and 12 weeks compared to Baseline |
| Safety Issue? | No |

Analysis Population Description
FAS, LOCF.

Reporting Groups

| | Description |
|---|---|
| Degarelix 240 mg/80 mg | Degarelix 240 mg (40 mg/mL) + 80 mg (20 mg/mL) |
| Goserelin (3.6 mg) + Bicalutamide (50 mg) | Goserelin (3.6 mg) + bicalutamide (50 mg) |

Measured Values

| | Degarelix 240 mg/80 mg | Goserelin (3.6 mg) + Bicalutamide (50 mg) |
|---|---|---|
| Number of Participants Analyzed | 27 | 12 |
| Percentage Change From Baseline in Prostate-specific Antigen (PSA) Concentration at Each Visit<br>[units: percentage]<br>Median (Full Range) | | |
| Week 4 | -85.72 (-97.87 to 234.97) | -93.44 (-98.33 to -87.09) |
| Week 8 | -89.2 (-99.47 to -31.62) | -97.26 (-99.72 to -87.56) |
| Week 12 | -93.87 (-99.83 to -64.71) | -97.78 (-99.72 to -94.52) |

8. 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'). The figures in the tables present the change (ie decrease) in IPSS QoL score, i.e. the bigger the decrease the better QoL. |
| Time Frame | After treatment of 4, 8 and 12 weeks compared to Baseline |
| Safety Issue? | No |

Analysis Population Description
FAS, OC.

Reporting Groups

| | Description |
|---|---|
| Degarelix 240 mg/80 mg | Degarelix 240 mg (40 mg/mL) + 80 mg (20 mg/mL) |
| Goserelin (3.6 mg) + Bicalutamide (50 mg) | Goserelin (3.6 mg) + bicalutamide (50 mg) |

Measured Values

| | Degarelix 240 mg/80 mg | Goserelin (3.6 mg) + Bicalutamide (50 mg) |
|---|---|---|
| Number of Participants Analyzed | 27 | 13 |
| Change From Baseline in Quality of Life (QoL) Related to Urinary Symptoms at Each Visit<br>[units: score on scale]<br>Mean (Standard Deviation) | | |
| Week 4 | -0.96 (0.92) | -0.54 (1.51) |
| Week 8 | -1.54 (1.42) | -0.73 (2.20) |
| Week 12 | -1.77 (1.73) | -0.55 (1.69) |

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

FAS. One participant in the degarelix group did not have any assessment of vital signs or body weight (the number of participants in this group is thus 26).

Reporting Groups

| | Description |
|---|---|
| Degarelix 240 mg/80 mg | Degarelix 240 mg (40 mg/mL) + 80 mg (20 mg/mL) |
| Goserelin (3.6 mg) + Bicalutamide (50 mg) | Goserelin (3.6 mg) + bicalutamide (50 mg) |

Measured Values

| | Degarelix 240 mg/80 mg | Goserelin (3.6 mg) + Bicalutamide (50 mg) |
|---|---|---|
| Number of Participants Analyzed | 26 | 13 |
| 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 | 0 |
| Systolic blood pressure <=90 and decrease >=20 | 0 | 0 |
| Systolic blood pressure >=180 and increase >=20 | 0 | 0 |
| Heart rate <=50 and decrease >=15 | 0 | 0 |
| Heart rate >=120 and increase >=15 | 0 | 0 |
| Body weight decrease of >=7 percent | 1 | 0 |
| Body weight increase of >=7 percent | 1 | 0 |

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 on participant with one abnormal value are presented, many more variables were included in the trial. |
| Time Frame | Baseline to 12 weeks of treatment |
| Safety Issue? | No |

Analysis Population Description

FAS.

Reporting Groups

| | Description |
|---|---|
| Degarelix 240 mg/80 mg | Degarelix 240 mg (40 mg/mL) + 80 mg (20 mg/mL) |
| Goserelin (3.6 mg) + Bicalutamide (50 mg) | Goserelin (3.6 mg) + bicalutamide (50 mg) |

Measured Values

| | Degarelix 240 mg/80 mg | Goserelin (3.6 mg) + Bicalutamide (50 mg) |
|---|---|---|
| Number of Participants Analyzed | 27 | 13 |
| Number of Participants With Markedly Abnormal Values in Safety Laboratory Variables [units: participants] | | |
| B-Haematocrit (Ratio) <=0.37 | 5 | 1 |
| B-Platelet count (10^9/L) <=75 | 1 | 0 |
| S-Calcium (mmol/L) <=1.8 | 1 | 0 |
| S-Potassium (mmol/L) >=5.8 | 0 | 1 |
| S-Urea nitrogen (mmol/L) >=10.7 | 1 | 2 |

## 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 | Degarelix 240 mg (40 mg/mL) + 80 mg (20 mg/mL) |
| Goserelin (3.6 mg) + Bicalutamide (50 mg) | Goserelin (3.6 mg) + bicalutamide (50 mg) |

Serious Adverse Events

| | Degarelix 240 mg/80 mg | | Goserelin (3.6 mg) + Bicalutamide (50 mg) | |
|---|---|---|---|---|
| | Affected/At Risk (%) | # Events | Affected/At Risk (%) | # Events |
| Total | 0/27 (0%) | | 1/13 (7.69%) | |
| Hepatobiliary disorders | | | | |

| | Degarelix 240 mg/80 mg | | Goserelin (3.6 mg) + Bicalutamide (50 mg) | |
|---|---|---|---|---|
| | Affected/At Risk (%) | # Events | Affected/At Risk (%) | # Events |
| Hepatic failure [A] † | 0/27 (0%) | 0 | 1/13 (7.69%) | 1 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | | |
| Prostate cancer [A] † | 0/27 (0%) | 0 | 1/13 (7.69%) | 1 |
| Renal and urinary disorders | | | | |
| Renal failure [A] † | 0/27 (0%) | 0 | 1/13 (7.69%) | 1 |
| Reproductive system and breast disorders | | | | |
| Prostatic obstruction [A] † | 0/27 (0%) | 0 | 1/13 (7.69%) | 1 |

† Indicates events were collected by systematic assessment.
A Term from vocabulary, MedDRA (10.1)

Other Adverse Events

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

| | Degarelix 240 mg/80 mg | | Goserelin (3.6 mg) + Bicalutamide (50 mg) | |
|---|---|---|---|---|
| | Affected/At Risk (%) | # Events | Affected/At Risk (%) | # Events |
| Total | 14/27 (51.85%) | | 7/13 (53.85%) | |
| Blood and lymphatic system disorders | | | | |
| Anaemia [A] † | 2/27 (7.41%) | 2 | 0/13 (0%) | 0 |
| Leukocytosis [A] † | 0/27 (0%) | 0 | 1/13 (7.69%) | 1 |
| Congenital, familial and genetic disorders | | | | |
| Reproductive tract hypoplasia, male [A] † | 2/27 (7.41%) | 2 | 0/13 (0%) | 0 |
| Gastrointestinal disorders | | | | |
| Constipation [A] † | 3/27 (11.11%) | 3 | 0/13 (0%) | 0 |
| General disorders | | | | |
| Fatigue [A] † | 2/27 (7.41%) | 2 | 0/13 (0%) | 0 |
| Injection site erythema [A] † | 3/27 (11.11%) | 5 | 0/13 (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] † | 6/27 (22.22%) | 16 | 0/13 (0%) | 0 |
| Pyrexia [A] † | 1/27 (3.7%) | 1 | 1/13 (7.69%) | 1 |
| Hepatobiliary disorders | | | | |
| Hepatic failure [A] † | 0/27 (0%) | 0 | 1/13 (7.69%) | 1 |
| Infections and infestations | | | | |
| Cystitis [A] † | 3/27 (11.11%) | 4 | 2/13 (15.38%) | 2 |
| Urinary tract infection [A] † | 1/27 (3.7%) | 1 | 2/13 (15.38%) | 2 |
| Investigations | | | | |
| Weight decreased [A] † | 3/27 (11.11%) | 3 | 0/13 (0%) | 0 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | | |
| Metastases to bone [A] † | 1/27 (3.7%) | 1 | 2/13 (15.38%) | 2 |
| Prostate cancer [A] † | 0/27 (0%) | 0 | 1/13 (7.69%) | 1 |
| Renal and urinary disorders | | | | |
| Renal cyst [A] † | 0/27 (0%) | 0 | 1/13 (7.69%) | 1 |
| Renal failure [A] † | 0/27 (0%) | 0 | 1/13 (7.69%) | 1 |
| Urinary retention [A] † | 0/27 (0%) | 0 | 1/13 (7.69%) | 2 |
| Reproductive system and breast disorders | | | | |
| Prostatic obstruction [A] † | 0/27 (0%) | 0 | 1/13 (7.69%) | 1 |
| Vascular disorders | | | | |
| Hot flush [A] † | 5/27 (18.52%) | 5 | 2/13 (15.38%) | 2 |

† Indicates events were collected by systematic assessment.
A Term from vocabulary, MedDRA (10.1)

## Limitations and Caveats

Early termination leading to small numbers of subjects analyzed.

## 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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