



Clinical trial results:

A Phase II, Multicentre, Open, Prospective, Randomised, Parallel-Group, Pharmacodynamic Equivalence study on Intramuscular Versus Subcutaneous applications of Triptorelin Pamoate (Pamorelin® LA 11.25 mg) in patients with Advanced Prostate Cancer

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2010-019632-12 |
| Trial protocol | DE |
| Global end of trial date | 07 May 2012 |

Results information

| | |
|--------------------------------|------------------|
| Result version number | v1 (current) |
| This version publication date | 04 February 2016 |
| First version publication date | 04 February 2016 |

Trial information

Trial identification

| | |
|-----------------------|----------------|
| Sponsor protocol code | A-94-52014-178 |
|-----------------------|----------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01257425 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | Ipsen Pharma GmbH |
| Sponsor organisation address | Willy-Brandt-Straße 3, Ettlingen, Germany, D-76275 |
| Public contact | Medical Director, Oncology, Ipsen, clinical.trials@ipsen.com |
| Scientific contact | Medical Director, Oncology, Ipsen, clinical.trials@ipsen.com |

Notes:

Paediatric regulatory details

| | |
|--|----|
| Is trial part of an agreed paediatric investigation plan (PIP) | No |
| Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial? | No |
| Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial? | No |

Notes:

Results analysis stage

| | |
|--|------------------|
| Analysis stage | Final |
| Date of interim/final analysis | 25 June 2013 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 13 February 2012 |
| Global end of trial reached? | Yes |
| Global end of trial date | 07 May 2012 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To demonstrate the pharmacodynamic equivalence of triptorelin pamoate (Pamorelin® LA 11.25 mg), applied either as intramuscular (IM) or subcutaneous (SC) injections, in terms of the area under the curve (AUC1-85d) for serum testosterone in patients with advanced prostate cancer.

Protection of trial subjects:

The study and the archiving of essential documents were performed in compliance with Good Clinical Practices (GCP) and in accordance with the Declaration of Helsinki. Triptorelin pamoate 3-month formulation (Pamorelin® LA 11.25 mg) has been investigated and is approved for intramuscular application only (5, 6). However, many elderly patients with prostate cancer suffer from accompanying diseases which require anticoagulant medication, and subcutaneous injections are often preferred in anticoagulated patients.

Background therapy: -

Evidence for comparator: -

| | |
|---|------------------|
| Actual start date of recruitment | 16 December 2010 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|--------------|
| Country: Number of subjects enrolled | Germany: 103 |
| Worldwide total number of subjects | 103 |
| EEA total number of subjects | 103 |

Notes:

Subjects enrolled per age group

| | |
|---|----|
| In utero | 0 |
| Preterm newborn - gestational age < 37 wk | 0 |
| Newborns (0-27 days) | 0 |
| Infants and toddlers (28 days-23 months) | 0 |
| Children (2-11 years) | 0 |
| Adolescents (12-17 years) | 0 |
| Adults (18-64 years) | 10 |
| From 65 to 84 years | 85 |

| | |
|-------------------|---|
| 85 years and over | 8 |
|-------------------|---|

Subject disposition

Recruitment

Recruitment details:

Patients diagnosed with advanced prostate cancer (locally advanced or metastatic, histologically proven) recruited at 23 investigational sites in Germany

Pre-assignment

Screening details:

109 patients screened and 6 of these did not fulfil randomisation criteria therefore 103 patients were randomised to either group of treatment with triptorelin pamoate 3-month formulation applied intramuscularly or subcutaneously.

Period 1

| | |
|------------------------------|--------------------------------|
| Period 1 title | Overall study (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Not blinded |

Arms

| | |
|------------------------------|--|
| Are arms mutually exclusive? | Yes |
| Arm title | Group A: Triptorelin Pamoate (Pamorelin® LA 11.25 mg) IM |

Arm description:

Pamorelin® LA 11.25 mg administered as standard IM injection (= reference group) at Day 1 and Day 85

| | |
|--|---|
| Arm type | Experimental |
| Investigational medicinal product name | Triptorelin Pamoate (Pamorelin® LA 11.25 mg) IM |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Powder and solvent for prolonged-release suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

Pamorelin® (triptorelin pamoate), 11.25 mg, intramuscular injection

| | |
|------------------|--|
| Arm title | Group B: Triptorelin Pamoate (Pamorelin® LA 11.25 mg) SC |
|------------------|--|

Arm description:

Pamorelin® LA 11.25 mg administered as SC injection at Day 1 and Day 85

| | |
|--|---|
| Arm type | Experimental |
| Investigational medicinal product name | Triptorelin Pamoate (Pamorelin® LA 11.25 mg) SC |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Powder and solvent for prolonged-release suspension for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Pamorelin® (triptorelin pamoate), 11.25 mg, subcutaneous injection

| Number of subjects in period 1 | Group A: Triptorelin Pamoate (Pamorelin® LA 11.25 mg) IM | Group B: Triptorelin Pamoate (Pamorelin® LA 11.25 mg) SC |
|---------------------------------------|--|--|
| Started | 51 | 52 |
| Completed | 45 | 46 |
| Not completed | 6 | 6 |
| Consent withdrawn by subject | 1 | - |
| Adverse event, non-fatal | 1 | 1 |
| Death | - | 1 |
| Protocol deviation | 1 | 1 |
| Lack of efficacy | 3 | 3 |

Baseline characteristics

Reporting groups

| | |
|--|--|
| Reporting group title | Group A: Triptorelin Pamoate (Pamorelin® LA 11.25 mg) IM |
| Reporting group description: Pamorelin® LA 11.25 mg administered as standard IM injection (= reference group) at Day 1 and Day 85 | |
| Reporting group title | Group B: Triptorelin Pamoate (Pamorelin® LA 11.25 mg) SC |
| Reporting group description: Pamorelin® LA 11.25 mg administered as SC injection at Day 1 and Day 85 | |

| Reporting group values | Group A: Triptorelin Pamoate (Pamorelin® LA 11.25 mg) IM | Group B: Triptorelin Pamoate (Pamorelin® LA 11.25 mg) SC | Total |
|---|--|--|-------|
| Number of subjects | 51 | 52 | 103 |
| Age categorical | | | |
| Units: Subjects | | | |
| 50 to < 60 | 2 | 2 | 4 |
| 60 to < 70 | 11 | 10 | 21 |
| 70 to < 80 | 31 | 30 | 61 |
| 80 to < 90 | 7 | 10 | 17 |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 73.3 | 73.4 | - |
| standard deviation | ± 7 | ± 6.7 | - |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 0 | 0 | 0 |
| Male | 51 | 52 | 103 |
| Race | | | |
| Units: Subjects | | | |
| Caucasian | 51 | 52 | 103 |
| Karnofsky index (%) | | | |
| Karnofsky index is a measure of performance status to quantify cancer patients' general well-being and activities of daily life. Karnofsky scores run from 100% (perfect health) to 0% (death). Analysed from Intent-to-treat (ITT) population comprised of 103 patients (SC:52 patients and IM:51 patients). | | | |
| Units: Subjects | | | |
| 100% | 27 | 21 | 48 |
| 90% | 12 | 18 | 30 |
| 80% | 12 | 13 | 25 |
| Prostate specific antigen (PSA) level | | | |
| Analysed from Intent-to-treat (ITT) population with one missing value in the IM group. | | | |
| Units: ng/mL | | | |
| arithmetic mean | 97.2 | 47.1 | - |
| standard deviation | ± 368 | ± 174.9 | - |
| Testosterone serum level | | | |
| Analysed from Intent-to-treat (ITT) population comprised of 103 patients (SC:52 patients and IM:51 patients). | | | |
| Units: ng/mL | | | |
| arithmetic mean | 3.12 | 3.23 | |

| | | | |
|---|--------|--------|---|
| standard deviation | ± 1.36 | ± 1.28 | - |
| Tumour-related pain | | | |
| Analysed from modified ITT population comprised of 98 patients (SC: 49 and IM: 49 patients). Tumour-related pain at baseline was rated by the patient by means of a 10-cm visual analogue scale (VAS), ranging from 0 (no pain) to 10 (maximum pain). | | | |
| Units: cm | | | |
| arithmetic mean | 0.37 | 0.25 | |
| standard deviation | ± 0.99 | ± 0.58 | - |

End points

End points reporting groups

| | |
|--|--|
| Reporting group title | Group A: Triptorelin Pamoate (Pamorelin® LA 11.25 mg) IM |
| Reporting group description: Pamorelin® LA 11.25 mg administered as standard IM injection (= reference group) at Day 1 and Day 85 | |
| Reporting group title | Group B: Triptorelin Pamoate (Pamorelin® LA 11.25 mg) SC |
| Reporting group description: Pamorelin® LA 11.25 mg administered as SC injection at Day 1 and Day 85 | |

Primary: Area under the curve of testosterone serum concentration (AUC1-85d)

| | |
|---|---|
| End point title | Area under the curve of testosterone serum concentration (AUC1-85d) |
| End point description: Area under the curve (AUC) calculated from serum testosterone concentration taken at intervals between the first administration (Day 1) of the study drug and Day 85 after dosing. From the curve describing serum testosterone concentration levels (ng/mL) over time, the AUC was calculated using numerical integration methods. This value was log-transformed to more closely meet the assumption of the statistical method. | |
| End point type | Primary |
| End point timeframe: Between Day 1 and Day 85 | |

| End point values | Group A: Triptorelin Pamoate (Pamorelin® LA 11.25 mg) IM | Group B: Triptorelin Pamoate (Pamorelin® LA 11.25 mg) SC | | |
|--------------------------------------|---|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 51 | 52 | | |
| Units: log(ng*day/mL) | | | | |
| arithmetic mean (standard deviation) | 4.23 (± 0.497) | 4.241 (± 0.396) | | |

Statistical analyses

| | |
|----------------------------|--|
| Statistical analysis title | Summary of AUC1-85d |
| Comparison groups | Group B: Triptorelin Pamoate (Pamorelin® LA 11.25 mg) SC v Group A: Triptorelin Pamoate (Pamorelin® LA 11.25 mg) IM |

| | |
|---|---------------------|
| Number of subjects included in analysis | 103 |
| Analysis specification | Pre-specified |
| Analysis type | equivalence |
| Parameter estimate | Ratio of AUC values |
| Point estimate | 0.977 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | 0.88 |
| upper limit | 1.08 |

Secondary: Area under the curve of testosterone serum concentration (AUC1-169d)

| | |
|------------------------|--|
| End point title | Area under the curve of testosterone serum concentration (AUC1-169d) |
| End point description: | Area under the curve calculated from serum testosterone concentration taken at intervals between the first administration (Day 1) of the study drug and Day 169 after dosing. From the curve describing serum testosterone concentration levels (ng/mL) over time, the AUC was calculated using numerical integration methods. This value was log-transformed to more closely meet the assumption of the statistical method. |
| End point type | Secondary |
| End point timeframe: | Between Day 1 and Day 169 |

| End point values | Group A: Triptorelin Pamoate (Pamorelin® LA 11.25 mg) IM | Group B: Triptorelin Pamoate (Pamorelin® LA 11.25 mg) SC | | |
|--------------------------------------|---|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 51 | 52 | | |
| Units: log(ng*day/mL) | | | | |
| arithmetic mean (standard deviation) | 4.524 (± 0.558) | 4.486 (± 0.422) | | |

Statistical analyses

| | |
|----------------------------|--|
| Statistical analysis title | Summary of AUC1-169d |
| Comparison groups | Group A: Triptorelin Pamoate (Pamorelin® LA 11.25 mg) IM v Group B: Triptorelin Pamoate (Pamorelin® LA 11.25 mg) SC |

| | |
|---|---------------------|
| Number of subjects included in analysis | 103 |
| Analysis specification | Pre-specified |
| Analysis type | equivalence |
| Parameter estimate | Ratio of AUC values |
| Point estimate | 0.932 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | 0.82 |
| upper limit | 1.06 |

Secondary: Area under the curve of testosterone serum concentration (AUC85-169d)

| | |
|-----------------|---|
| End point title | Area under the curve of testosterone serum concentration (AUC85-169d) |
|-----------------|---|

End point description:

Area under the curve calculated from serum testosterone concentration taken at intervals between Day 85 and Day 169 after dosing. From the curve describing serum testosterone concentration levels (ng/mL) over time, the AUC was calculated using numerical integration methods. This value was log-transformed to more closely meet the assumption of the statistical method.

95 patients (IM: 47 patients, SC: 48 patients) received a second injection of the study drug.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Between Day 85 and Day 169

| End point values | Group A: Triptorelin Pamoate (Pamorelin® LA 11.25 mg) IM | Group B: Triptorelin Pamoate (Pamorelin® LA 11.25 mg) SC | | |
|--------------------------------------|---|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 47 | 48 | | |
| Units: log(ng*day/mL) | | | | |
| arithmetic mean (standard deviation) | 2.884 (± 0.381) | 2.799 (± 0.451) | | |

Statistical analyses

| | |
|----------------------------|--|
| Statistical analysis title | Summary of AUC85-169d |
| Comparison groups | Group A: Triptorelin Pamoate (Pamorelin® LA 11.25 mg) IM v Group B: Triptorelin Pamoate (Pamorelin® LA 11.25 mg) SC |

| | |
|---|---------------------|
| Number of subjects included in analysis | 95 |
| Analysis specification | Pre-specified |
| Analysis type | equivalence |
| Parameter estimate | Ratio of AUC values |
| Point estimate | 0.91 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | 0.81 |
| upper limit | 1.02 |

Secondary: Maximum concentration of serum testosterone (Cmax) - Raw Data

| | |
|-----------------|---|
| End point title | Maximum concentration of serum testosterone (Cmax) - Raw Data |
|-----------------|---|

End point description:

Cmax was assessed as the maximum testosterone serum concentration between the first administration of the study drug and Day 169.

Analysed for intent-to-treat (ITT) population comprised of 103 patients (IM: 51 and SC: 52 patients).

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Between Day 1 and Day 169

| End point values | Group A: Triptorelin Pamoate (Pamorelin® LA 11.25 mg) IM | Group B: Triptorelin Pamoate (Pamorelin® LA 11.25 mg) SC | | |
|--------------------------------------|---|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 51 | 52 | | |
| Units: ng/mL | | | | |
| arithmetic mean (standard deviation) | 5.495 (± 2.348) | 5.738 (± 2.333) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum concentration of serum testosterone (Cmax) - Log-transformed Data

| | |
|-----------------|---|
| End point title | Maximum concentration of serum testosterone (Cmax) - Log-transformed Data |
|-----------------|---|

End point description:

Cmax was assessed as the maximum testosterone serum concentration between the first administration of the study drug and Day 169.

Analysed for intent-to-treat (ITT) population comprised of 103 patients (IM: 51 and SC: 52 patients).

| | |
|---------------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Between Day 1 and Day 169 | |

| End point values | Group A: Triptorelin Pamoate (Pamorelin® LA 11.25 mg) IM | Group B: Triptorelin Pamoate (Pamorelin® LA 11.25 mg) SC | | |
|--------------------------------------|---|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 51 | 52 | | |
| Units: log(ng/mL) | | | | |
| arithmetic mean (standard deviation) | 1.62 (± 0.415) | 1.665 (± 0.423) | | |

Statistical analyses

| Statistical analysis title | Summary of Cmax Log-transformed Data |
|---|---|
| Comparison groups | Group A: Triptorelin Pamoate (Pamorelin® LA 11.25 mg) IM v Group B: Triptorelin Pamoate (Pamorelin® LA 11.25 mg) SC |
| Number of subjects included in analysis | 103 |
| Analysis specification | Pre-specified |
| Analysis type | equivalence |
| P-value | = 0.8516 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (net) |
| Point estimate | 0.01 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.09 |
| upper limit | 0.11 |

Secondary: Time to Castration [Tcast] - Testosterone Level Less Than or Equal to 0.5 ng/mL

| | |
|-----------------|---|
| End point title | Time to Castration [Tcast] - Testosterone Level Less Than or Equal to 0.5 ng/mL |
|-----------------|---|

End point description:

tcast is the number of days between day of first administration of the study drug and the day the testosterone level reaches the limit of castration defined as testosterone level less than or equal to 0.5 ng/mL for the first time. Analysis of tcast was based on the Kaplan-Meier estimator.

Analysed for intent-to-treat (ITT) population comprised of 103 patients (IM: 51 and SC: 52 patients).

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| 12 weeks | |

| End point values | Group A: Triptorelin Pamoate (Pamorelin® LA 11.25 mg) IM | Group B: Triptorelin Pamoate (Pamorelin® LA 11.25 mg) SC | | |
|----------------------------------|---|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 51 | 52 | | |
| Units: days | | | | |
| median (confidence interval 95%) | 22 (22 to 23) | 22 (22 to 23) | | |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Summary of [Tcast] Testosterone Level \leq 0.5 ng/mL |
| Comparison groups | Group A: Triptorelin Pamoate (Pamorelin® LA 11.25 mg) IM v Group B: Triptorelin Pamoate (Pamorelin® LA 11.25 mg) SC |
| Number of subjects included in analysis | 103 |
| Analysis specification | Pre-specified |
| Analysis type | equivalence |
| P-value | = 0.98 |
| Method | Logrank |

Secondary: Time to Castration [Tcast] - Testosterone Level Less Than 0.5 ng/mL

| | |
|-----------------|---|
| End point title | Time to Castration [Tcast] - Testosterone Level Less Than 0.5 ng/mL |
|-----------------|---|

End point description:

tcast is the number of days between day of first administration of the study drug and the day the testosterone level reaches the limit of castration defined as testosterone level less than 0.5 ng/mL for the first time. Analysis of tcast was based on the Kaplan-Meier estimator.

Analysed for intent-to-treat (ITT) population comprised of 103 patients (IM: 51 and SC: 52 patients).

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| 12 weeks | |

| End point values | Group A: Triptorelin Pamoate (Pamorelin® LA 11.25 mg) IM | Group B: Triptorelin Pamoate (Pamorelin® LA 11.25 mg) SC | | |
|----------------------------------|---|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 51 | 52 | | |
| Units: days | | | | |
| median (confidence interval 95%) | 22 (22 to 23) | 22 (22 to 23) | | |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Summary of [Tcast] Testosterone Level < 0.5 ng/mL |
| Comparison groups | Group A: Triptorelin Pamoate (Pamorelin® LA 11.25 mg) IM v Group B: Triptorelin Pamoate (Pamorelin® LA 11.25 mg) SC |
| Number of subjects included in analysis | 103 |
| Analysis specification | Pre-specified |
| Analysis type | equivalence |
| P-value | = 0.84 |
| Method | Logrank |

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to Day 169

Adverse event reporting additional description:

All AEs which occurred from the time that the subject gave informed consent to the end of the study (visit D169) were considered for analysis

| | |
|-----------------|----------------|
| Assessment type | Non-systematic |
|-----------------|----------------|

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|------|
| Dictionary version | 15.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|--|
| Reporting group title | Group A: Triptorelin Pamoate (Pamorelin® LA 11.25 mg) IM |
|-----------------------|--|

Reporting group description: -

| | |
|-----------------------|--|
| Reporting group title | Group B: Triptorelin Pamoate (Pamorelin® LA 11.25 mg) SC |
|-----------------------|--|

Reporting group description: -

| Serious adverse events | Group A: Triptorelin Pamoate (Pamorelin® LA 11.25 mg) IM | Group B: Triptorelin Pamoate (Pamorelin® LA 11.25 mg) SC | |
|---|--|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 7 / 51 (13.73%) | 11 / 52 (21.15%) | |
| number of deaths (all causes) | 0 | 1 | |
| number of deaths resulting from adverse events | 0 | 1 | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Colon Cancer | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 1 / 52 (1.92%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lymphoma | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 1 / 52 (1.92%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metastasis | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 1 / 52 (1.92%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 1 / 1 | |
| Plasmacytoma | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 52 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Injury, poisoning and procedural complications | | | |
| Subdural Haematoma | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 52 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 52 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac disorders | | | |
| Coronary Artery Disease | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 1 / 52 (1.92%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Coronary Artery Stenosis | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 1 / 52 (1.92%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Angina Pectoris | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 1 / 52 (1.92%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nervous system disorders | | | |
| Cerebrovascular Accident | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 1 / 52 (1.92%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Transient Ischaemic Attack | | | |

| | | | |
|--|----------------|----------------|--|
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 52 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Inguinal Hernia, Obstructive | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 1 / 52 (1.92%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Inguinal Hernia | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 1 / 52 (1.92%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Umbilical Hernia | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 1 / 52 (1.92%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vomiting | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 1 / 52 (1.92%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Dyspnoea | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 1 / 52 (1.92%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory Failure | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 1 / 52 (1.92%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal and urinary disorders | | | |
| Bladder outlet obstruction | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 52 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|----------------|----------------|--|
| Haematuria | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 1 / 52 (1.92%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pyuria | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 52 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal Failure | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 1 / 52 (1.92%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal Failure Acute | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 52 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urethral Stenosis | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 52 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urinary Retention | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 1 / 52 (1.92%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Urosepsis | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 1 / 52 (1.92%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bronchitis | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 1 / 52 (1.92%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cellulitis | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 0 / 51 (0.00%) | 1 / 52 (1.92%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Mediastinitis | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 1 / 52 (1.92%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Peritonitis | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 1 / 52 (1.92%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Rectal abscess | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 52 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sepsis | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 1 / 52 (1.92%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| Non-serious adverse events | Group A: Triptorelin Pamoate (Pamorelin® LA 11.25 mg) IM | Group B: Triptorelin Pamoate (Pamorelin® LA 11.25 mg) SC | |
|---|--|--|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 25 / 51 (49.02%) | 32 / 52 (61.54%) | |
| Vascular disorders | | | |
| Hot flush | | | |
| subjects affected / exposed | 14 / 51 (27.45%) | 15 / 52 (28.85%) | |
| occurrences (all) | 14 | 15 | |
| General disorders and administration site conditions | | | |
| Fatigue | | | |
| subjects affected / exposed | 3 / 51 (5.88%) | 0 / 52 (0.00%) | |
| occurrences (all) | 3 | 0 | |

| | | | |
|---|---------------------|---------------------|--|
| Skin and subcutaneous tissue disorders Hyperhidrosis subjects affected / exposed occurrences (all) | 4 / 51 (7.84%) 4 | 5 / 52 (9.62%) 5 | |
| Renal and urinary disorders Nocturia subjects affected / exposed occurrences (all) | 0 / 51 (0.00%) 0 | 3 / 52 (5.77%) 3 | |
| Psychiatric disorders Sleep disorder subjects affected / exposed occurrences (all) | 0 / 51 (0.00%) 0 | 3 / 52 (5.77%) 3 | |
| Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) | 1 / 51 (1.96%) 1 | 3 / 52 (5.77%) 5 | |
| Infections and infestations Urinary Tract Infection subjects affected / exposed occurrences (all) | 3 / 51 (5.88%) 4 | 3 / 52 (5.77%) 4 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|----------------|---|
| 16 August 2010 | The first amendment, dated 16 August 2010, was substantial and aimed to change the wording (linguistic change) in definition of pharmacodynamic equivalence between the two modes of administration and to add a further exclusion criterion (to exclude participation in another clinical trial within the last 30 days or simultaneous participation in another clinical trial). As this amendment was in place prior to enrolment of the first patient into the study, it did not affect the conduct of the study. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported