



## Clinical trial results:

### Prostate Cancer Antigen-3 (PCA-3) and TMPRSS2-ERG Score changes during initiation of Androgen Deprivation Therapy (ADT) with triptorelin (22.5 mg) in patients with advanced prostate cancer (PCa): A phase III, single arm multicentre study

#### Summary

|                          |                         |
|--------------------------|-------------------------|
| EudraCT number           | 2009-012786-58          |
| Trial protocol           | GB ES LV FR NL LT BE IT |
| Global end of trial date | 28 June 2013            |

#### Results information

|                                |  |
|--------------------------------|--|
| Result version number          | v2 (current)   |
| This version publication date  | 26 February 2016   |
| First version publication date | 03 July 2015   |
| Version creation reason        | <ul style="list-style-type: none"><li>Correction of full data set Review and correction.</li></ul> |

#### Trial information

##### Trial identification

|                       |                |
|-----------------------|----------------|
| Sponsor protocol code | 8-79-52014-168 |
|-----------------------|----------------|

##### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT01020448 |
| WHO universal trial number (UTN)   | -           |

Notes:

#### Sponsors

|                              |   |
|------------------------------|---|
| Sponsor organisation name    | Ipsen Pharma sas  |
| Sponsor organisation address | 65, quai Georges Gorse, Boulogne-Billancourt, France, F-92100           |
| Public contact               | Medical Director, Oncology, Ipsen Pharma sas, clinical.trials@ipsen.com |
| Scientific contact           | Medical Director, Oncology, Ipsen Pharma sas, 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                       | 06 September 2013 |
| Is this the analysis of the primary completion data? | Yes               |
| Primary completion date                              | 02 November 2011  |
| Global end of trial reached?                         | Yes               |
| Global end of trial date                             | 28 June 2013      |
| Was the trial ended prematurely?                     | No                |

Notes:

## General information about the trial

Main objective of the trial:

To model the PCA-3 change at Month 6 (M6) post treatment assessment.

Protection of trial subjects:

In compliance with Good Clinical Practice (GCP), the medical records/medical notes etc. had to be clearly marked and permit easy identification of a patient's participation in the specified clinical trial. The dose of triptorelin sustained release (SR) 22.5 mg used in this study has been previously investigated in a multicentre, non-comparative phase III study in patients with advanced PCa.

Background therapy: -

Evidence for comparator: -

|   |                  |
|---|------------------|
| Actual start date of recruitment                          | 30 November 2009 |
| Long term follow-up planned                               | Yes              |
| Long term follow-up rationale                             | Safety           |
| Long term follow-up duration                              | 6 Months         |
| Independent data monitoring committee (IDMC) involvement? | No               |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |                    |
|--------------------------------------|--------------------|
| Country: Number of subjects enrolled | Netherlands: 14    |
| Country: Number of subjects enrolled | Romania: 34        |
| Country: Number of subjects enrolled | Spain: 36          |
| Country: Number of subjects enrolled | United Kingdom: 51 |
| Country: Number of subjects enrolled | Belgium: 10        |
| Country: Number of subjects enrolled | Denmark: 24        |
| Country: Number of subjects enrolled | France: 89         |
| Country: Number of subjects enrolled | Latvia: 26         |
| Country: Number of subjects enrolled | Lithuania: 41      |
| Worldwide total number of subjects   | 325                |
| EEA total number of subjects         | 325                |

Notes:

### Subjects enrolled per age group

|  |   |
|--|---|
| In utero                               | 0 |
| Preterm newborn - gestational age < 37 | 0 |

|  |     |
|--|-----|
| wk                                       |     |
| 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)                     | 60  |
| From 65 to 84 years                      | 245 |
| 85 years and over                        | 20  |

## Subject disposition

### Recruitment

Recruitment details:

Study Initiation Date: 30-Nov-2009. Subjects screened were 339 and screen failures were 13.

### Pre-assignment

Screening details:

326 of the 339 patients screened for this study were included; one patient was excluded from the safety population as no post-baseline assessment was available. The other 325 patients were included in the treatment group.

### Period 1

|                              |  |
|------------------------------|--|
| Period 1 title               | Triptorelin (Decapeptyl®) 22.5 mg (overall period) |
| Is this the baseline period? | Yes  |
| Allocation method            | Non-randomised - controlled                        |
| Blinding used                | Not blinded  |

### Arms

|                  |                                   |
|------------------|-----------------------------------|
| <b>Arm title</b> | Triptorelin (Decapeptyl®) 22.5 mg |
|------------------|-----------------------------------|

Arm description:

Triptorelin (Decapeptyl®): One intramuscular injection of triptorelin (Decapeptyl®) 22.5 mg performed once all baseline procedures and assessments have been completed.

|  |                           |
|--|---------------------------|
| Arm type                               | Experimental              |
| Investigational medicinal product name | Triptorelin (Decapeptyl®) |
| Investigational medicinal product code |                           |
| Other name                             |                           |
| Pharmaceutical forms                   | Injection                 |
| Routes of administration               | Intramuscular use         |

Dosage and administration details:

One intramuscular injection of triptorelin (Decapeptyl®) 22.5mg performed once all baseline procedures and assessments have been completed.

| <b>Number of subjects in period 1</b> | Triptorelin (Decapeptyl®) 22.5 mg |
|---------------------------------------|-----------------------------------|
| Started                               | 325                               |
| Completed                             | 299                               |
| Not completed                         | 26                                |
| Consent withdrawn by subject          | 3                                 |
| Adverse event, non-fatal              | 11                                |
| Lost to follow-up                     | 2                                 |
| Disease Progression                   | 2                                 |
| Lack of efficacy                      | 8                                 |

## Baseline characteristics

### Reporting groups

|                       |                                   |
|-----------------------|-----------------------------------|
| Reporting group title | Triptorelin (Decapeptyl®) 22.5 mg |
|-----------------------|-----------------------------------|

Reporting group description: -

| Reporting group values   | Triptorelin<br>(Decapeptyl®) 22.5<br>mg | Total |  |
|--|---|-------|--|
| Number of subjects   | 325                                     | 325   |  |
| Age categorical<br>Units: Subjects   |   |       |  |
| In utero   | 0                                       | 0     |  |
| Preterm newborn infants<br>(gestational age < 37 wks)  | 0                                       | 0     |  |
| Newborns (0-27 days)   | 0                                       | 0     |  |
| Infants and toddlers (28 days-23<br>months)  | 0                                       | 0     |  |
| Children (2-11 years)  | 0                                       | 0     |  |
| Adolescents (12-17 years)  | 0                                       | 0     |  |
| Adults (18-64 years)   | 60                                      | 60    |  |
| From 65-84 years   | 245                                     | 245   |  |
| 85 years and over  | 20                                      | 20    |  |
| Age continuous<br>Units: years   |   |       |  |
| arithmetic mean  | 72.6                                    |       |  |
| standard deviation   | ± 8.4                                   | -     |  |
| Gender categorical<br>Units: Subjects  |   |       |  |
| Female   | 0                                       | 0     |  |
| Male   | 325                                     | 325   |  |
| Race (NIH/OMB)<br>Units: Subjects  |   |       |  |
| American Indian or Alaska Native   | 0                                       | 0     |  |
| Asian  | 1                                       | 1     |  |
| Native Hawaiian or Other Pacific<br>Islander   | 0                                       | 0     |  |
| Black or African American  | 7                                       | 7     |  |
| White  | 307                                     | 307   |  |
| More than one race   | 0                                       | 0     |  |
| Unknown or Not Reported  | 10                                      | 10    |  |
| PCA-3 Score  |   |       |  |
| PCA-3 score = (mRNA PCA3/mRNA PSA)x1000<br>• Non-assessable = Associated PSA mRNA <7500 copies/mL<br>• ≤BLQ = PCA-3 mRNA is below the concentration of the calibrator and associated PSA mRNA >7500<br>copies/mL<br>• <35 = PCA-3 mRNA above BLQ and less than 35<br>• ≥35 = PCA-3 mRNA greater or equal to 35 |   |       |  |
| Units: Subjects  |   |       |  |
| Non-assessable   | 39                                      | 39    |  |
| ≤BLQ   | 15                                      | 15    |  |
| <35  | 89                                      | 89    |  |

|                                   |     |     |  |
|-----------------------------------|-----|-----|--|
| ≥35                               | 179 | 179 |  |
| Missing - No sample analysis done | 3   | 3   |  |

|                    |        |   |  |
|--------------------|--------|---|--|
| Height             |        |   |  |
| n=315, missing=10  |        |   |  |
| Units: Cm          |        |   |  |
| arithmetic mean    | 172.3  |   |  |
| standard deviation | ± 6.5  | - |  |
| Weight             |        |   |  |
| n=317, missing=8   |        |   |  |
| Units: KG          |        |   |  |
| arithmetic mean    | 79.6   |   |  |
| standard deviation | ± 13.4 | - |  |
| BMI                |        |   |  |
| n=314, missing=11  |        |   |  |
| Units: kg/m²       |        |   |  |
| arithmetic mean    | 26.79  |   |  |
| standard deviation | ± 4.23 | - |  |

## End points

### End points reporting groups

|   |                                   |
|---|-----------------------------------|
| Reporting group title   | Triptorelin (Decapeptyl®) 22.5 mg |
| Reporting group description:  |                                   |
| Triptorelin (Decapeptyl®): One intramuscular injection of triptorelin (Decapeptyl®) 22.5 mg performed once all baseline procedures and assessments have been completed. |                                   |

### Primary: PCA3 Score Expressed as a Ratio of PCA3 mRNA (Messenger Ribonucleic Acid) Over PSA (Prostate Specific Antigen) mRNA

|                 |  |
|-----------------|--|
| End point title | PCA3 Score Expressed as a Ratio of PCA3 mRNA (Messenger Ribonucleic Acid) Over PSA (Prostate Specific Antigen) mRNA <sup>[1]</sup> |
|-----------------|--|

End point description:

PCA-3 score = (mRNA PCA3/mRNA PSA)×1000

- Non-assessable = Associated PSA mRNA <7500 copies/mL
- ≤BLQ = PCA-3 mRNA is below the concentration of the calibrator and associated PSA mRNA >7500 copies/mL
- <35 = PCA-3 mRNA above BLQ and less than 35
- ≥35 = PCA-3 mRNA greater or equal to 35

Number of participants analyzed were 298 as one participant was admitted to an asylum and was withdrawn before month 1 visit was scheduled. No postbaseline assessment was available for this patient.

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

At month 6 post-treatment

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: No statistical analysis for this endpoint

| End point values                   | Triptorelin (Decapeptyl®) 22.5 mg |  |  |  |
|------------------------------------|-----------------------------------|--|--|--|
| Subject group type                 | Reporting group                   |  |  |  |
| Number of subjects analysed        | 298                               |  |  |  |
| Units: Number of subjects analysed |                                   |  |  |  |
| Non-assessable                     | 232                               |  |  |  |
| ≤BLQ                               | 27                                |  |  |  |
| <35                                | 10                                |  |  |  |
| ≥35                                | 24                                |  |  |  |
| Missing - No sample analysis done  | 5                                 |  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: PCA3 Score Expressed as a Ratio of PCA3 mRNA Over PSA mRNA

|                 |  |
|-----------------|--|
| End point title | PCA3 Score Expressed as a Ratio of PCA3 mRNA Over PSA mRNA |
|-----------------|--|

End point description:

PCA-3 score = (mRNA PCA3/mRNA PSA)x1000

- Non-assessable = Associated PSA mRNA <7500 copies/mL
- ≤BLQ = PCA-3 mRNA is below the concentration of the calibrator and associated PSA mRNA >7500 copies/mL
- <35 = PCA-3 mRNA above BLQ and less than 35
- ≥35 = PCA-3 mRNA greater or equal to 35

Analysis based on number (N) of patients with a valid value. Intention-to-treat (ITT) population.

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

End point timeframe:

At month 1 and 3 post-treatment

| End point values                                    | Triptorelin<br>(Decapeptyl®)<br>22.5 mg |  |  |  |
|---|---|--|--|--|
| Subject group type                                  | Reporting group                         |  |  |  |
| Number of subjects analysed                         | 322                                     |  |  |  |
| Units: Number of Participants                       |   |  |  |  |
| Month 1: Non-assessable (N=322)                     | 109                                     |  |  |  |
| Month 1: ≤BLQ (N=322)                               | 40                                      |  |  |  |
| Month 1: <35 (N=322)                                | 80                                      |  |  |  |
| Month 1: ≥35 (N=322)                                | 91                                      |  |  |  |
| Month 1: Missing-No sample analysis<br>done (N=322) | 2                                       |  |  |  |
| Month 3: Non-assessable (N=313)                     | 215                                     |  |  |  |
| Month 3: ≤BLQ (N=313)                               | 31                                      |  |  |  |
| Month 3: <35 (N=313)                                | 34                                      |  |  |  |
| Month 3: ≥35 (N=313)                                | 31                                      |  |  |  |
| Month 3: Missing-No sample analysis<br>done (N=313) | 2                                       |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: TMPRSS2-ERG Score (Expressed as a Ratio of T2-ERG mRNA Over PSA mRNA)

|                 |   |
|-----------------|---|
| End point title | TMPRSS2-ERG Score (Expressed as a Ratio of T2-ERG mRNA Over PSA mRNA) |
|-----------------|---|

End point description:

TMPRSS2-ERG = (TMPRSS2-ERG mRNA / PSA mRNA) x 100000

A TMPRSS2-ERG score <35 was described as 'negative' and a TMPRSS2-ERG score ≥35 as 'positive.'

Analysis based on number (N) of patients with a valid value. ITT population.

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

End point timeframe:

At baseline, month 1, 3 and 6 post-treatment



| End point values                                    | Triptorelin<br>(Decapeptyl®)<br>22.5 mg |  |  |  |
|---|---|--|--|--|
| Subject group type                                  | Reporting group                         |  |  |  |
| Number of subjects analysed                         | 322                                     |  |  |  |
| Units: Number of subjects                           |   |  |  |  |
| Baseline: Non-assessable (N=322)                    | 33                                      |  |  |  |
| Baseline: <35 negative (N=322)                      | 140                                     |  |  |  |
| Baseline: ≥35 positive (N=322)                      | 149                                     |  |  |  |
| Month 1: Non-assessable (N=322)                     | 117                                     |  |  |  |
| Month 1: <35 negative (N=322)                       | 97                                      |  |  |  |
| Month 1: ≥35 positive (N=322)                       | 106                                     |  |  |  |
| Month 1: Missing-No sample analysis<br>done (N=322) | 2                                       |  |  |  |
| Month 3: Non-assessable (N=313)                     | 213                                     |  |  |  |
| Month 3: <35 negative (N=313)                       | 45                                      |  |  |  |
| Month 3: ≥35 positive (N=313)                       | 53                                      |  |  |  |
| Month 3: Missing-No sample analysis<br>done (N=313) | 2                                       |  |  |  |
| Month 6: Non-assessable (N=298)                     | 241                                     |  |  |  |
| Month 6: <35 negative (N=298)                       | 24                                      |  |  |  |
| Month 6: ≥35 positive (N=298)                       | 27                                      |  |  |  |
| Month 6: Missing-No sample analysis<br>done (N=298) | 6                                       |  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Proportion of Patients Medically Castrated (i.e. With Serum Testosterone Levels of <50 ng/dL)

|  |   |
|--|---|
| End point title  | Proportion of Patients Medically Castrated (i.e. With Serum Testosterone Levels of <50 ng/dL) |
| End point description:   |   |
| Analysis based on number (N) of patients with a valid value. ITT population. |   |
| End point type   | Secondary   |
| End point timeframe:   |   |
| At month 1, 3 and 6 post-treatment   |   |

|                                   |   |  |  |  |
|-----------------------------------|---|--|--|--|
| <b>End point values</b>           | Triptorelin<br>(Decapeptyl®)<br>22.5 mg |  |  |  |
| Subject group type                | Reporting group                         |  |  |  |
| Number of subjects analysed       | 322                                     |  |  |  |
| Units: Percentage of participants |   |  |  |  |
| number (not applicable)           |   |  |  |  |
| Month 1 (N=322)                   | 94.7                                    |  |  |  |
| Month 3 (N=313)                   | 95.2                                    |  |  |  |
| Month 6 (N=298)                   | 90.9                                    |  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: PSA Level

|  |           |
|--|-----------|
| End point title  | PSA Level |
| End point description:   |           |
| Analysis based on number (N) of patients with a valid value. ITT population. |           |
| End point type   | Secondary |
| End point timeframe:   |           |
| At baseline, month 1, 3 and 6 post-treatment                                 |           |

|                               |   |  |  |  |
|-------------------------------|---|--|--|--|
| <b>End point values</b>       | Triptorelin<br>(Decapeptyl®)<br>22.5 mg |  |  |  |
| Subject group type            | Reporting group                         |  |  |  |
| Number of subjects analysed   | 322                                     |  |  |  |
| Units: µg/L                   |   |  |  |  |
| median (full range (min-max)) |   |  |  |  |
| Baseline (N=321)              | 45.4 (1 to 12239)                       |  |  |  |
| Month 1 (N=320)               | 8.3 (0 to 581)                          |  |  |  |
| Month 3 (N=311)               | 1.8 (0 to 969)                          |  |  |  |
| Month 6 (N=296)               | 1.2 (0 to 1251)                         |  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Safety, Assessed Through the Collection of Adverse Events (AEs)

|                        |   |
|------------------------|---|
| End point title        | Safety, Assessed Through the Collection of Adverse Events (AEs) |
| End point description: |   |
| End point type         | Secondary   |

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End point timeframe:

For the duration of the study (up to month 6)

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|  |   |  |  |  |
|--|---|--|--|--|
| <b>End point values</b>                          | Triptorelin<br>(Decapeptyl®)<br>22.5 mg |  |  |  |
| Subject group type                               | Reporting group                         |  |  |  |
| Number of subjects analysed                      | 325                                     |  |  |  |
| Units: Number of subjects                        |   |  |  |  |
| Any Adverse Events (AEs)                         | 193                                     |  |  |  |
| Any Treatment Emergent Adverse<br>Events (TEAEs) | 190                                     |  |  |  |
| TEAEs Leading to Withdrawal                      | 11                                      |  |  |  |
| TEAEs Leading to Death                           | 11                                      |  |  |  |
| Serious Adverse Events (SAEs)                    | 37                                      |  |  |  |

### Statistical analyses

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No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Up to month 6

|                 |            |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 13.1 |
|--------------------|------|

### Reporting groups

|                       |                                   |
|-----------------------|-----------------------------------|
| Reporting group title | Triptorelin (Decapeptyl®) 22.5 mg |
|-----------------------|-----------------------------------|

Reporting group description:

Triptorelin (Decapeptyl®): One intramuscular injection of triptorelin (Decapeptyl®) 22.5 mg performed once all baseline procedures and assessments have been completed.

| Serious adverse events   | Triptorelin<br>(Decapeptyl®) 22.5<br>mg |  |  |
|--|---|--|--|
| Total subjects affected by serious<br>adverse events                   |   |  |  |
| subjects affected / exposed  | 37 / 325 (11.38%)                       |  |  |
| number of deaths (all causes)  | 11                                      |  |  |
| number of deaths resulting from<br>adverse events                      |   |  |  |
| Neoplasms benign, malignant and<br>unspecified (incl cysts and polyps) |   |  |  |
| Bone pain due to metastasis  |   |  |  |
| subjects affected / exposed  | 2 / 325 (0.62%)                         |  |  |
| occurrences causally related to<br>treatment / all                     | 0 / 2                                   |  |  |
| deaths causally related to<br>treatment / all                          | 0 / 0                                   |  |  |
| Rectum tumor   |   |  |  |
| subjects affected / exposed  | 1 / 325 (0.31%)                         |  |  |
| occurrences causally related to<br>treatment / all                     | 0 / 1                                   |  |  |
| deaths causally related to<br>treatment / all                          | 0 / 0                                   |  |  |
| Larynx adenocarcinoma  |   |  |  |
| subjects affected / exposed  | 1 / 325 (0.31%)                         |  |  |
| occurrences causally related to<br>treatment / all                     | 0 / 1                                   |  |  |
| deaths causally related to<br>treatment / all                          | 0 / 0                                   |  |  |
| Cancer progression   |   |  |  |

|  |                 |  |  |
|--|-----------------|--|--|
| subjects affected / exposed                          | 1 / 325 (0.31%) |  |  |
| occurrences causally related to treatment / all      | 0 / 1           |  |  |
| deaths causally related to treatment / all           | 0 / 1           |  |  |
| Urothelial tumor in the bladder                      |                 |  |  |
| subjects affected / exposed                          | 1 / 325 (0.31%) |  |  |
| occurrences causally related to treatment / all      | 0 / 1           |  |  |
| deaths causally related to treatment / all           | 0 / 0           |  |  |
| Right central pulmonary tumor malignant              |                 |  |  |
| subjects affected / exposed                          | 1 / 325 (0.31%) |  |  |
| occurrences causally related to treatment / all      | 0 / 1           |  |  |
| deaths causally related to treatment / all           | 0 / 0           |  |  |
| Vascular disorders                                   |                 |  |  |
| Claudication   |                 |  |  |
| subjects affected / exposed                          | 1 / 325 (0.31%) |  |  |
| occurrences causally related to treatment / all      | 0 / 1           |  |  |
| deaths causally related to treatment / all           | 0 / 0           |  |  |
| General disorders and administration site conditions |                 |  |  |
| Asthenia   |                 |  |  |
| subjects affected / exposed                          | 1 / 325 (0.31%) |  |  |
| occurrences causally related to treatment / all      | 0 / 1           |  |  |
| deaths causally related to treatment / all           | 0 / 0           |  |  |
| Blocked nephrostomy catheter                         |                 |  |  |
| subjects affected / exposed                          | 1 / 325 (0.31%) |  |  |
| occurrences causally related to treatment / all      | 0 / 1           |  |  |
| deaths causally related to treatment / all           | 0 / 0           |  |  |
| Septic venous thrombophlebitis                       |                 |  |  |
| subjects affected / exposed                          | 1 / 325 (0.31%) |  |  |
| occurrences causally related to treatment / all      | 0 / 1           |  |  |
| deaths causally related to treatment / all           | 0 / 0           |  |  |
| Fever  |                 |  |  |
| subjects affected / exposed                          | 1 / 325 (0.31%) |  |  |
| occurrences causally related to treatment / all      | 0 / 1           |  |  |
| deaths causally related to treatment / all           | 0 / 0           |  |  |

|   |                 |  |  |
|---|-----------------|--|--|
| Sudden death                                    |                 |  |  |
| subjects affected / exposed                     | 1 / 325 (0.31%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 1           |  |  |
| Unspecific thoracic pain                        |                 |  |  |
| subjects affected / exposed                     | 1 / 325 (0.31%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Thoracic pain                                   |                 |  |  |
| subjects affected / exposed                     | 1 / 325 (0.31%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Immune system disorders                         |                 |  |  |
| Allergy to conc med                             |                 |  |  |
| subjects affected / exposed                     | 1 / 325 (0.31%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Reproductive system and breast disorders        |                 |  |  |
| Hemorrhage prostate                             |                 |  |  |
| subjects affected / exposed                     | 1 / 325 (0.31%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Respiratory, thoracic and mediastinal disorders |                 |  |  |
| Bilateral pleural effusion                      |                 |  |  |
| subjects affected / exposed                     | 1 / 325 (0.31%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Acute respiratory failure                       |                 |  |  |
| subjects affected / exposed                     | 1 / 325 (0.31%) |  |  |
| occurrences causally related to treatment / all | 0 / 2           |  |  |
| deaths causally related to treatment / all      | 0 / 1           |  |  |
| Right pleurisy                                  |                 |  |  |

|   |                 |  |  |
|---|-----------------|--|--|
| subjects affected / exposed                     | 1 / 325 (0.31%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Chronic obstructive pulmonary disease           |                 |  |  |
| subjects affected / exposed                     | 1 / 325 (0.31%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Psychiatric disorders                           |                 |  |  |
| Depression                                      |                 |  |  |
| subjects affected / exposed                     | 1 / 325 (0.31%) |  |  |
| occurrences causally related to treatment / all | 1 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Suicide   |                 |  |  |
| subjects affected / exposed                     | 1 / 325 (0.31%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 1           |  |  |
| Investigations                                  |                 |  |  |
| Weight gain                                     |                 |  |  |
| subjects affected / exposed                     | 1 / 325 (0.31%) |  |  |
| occurrences causally related to treatment / all | 1 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Injury, poisoning and procedural complications  |                 |  |  |
| Deliberate medication overdose                  |                 |  |  |
| subjects affected / exposed                     | 1 / 325 (0.31%) |  |  |
| occurrences causally related to treatment / all | 1 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Hip fracture                                    |                 |  |  |
| subjects affected / exposed                     | 1 / 325 (0.31%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Fall  |                 |  |  |

|   |                 |  |  |
|---|-----------------|--|--|
| subjects affected / exposed                     | 2 / 325 (0.62%) |  |  |
| occurrences causally related to treatment / all | 0 / 2           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Cardiac disorders                               |                 |  |  |
| Cardio respiratory arrest                       |                 |  |  |
| subjects affected / exposed                     | 1 / 325 (0.31%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 1           |  |  |
| Atrial fibrillation                             |                 |  |  |
| subjects affected / exposed                     | 1 / 325 (0.31%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Myocardial infarction                           |                 |  |  |
| subjects affected / exposed                     | 1 / 325 (0.31%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Heart failure                                   |                 |  |  |
| subjects affected / exposed                     | 3 / 325 (0.92%) |  |  |
| occurrences causally related to treatment / all | 0 / 3           |  |  |
| deaths causally related to treatment / all      | 0 / 3           |  |  |
| Chronic heart failure                           |                 |  |  |
| subjects affected / exposed                     | 1 / 325 (0.31%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 1           |  |  |
| Nervous system disorders                        |                 |  |  |
| Paraplegia                                      |                 |  |  |
| subjects affected / exposed                     | 1 / 325 (0.31%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Spinal cord compression                         |                 |  |  |
| subjects affected / exposed                     | 1 / 325 (0.31%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Blood and lymphatic system disorders            |                 |  |  |



|   |                 |  |  |
|---|-----------------|--|--|
| Severe anemia                                   |                 |  |  |
| subjects affected / exposed                     | 2 / 325 (0.62%) |  |  |
| occurrences causally related to treatment / all | 0 / 2           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Anaemia   |                 |  |  |
| subjects affected / exposed                     | 1 / 325 (0.31%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Gastrointestinal disorders                      |                 |  |  |
| Diarrhoea                                       |                 |  |  |
| subjects affected / exposed                     | 1 / 325 (0.31%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Fecal peritonitis                               |                 |  |  |
| subjects affected / exposed                     | 1 / 325 (0.31%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 1           |  |  |
| Entero-cutaneous fistula                        |                 |  |  |
| subjects affected / exposed                     | 1 / 325 (0.31%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Perforated colon                                |                 |  |  |
| subjects affected / exposed                     | 1 / 325 (0.31%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Perforated gall bladder                         |                 |  |  |
| subjects affected / exposed                     | 1 / 325 (0.31%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Right inguinal hernia                           |                 |  |  |
| subjects affected / exposed                     | 1 / 325 (0.31%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Subileus  |                 |  |  |

|   |                 |  |  |
|---|-----------------|--|--|
| subjects affected / exposed                     | 1 / 325 (0.31%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Hepatobiliary disorders                         |                 |  |  |
| Liver failure                                   |                 |  |  |
| subjects affected / exposed                     | 1 / 325 (0.31%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Renal and urinary disorders                     |                 |  |  |
| Haematuria                                      |                 |  |  |
| subjects affected / exposed                     | 1 / 325 (0.31%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Acute renal failure                             |                 |  |  |
| subjects affected / exposed                     | 1 / 325 (0.31%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| End stage renal failure                         |                 |  |  |
| subjects affected / exposed                     | 1 / 325 (0.31%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Renal failure                                   |                 |  |  |
| subjects affected / exposed                     | 4 / 325 (1.23%) |  |  |
| occurrences causally related to treatment / all | 0 / 4           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Urinary retention                               |                 |  |  |
| subjects affected / exposed                     | 1 / 325 (0.31%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Urethral stricture                              |                 |  |  |
| subjects affected / exposed                     | 1 / 325 (0.31%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Musculoskeletal and connective tissue           |                 |  |  |

|   |                 |  |  |  |
|---|-----------------|--|--|--|
| disorders                                       |                 |  |  |  |
| Increased pain in right thigh                   |                 |  |  |  |
| subjects affected / exposed                     | 1 / 325 (0.31%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| Worsening of chronic lumbago                    |                 |  |  |  |
| subjects affected / exposed                     | 1 / 325 (0.31%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| Infections and infestations                     |                 |  |  |  |
| Chest infection                                 |                 |  |  |  |
| subjects affected / exposed                     | 1 / 325 (0.31%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| Appendicitis acute                              |                 |  |  |  |
| subjects affected / exposed                     | 1 / 325 (0.31%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| Bronchitis                                      |                 |  |  |  |
| subjects affected / exposed                     | 1 / 325 (0.31%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| Acute pneumonia                                 |                 |  |  |  |
| subjects affected / exposed                     | 2 / 325 (0.62%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 2           |  |  |  |
| deaths causally related to treatment / all      | 0 / 2           |  |  |  |
| Pneumonia pneumocystis                          |                 |  |  |  |
| subjects affected / exposed                     | 1 / 325 (0.31%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| Septicaemia                                     |                 |  |  |  |
| subjects affected / exposed                     | 1 / 325 (0.31%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |

|   |                 |  |  |
|---|-----------------|--|--|
| Urosepsis                                       |                 |  |  |
| subjects affected / exposed                     | 1 / 325 (0.31%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Septicemia due to catheter                      |                 |  |  |
| subjects affected / exposed                     | 1 / 325 (0.31%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Metabolism and nutrition disorders              |                 |  |  |
| Hypocalcemia                                    |                 |  |  |
| subjects affected / exposed                     | 1 / 325 (0.31%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |

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

|   |   |  |  |
|---|---|--|--|
| <b>Non-serious adverse events</b>                     | Triptorelin<br>(Decapeptyl®) 22.5<br>mg |  |  |
| Total subjects affected by non-serious adverse events |   |  |  |
| subjects affected / exposed                           | 89 / 325 (27.38%)                       |  |  |
| Vascular disorders                                    |   |  |  |
| Hot flush   |   |  |  |
| subjects affected / exposed                           | 89 / 325 (27.38%)                       |  |  |
| occurrences (all)                                     | 89                                      |  |  |

## **More information**

### **Substantial protocol amendments (globally)**

Were there any global substantial amendments to the protocol? No

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### **Interruptions (globally)**

Were there any global interruptions to the trial? No

### **Limitations and caveats**

None reported