



Clinical trial results:

An Open-Label, Single-Arm Study of the Safety, Efficacy, and Pharmacokinetic Behavior of Leuprolide Mesylate for Injectable Suspension (LMIS 50 mg) in Subjects with Advanced Prostate Carcinoma

Summary

| | |
|--------------------------|-------------------|
| EudraCT number | 2013-001790-25 |
| Trial protocol | AT DE CZ SK LT PL |
| Global end of trial date | 02 September 2016 |

Results information

| | |
|--------------------------------|---|
| Result version number | v2 (current) |
| This version publication date | 22 April 2020 |
| First version publication date | 27 October 2018 |
| Version creation reason | <ul style="list-style-type: none">• Correction of full data set Version 2 contains the same data as version 1. Version 2 was created in order to correct IT issues. |

Trial information

Trial identification

| | |
|-----------------------|--------------|
| Sponsor protocol code | FP01C-13-001 |
|-----------------------|--------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02234115 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | Foresee Pharmaceuticals Co., Ltd |
| Sponsor organisation address | 3F., No. 19-3, Sanchong Rd., Nangang Dist., Taipei City, Taiwan, 115 |
| Public contact | Clinical Trials Information, QPS Austria, 0043 316258111, |
| Scientific contact | Clinical Trials Information, QPS Austria, 0043 316258111, |

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 | 13 February 2018 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 30 August 2016 |
| Global end of trial reached? | Yes |
| Global end of trial date | 02 September 2016 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

Primary objectives:

1. Determine the safety and tolerability of LMIS 50 mg for up to 1 year of exposure following 2 subcutaneous doses given at 6 months apart in subjects with advanced prostate carcinoma;
2. Establish the efficacy of LMIS 50 mg for up to 1 year following 2 subcutaneous doses given at 6 months apart in subjects with advanced prostate carcinoma, as determined by the magnitude and duration of suppression of serum testosterone levels; and
3. Evaluate the pharmacokinetic behavior of serum leuprolide following 2 subcutaneous injections of LMIS 50 mg given 6 months apart.

Protection of trial subjects:

This study was conducted in accordance with International Conference on Harmonization (ICH) Good Clinical Practice, and the principles of the Declaration of Helsinki, in addition to following the laws and regulations of the countries in which a study is conducted.

Background therapy: -

Evidence for comparator: -

| | |
|---|--------------|
| Actual start date of recruitment | 01 July 2014 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|--------------------|
| Country: Number of subjects enrolled | Poland: 5 |
| Country: Number of subjects enrolled | Slovakia: 18 |
| Country: Number of subjects enrolled | Austria: 1 |
| Country: Number of subjects enrolled | Czech Republic: 17 |
| Country: Number of subjects enrolled | Germany: 1 |
| Country: Number of subjects enrolled | Lithuania: 29 |
| Country: Number of subjects enrolled | United States: 64 |
| Country: Number of subjects enrolled | Taiwan: 2 |
| Worldwide total number of subjects | 137 |
| EEA total number of subjects | 71 |

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) | 45 |
| From 65 to 84 years | 82 |
| 85 years and over | 10 |

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Male adult subjects with histologically confirmed prostate carcinoma were screened based on baseline morning serum testosterone level , ECOG performance, lab chemistry results for lipid profile, serum glucose, HgbA1c, clinical chemistries (K, Na, Mg, Ca and P), and urinalysis range.

Period 1

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

Arms

| | |
|--|------------------|
| Arm title | LMIS 50 mg |
| Arm description: - | |
| Arm type | Experimental |
| Investigational medicinal product name | LMIS 50 mg |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

LMIS 50 mg was given SC once every 24 weeks for up to 1 years.

| Number of subjects in period 1 | LMIS 50 mg |
|--------------------------------|------------|
| Started | 137 |
| Completed | 122 |
| Not completed | 15 |
| Adverse event, serious fatal | 3 |
| Consent withdrawn by subject | 3 |
| Disease progression | 1 |
| Adverse event, non-fatal | 2 |
| Lost to follow-up | 1 |
| Lack of efficacy | 1 |
| Protocol deviation | 4 |

Baseline characteristics

Reporting groups

| Reporting group title | Overall trial |
|--------------------------------|---------------|
| Reporting group description: - | |

| Reporting group values | Overall trial | Total | |
|---|---------------|-------|--|
| Number of subjects | 137 | 137 | |
| Age categorical | | | |
| Units: Subjects | | | |
| Adults (18-64 years) | 45 | 45 | |
| From 65-84 years | 82 | 82 | |
| 85 years and over | 10 | 10 | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 0 | 0 | |
| Male | 137 | 137 | |
| Ethnicity | | | |
| Units: Subjects | | | |
| Hispanic or Latino | 3 | 3 | |
| Not Hispanic or Latino | 61 | 61 | |
| Unknown or Not Reported | 73 | 73 | |
| Race | | | |
| Units: Subjects | | | |
| American Indian or Alaska Native | 0 | 0 | |
| Asian | 5 | 5 | |
| Native Hawaiian or Other Pacific Islander | 0 | 0 | |
| Black or African American | 8 | 8 | |
| White | 123 | 123 | |
| More than one race | 0 | 0 | |
| Unknown or Not Reported | 1 | 1 | |
| Region of Enrollment | | | |
| Units: Subjects | | | |
| Austria | 1 | 1 | |
| United States | 64 | 64 | |
| Czech Republic | 17 | 17 | |
| Taiwan | 2 | 2 | |
| Poland | 5 | 5 | |
| Slovakia | 18 | 18 | |
| Lithuania | 29 | 29 | |
| Germany | 1 | 1 | |

End points

End points reporting groups

| | |
|--|--------------------|
| Reporting group title | LMIS 50 mg |
| Reporting group description: - | |
| Subject analysis set title | Full analysis |
| Subject analysis set type | Intention-to-treat |
| Subject analysis set description: | |
| Any subject who received at least one dose of LMIS 50 mg was included in the analysis. | |

Primary: Proportion of subjects with a serum testosterone concentration suppressed to castrate levels from Day 28 through Day 336

| | |
|-----------------|---|
| End point title | Proportion of subjects with a serum testosterone concentration suppressed to castrate levels from Day 28 through Day 336 ^[1] |
|-----------------|---|

End point description:

The percentage of subjects with a serum testosterone concentration suppressed to castrate levels (≤ 50 ng/dL) following the first injection of LMIS 50 mg from Day 28 through Day 336 (remaining duration of the study).

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

End point timeframe:

Baseline to 28 days, 28 days to 336 days

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: Descriptive statistics are sufficient for this single-arm study.

| | | | | |
|---|---------------------|--|--|--|
| End point values | LMIS 50 mg | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 137 | | | |
| Units: Percentage | | | | |
| arithmetic mean (confidence interval 95%) | 97.0 (92.2 to 98.9) | | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

336 days

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 19.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|--------------|
| Reporting group title | All subjects |
|-----------------------|--------------|

Reporting group description: -

| Serious adverse events | All subjects | | |
|---|-------------------|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 20 / 137 (14.60%) | | |
| number of deaths (all causes) | 3 | | |
| number of deaths resulting from adverse events | | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Colon adenoma | | | |
| subjects affected / exposed | 1 / 137 (0.73%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Colon cancer | | | |
| subjects affected / exposed | 1 / 137 (0.73%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Prostate cancer metastatic | | | |
| subjects affected / exposed | 1 / 137 (0.73%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| Vascular disorders | | | |
| Intermittent claudication | | | |
| subjects affected / exposed | 1 / 137 (0.73%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | |
|--|-----------------|--|--|
| Peripheral artery occlusion | | | |
| subjects affected / exposed | 1 / 137 (0.73%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 1 / 137 (0.73%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Death | | | |
| subjects affected / exposed | 1 / 137 (0.73%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| Non-cardiac chest pain | | | |
| subjects affected / exposed | 1 / 137 (0.73%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Acute respiratory failure | | | |
| subjects affected / exposed | 1 / 137 (0.73%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Asthma | | | |
| subjects affected / exposed | 1 / 137 (0.73%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Chronic obstructive pulmonary disease | | | |
| subjects affected / exposed | 1 / 137 (0.73%) | | |
| occurrences causally related to treatment / all | 0 / 3 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pneumothorax spontaneous | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 1 / 137 (0.73%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Injury, poisoning and procedural complications | | | |
| Hip fracture | | | |
| subjects affected / exposed | 1 / 137 (0.73%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Joint dislocation | | | |
| subjects affected / exposed | 1 / 137 (0.73%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Subdural haematoma | | | |
| subjects affected / exposed | 2 / 137 (1.46%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cardiac disorders | | | |
| Angina pectoris | | | |
| subjects affected / exposed | 1 / 137 (0.73%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Atrial fibrillation | | | |
| subjects affected / exposed | 1 / 137 (0.73%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Myocardial infarction | | | |
| subjects affected / exposed | 1 / 137 (0.73%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Nervous system disorders | | | |
| Cerebrovascular accident | | | |
| subjects affected / exposed | 1 / 137 (0.73%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 1 | | |

| | | | |
|---|-----------------|--|--|
| Metabolic encephalopathy | | | |
| subjects affected / exposed | 1 / 137 (0.73%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Ear and labyrinth disorders | | | |
| Vertigo | | | |
| subjects affected / exposed | 1 / 137 (0.73%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Eye disorders | | | |
| Vision blurred | | | |
| subjects affected / exposed | 1 / 137 (0.73%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrointestinal disorders | | | |
| Dysphagia | | | |
| subjects affected / exposed | 1 / 137 (0.73%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Skin and subcutaneous tissue disorders | | | |
| Diabetic foot | | | |
| subjects affected / exposed | 1 / 137 (0.73%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Musculoskeletal and connective tissue disorders | | | |
| Osteoarthritis | | | |
| subjects affected / exposed | 1 / 137 (0.73%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infections and infestations | | | |
| Bronchitis bacterial | | | |
| subjects affected / exposed | 1 / 137 (0.73%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Clostridium difficile colitis | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 1 / 137 (0.73%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pneumonia | | | |
| subjects affected / exposed | 1 / 137 (0.73%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Metabolism and nutrition disorders | | | |
| Dehydration | | | |
| subjects affected / exposed | 1 / 137 (0.73%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

Frequency threshold for reporting non-serious adverse events: 0.05 %

| Non-serious adverse events | All subjects | | |
|---|--------------------|--|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 114 / 137 (83.21%) | | |
| Vascular disorders | | | |
| Hot flush | | | |
| subjects affected / exposed | 67 / 137 (48.91%) | | |
| occurrences (all) | 69 | | |
| Hypertension | | | |
| subjects affected / exposed | 20 / 137 (14.60%) | | |
| occurrences (all) | 23 | | |
| General disorders and administration site conditions | | | |
| Fatigue | | | |
| subjects affected / exposed | 9 / 137 (6.57%) | | |
| occurrences (all) | 10 | | |
| Injection site pain | | | |
| subjects affected / exposed | 10 / 137 (7.30%) | | |
| occurrences (all) | 13 | | |
| Renal and urinary disorders | | | |
| Nocturia | | | |

| | | | |
|---|------------------------|--|--|
| subjects affected / exposed occurrences (all) | 8 / 137 (5.84%) 9 | | |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia subjects affected / exposed occurrences (all) | 9 / 137 (6.57%) 12 | | |
| Back pain subjects affected / exposed occurrences (all) | 7 / 137 (5.11%) 7 | | |
| Pain in extremity subjects affected / exposed occurrences (all) | 13 / 137 (9.49%) 18 | | |
| Infections and infestations | | | |
| Nasopharyngitis subjects affected / exposed occurrences (all) | 7 / 137 (5.11%) 9 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported