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	• 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

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