Clinical trial results:
An Open-Label, Single-Arm Study of The Efficacy, Safety, and Pharmacokinetic Behavior of Leuprolide Mesylate Injectable Suspension (LMIS 25 mg) in Subjects with Prostate Cancer

Summary

EudraCT number	2017-001333-88
Trial protocol	LT SK CZ
Global end of trial date	02 September 2019

Results information

Result version number	v1 (current)
This version publication date	17 March 2021
First version publication date	17 March 2021

Trial information

Trial identification

Sponsor protocol code	FP01C-17-001

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03261999
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Foresee Pharmaceuticals, Co., Ltd.
Sponsor organisation address	9F-2, No. 19-3, Sanchong Rd., Nangang Dist., Taipei, Taiwan,
Public contact	Yen-Ling Lin, Ph.D., Foresee Pharmaceuticals, Co., Ltd., yenling.lin@foreseepharma.com
Scientific contact	Yisheng Lee, Ph.D., Foresee Pharmaceuticals, Co., Ltd., yisheng.lee@foreseepharma.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	02 September 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	02 September 2019
Global end of trial reached?	Yes
Global end of trial date	02 September 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the efficacy and safety of LMIS 25 mg for up to 24 weeks following 2 subcutaneous doses given 12 weeks apart in subjects with prostate cancer.

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	26 September 2017
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	Korea, Republic of: 16
Country: Number of subjects enrolled	United States: 8
Country: Number of subjects enrolled	Slovakia: 34
Country: Number of subjects enrolled	Czech Republic: 9
Country: Number of subjects enrolled	Lithuania: 77
Worldwide total number of subjects	144
EEA total number of subjects	120

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)	37

From 65 to 84 years	103
85 years and over	4

Subject disposition

Recruitment

Recruitment details:

EEA area: 120 subjects (September 2017 to May 2018), Republic of Korea: 16 subjects (January 2018 to May 2018), United States: 8 subjects (November 2017 to April 2018)

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 25mg

Arm description:

Any subject who received at least one dose of LMIS 25 mg (Intention-To-Treat population N = 144). Thereof, subjects with a serum testosterone concentration suppressed to castrate levels (≤ 50 ng/dL) Day 28 (V9): n = 143

Arm type	Experimental
Investigational medicinal product name	LEUPROLIDE MESYLATE INJECTABLE SUSPENSION 25 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Two separate doses of LMIS 25 mg with approx. 12-week apart

Number of subjects in period 1	LMIS 25mg
Started	144
Completed	129
Not completed	15
Consent withdrawn by subject	7
Adverse event, non-fatal	1
sponsor's decision	5
Protocol deviation	2

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial (overall period)

Reporting group description: -

Reporting group values	Overall trial (overall period)	Total	
Number of subjects	144	144	
Age categorical Units: Subjects			
Adults (18-64 years)	37	37	
From 65-84 years	103	103	
85 years and over	4	4	
Age continuous Units: years			
arithmetic mean	69.8		
standard deviation	± 7.93	-	
Gender categorical Units: Subjects			
Female	0	0	
Male	144	144	

End points

End points reporting groups

Reporting group title	LMIS 25mg

Reporting group description:

Any subject who received at least one dose of LMIS 25 mg (Intention-To-Treat population N = 144). Thereof, subjects with a serum testosterone concentration suppressed to castrate levels (≤ 50 ng/dL) Day 28 (V9): n = 143

Primary: Proportion of subjects with serum testosterone concentration suppressed to castrate levels from Day 28 through Day 168

End point title	Proportion of subjects with serum testosterone concentration suppressed to castrate levels from Day 28 through Day 168[1]

End point description:

The primary endpoint of efficacy was to determine the percentage of subjects with a serum testosterone concentration suppressed to castrate levels (≤ 50 ng/dL) on Day 28 ± 1 day (week 4) following the first injection of LMIS 25 mg, and the proportion of subjects with serum testosterone suppression (≤ 50 ng/dL) from Day 28 ± 1 day (week 4) through Day 168 ± 5 days (week 24) until the end of the study. Note: Descriptive statistics are sufficient for this single-arm study, therefore no statistical analyses for this endpoint specified.

End point type	Primary

End point timeframe:

Baseline to 28 days (week 4), 28 days to 168 days (week 24)

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: This clinical study was open-label by design, therefore no comparison with a control group has been made.

End point values	LMIS 25mg			
Subject group type	Reporting group			
Number of subjects analysed	143			
Units: percent				
arithmetic mean (confidence interval 95%)	97.9 (93.5 to 99.3)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

168 days per subject; Screening till End of Study Visit (Follow up for drop outs 12 weeks after last injection)

Adverse event reporting additional description:

Subjects who were withdrawn due to AEs or SAEs have been be followed until these events were resolved or until the event was considered stable.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	21.1

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	9 / 144 (6.25%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 144 (0.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Oropharyngeal neoplasm			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 144 (0.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Tendon rupture			
alternative assessment type: Systematic			

subjects affected / exposed	1 / 144 (0.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Acute myocardial infarction			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 144 (0.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Surgical and medical procedures			
Rehabilitation therapy			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 144 (0.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Cerebrovascular accident			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 144 (0.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Sciatica			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 144 (0.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Pancreatitis acute			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 144 (0.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Drug-induced liver injury			
alternative assessment type:			

Systematic			
subjects affected / exposed	1 / 144 (0.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Urethral stenosis			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 144 (0.69%)		
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 %

Non-serious adverse events	All subjects		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	90 / 144 (62.50%)		
Investigations			
Weight increased			
alternative assessment type: Systematic			
subjects affected / exposed	11 / 144 (7.64%)		
occurrences (all)	11		
Electrocardiogram QT prolonged			
subjects affected / exposed	1 / 144 (0.69%)		
occurrences (all)	1		
Alanine aminotransferase increased			
subjects affected / exposed	1 / 144 (0.69%)		
occurrences (all)	1		
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 144 (0.69%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			
Post procedural complication			
subjects affected / exposed	2 / 144 (1.39%)		
occurrences (all)	3		
Vascular disorders			

Hot flush			
alternative assessment type: Systematic			
subjects affected / exposed	35 / 144 (24.31%)		
occurrences (all)	35		
Hypertension			
alternative assessment type: Systematic			
subjects affected / exposed	16 / 144 (11.11%)		
occurrences (all)	18		
General disorders and administration site conditions			
Injection site haemorrhage			
alternative assessment type: Systematic			
subjects affected / exposed	8 / 144 (5.56%)		
occurrences (all)	9		
Injection site erythema			
subjects affected / exposed	2 / 144 (1.39%)		
occurrences (all)	2		
Injection site nodule			
subjects affected / exposed	2 / 144 (1.39%)		
occurrences (all)	3		
Asthenia			
subjects affected / exposed	1 / 144 (0.69%)		
occurrences (all)	1		
Injection site induration			
subjects affected / exposed	1 / 144 (0.69%)		
occurrences (all)	1		
Injection site pain			
subjects affected / exposed	1 / 144 (0.69%)		
occurrences (all)	1		
Injection site reaction			
subjects affected / exposed	1 / 144 (0.69%)		
occurrences (all)	1		
Localised oedema			
subjects affected / exposed	1 / 144 (0.69%)		
occurrences (all)	1		
Infections and infestations			

Nasopharyngitis subjects affected / exposed occurrences (all)	6 / 144 (4.17%) 6		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
02 January 2018	The protocol was revised because of administrative changes, changes for one of the exclusion criteria*, and correction for typos. *Patients previously enrolled in the LMIS 50 mg study were not excluded in version 1.0. Thus, this criterion was added in version 1.1 as in Exclusion criteria (6) to avoid potential patient selection bias and for clarification.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Site CZ03 was found with significant GCP violation during the study conduct; thus, the sensitivity analysis for the primary efficacy endpoint excluding subjects from CZ03 was performed.

Notes: