Clinical trial results:
Interventional, open-label, flexible-dose, long-term safety study of Lu AF35700 in adult patients with schizophrenia

Summary

EudraCT number	2015-003284-11
Trial protocol	ES CZ SK EE FI BG PL
Global end of trial date	10 October 2019

Results information

Result version number	v1 (current)
This version publication date	16 October 2020
First version publication date	16 October 2020

Trial information

Trial identification

Sponsor protocol code	16159B Debut

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02892422
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	H. Lundbeck A/S
Sponsor organisation address	Ottiliavej 9, Valby, Denmark, 2500
Public contact	LundbeckClinicalTrials@lundbeck.com, H. Lundbeck A/S, 45 36301311, LundbeckClinicalTrials@lundbeck.com
Scientific contact	LundbeckClinicalTrials@lundbeck.com, H. Lundbeck A/S, 45 36301311, LundbeckClinicalTrials@lundbeck.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	10 October 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	10 October 2019
Global end of trial reached?	Yes
Global end of trial date	10 October 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the safety and tolerability of the long-term treatment with Lu AF35700

Protection of trial subjects:

The trial was conducted in accordance with the Declaration of Helsinki (2013) and ICH Good Clinical Practice (1996)

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 July 2016
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	United States: 98
Country: Number of subjects enrolled	Ukraine: 48
Country: Number of subjects enrolled	Canada: 3
Country: Number of subjects enrolled	Mexico: 57
Country: Number of subjects enrolled	Poland: 19
Country: Number of subjects enrolled	Slovakia: 8
Country: Number of subjects enrolled	Spain: 3
Country: Number of subjects enrolled	Bulgaria: 107
Country: Number of subjects enrolled	Czech Republic: 11
Country: Number of subjects enrolled	Estonia: 16
Country: Number of subjects enrolled	Russian Federation: 112
Country: Number of subjects enrolled	Serbia: 43
Country: Number of subjects enrolled	Romania: 3
Worldwide total number of subjects	528
EEA total number of subjects	167

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)	513
From 65 to 84 years	15
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Subjects who met each of the inclusion and none of the exclusion criteria were eligible to participate in the study.

Period 1

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

Arms

Arm title	Lu AF35700 Flexible dose

Arm description:

Lu AF35700: flexible dose of Lu AF35700, 10 or 20 mg/day, tablets, orally

Arm type	Experimental
Investigational medicinal product name	Lu AF35700
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Lu AF35700 - 10, 20 or 70 mg/day, tablets, orally, once daily

Number of subjects in period 1	Lu AF35700 Flexible dose
Started	528
Completed	318
Not completed	210
Physician decision	1
Withdrawal of consent	13
Patient legally incapable	1
Consent withdrawn by subject	56
Patient decision	7
Adverse event, non-fatal	38
Sponsor information 16159A results	21
Moving elsewhere	4
Exclusion crietria met	3
Non-compliance	10
Non-compliance with study drug	11

Lost to follow-up	5
Enrolled but not treated	4
Lack of efficacy	32
Protocol deviation	4

Baseline characteristics

Reporting groups	
Reporting group title	Overall study

Reporting group description: -

Reporting group values	Overall study	Total	
Number of subjects	528	528	
Age categorical Units: Subjects			
Adults (18-64 years)	513	513	
From 65-84 years	15	15	
Age continuous Units: years			
geometric mean	41.3		
standard deviation	± 11.67	-	
Gender categorical Units: Subjects			
Female	220	220	
Male	308	308	

End points

End points reporting groups

Reporting group title	Lu AF35700 Flexible dose

Reporting group description:

Lu AF35700: flexible dose of Lu AF35700, 10 or 20 mg/day, tablets, orally

Primary: Number of participants with Treatment-Emergent Adverse Events

End point title	Number of participants with Treatment-Emergent Adverse Events[1]

End point description:

Based on the safety assessments (e.g. clinical safety laboratory tests, vital signs, weight, waist circumference and ECG)

End point type	Primary

End point timeframe:

From dosing to end of study (57 weeks)

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: Only descriptive statistics

End point values	Lu AF35700 Flexible dose			
Subject group type	Reporting group			
Number of subjects analysed	524			
Units: participants	289			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: 58 weeks	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	22.0

Reporting groups	
Reporting group title	AF35700 flex-dose

Reporting group description: -

Serious adverse events	AF35700 flex-dose		
Total subjects affected by serious adverse events			
subjects affected / exposed	28 / 524 (5.34%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Injury, poisoning and procedural complications			
Hip fracture			
subjects affected / exposed	1 / 524 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Intentional overdose			
subjects affected / exposed	2 / 524 (0.38%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	1 / 524 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Coma			
subjects affected / exposed	1 / 524 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Parkinsonism				
subjects affected / exposed	1 / 524 (0.19%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Pulmonary embolism				
subjects affected / exposed	1 / 524 (0.19%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Psychiatric disorders				
Acute psychosis				
subjects affected / exposed	1 / 524 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Alcohol withdrawal syndrome				
subjects affected / exposed	1 / 524 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Disinhibition				
subjects affected / exposed	1 / 524 (0.19%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Hallucination, auditory				
subjects affected / exposed	1 / 524 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Insomnia				
subjects affected / exposed	1 / 524 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Psychotic disorder				
subjects affected / exposed	3 / 524 (0.57%)			
occurrences causally related to treatment / all	3 / 3			
deaths causally related to treatment / all	0 / 0			

Schizophrenia			
subjects affected / exposed	16 / 524 (3.05%)		
occurrences causally related to treatment / all	10 / 19		
deaths causally related to treatment / all	0 / 0		
Suicide attempt			
subjects affected / exposed	2 / 524 (0.38%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	AF35700 flex-dose		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	43 / 524 (8.21%)		
Nervous system disorders			
Headache			
subjects affected / exposed	43 / 524 (8.21%)		
occurrences (all)	49		

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