



## Clinical trial results:

### A Randomized, Double-blind, Placebo-controlled, Parallel Group, Comparative, Multicenter, Phase 2 Clinical Study to Evaluate Efficacy and Safety of Two Doses of LND101001 Monotherapy in Patients with Mild to Moderate Alzheimer's Disease.

#### Summary

EudraCT number	2013-001851-11
Trial protocol	GB CZ LT PL IT ES HR
Global end of trial date	29 August 2016

#### Results information

Result version number	v1 (current)
This version publication date	13 September 2017
First version publication date	13 September 2017

#### Trial information

##### Trial identification

Sponsor protocol code	LRP/LND101001/2013/001
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##### Additional study identifiers

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

Notes:

#### Sponsors

Sponsor organisation name	Lupin Limited
Sponsor organisation address	Survey no. 46A/47A, Nande Village, Mulshi, Pune, India,
Public contact	Dr. Neelam Kardekar, Lupin Limited, neelamkardekar@lupin.com
Scientific contact	Dr. Narendra Maharaj, Lupin Limited, narendramaharaj@lupin.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	29 August 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	29 August 2016
Global end of trial reached?	Yes
Global end of trial date	29 August 2016
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

To evaluate the efficacy of two different doses of LND101001 in improving cognitive function in patients with dementia of the Alzheimer's type in comparison with placebo, using the Alzheimer's Disease Assessment Scale - Cognitive Subscale - 13 (ADAS Cog-13) total score.

Protection of trial subjects:

The Guidelines of the World Medical Association Declaration of Helsinki in its revised edition (64th World Medical Association General Assembly, Fortaleza, Brazil, October 2013), the Guidelines of International Conference of Harmonization (ICH) Good

Clinical Practice (GCP) (Committee for Proprietary Medicinal Products [CPMP]/ICH/135/95), and the demands of national drug and data protection laws and other applicable regulatory requirements were strictly followed during this study.

Each patient had an identified, reliable caregiver who was willing to provide support, ensure compliance, correct storage, preparation and administration of the study medication and ready to accompany the patient to study visits whenever required, as well as to provide information about patient's physical and behavioral symptoms and changes.

Concomitant medication/treatment, which was considered necessary for the patient's safety and well-being, could be given at the discretion of the Investigator

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	09 June 2015
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	Poland: 40
Country: Number of subjects enrolled	Spain: 28
Country: Number of subjects enrolled	United Kingdom: 10
Country: Number of subjects enrolled	Croatia: 20
Country: Number of subjects enrolled	Czech Republic: 57
Country: Number of subjects enrolled	Romania: 22
Worldwide total number of subjects	177
EEA total number of subjects	177

Notes:

<b>Subjects enrolled per age group</b>	
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)	19
From 65 to 84 years	155
85 years and over	3

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

Of the 247 patients who were screened for the study, 69 patients failed screening and 177 patients, who met the eligibility criteria were randomized and received at least one dose of investigational product.

### Period 1

Period 1 title	Overall Trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Carer, Assessor

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	LND101001 5 mg

Arm description: -

Arm type	Experimental
Investigational medicinal product name	LND101001
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, soft
Routes of administration	Oral use

Dosage and administration details:

Administered once a day everyday for 90 days

<b>Arm title</b>	LND101001 25 mg
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Arm description: -

Arm type	Experimental
Investigational medicinal product name	LND101001
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, soft
Routes of administration	Oral use

Dosage and administration details:

Administered once a day everyday for 90 days

<b>Arm title</b>	Placebo
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Arm description: -

Arm type	Placebo
Investigational medicinal product name	Placebo of LND101001
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, soft
Routes of administration	Oral use

Dosage and administration details:

Administered once a day everyday for 90 Days

<b>Number of subjects in period 1</b>	LND101001 5 mg	LND101001 25 mg	Placebo
Started	56	60	61
Completed	50	55	56
Not completed	6	5	5
Adverse event, serious fatal	1	-	-
Consent withdrawn by subject	3	3	1
Adverse event, non-fatal	2	2	3
Lost to follow-up	-	-	1

## Baseline characteristics

### Reporting groups

Reporting group title	LND101001 5 mg
Reporting group description: -	
Reporting group title	LND101001 25 mg
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Reporting group values	LND101001 5 mg	LND101001 25 mg	Placebo
Number of subjects	56	60	61
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	6	4	9
From 65-84 years	49	55	51
85 years and over	1	1	1
Age continuous			
Units: years			
arithmetic mean	73.3	73.7	72.5
standard deviation	± 7.87	± 6.21	± 7.81
Gender categorical			
Units: Subjects			
Female	43	35	41
Male	13	25	20

Reporting group values	Total		
Number of subjects	177		
Age categorical			
Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	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)	19		
From 65-84 years	155		
85 years and over	3		

Age continuous Units: years arithmetic mean standard deviation	-		
Gender categorical Units: Subjects			
Female	119		
Male	58		

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### Subject analysis sets

Subject analysis set title	Safety Population
Subject analysis set type	Safety analysis

Subject analysis set description:

The Safety population will include all patients who have received at least one dose of study medication.

Subject analysis set title	Per Protocol
Subject analysis set type	Per protocol

Subject analysis set description:

The Per Protocol (PP) population will include all patients who satisfactorily complete the study and fully comply with the requirements of the protocol.

Reporting group values	Safety Population	Per Protocol	
Number of subjects	177	158	
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous Units: years arithmetic mean standard deviation	73.2 ± 7.31	±	
Gender categorical Units: Subjects			
Female	119		
Male	58		

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## End points

### End points reporting groups

Reporting group title	LND101001 5 mg
Reporting group description: -	
Reporting group title	LND101001 25 mg
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	
Subject analysis set title	Safety Population
Subject analysis set type	Safety analysis
Subject analysis set description:	
The Safety population will include all patients who have received at least one dose of study medication.	
Subject analysis set title	Per Protocol
Subject analysis set type	Per protocol
Subject analysis set description:	
The Per Protocol (PP) population will include all patients who satisfactorily complete the study and fully comply with the requirements of the protocol.	

### Primary: Change from Baseline in ADAS-Cog-13 Total Score

End point title	Change from Baseline in ADAS-Cog-13 Total Score
End point description:	
End point type	Primary
End point timeframe:	
Mean change from baseline in the ADAS-Cog-13 total score at 90 days.	

End point values	LND101001 5 mg	LND101001 25 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	50	52	56	
Units: No unit				
arithmetic mean (standard deviation)	-0.2 (± 5.71)	-0.4 (± 4.96)	-1.7 (± 5.87)	

### Statistical analyses

Statistical analysis title	Primary Analysis: LND101001 5mg Vs Placebo
Comparison groups	LND101001 5 mg v Placebo
Number of subjects included in analysis	106
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.103
Method	ANCOVA



<b>Statistical analysis title</b>	Primary Analysis: LND101001 25mg Vs Placebo
Comparison groups	LND101001 25 mg v Placebo
Number of subjects included in analysis	108
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.143
Method	ANCOVA

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

The period of observation of AEs was from the time when the informed consent form was signed until 30 days after last administration of study medication i.e. Day 90

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	18.0
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### Reporting groups

Reporting group title	LND101001 5mg
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Reporting group description: -

Reporting group title	LND101001 25 mg
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Reporting group description: -

Reporting group title	Placebo
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Reporting group description: -

Serious adverse events	LND101001 5mg	LND101001 25 mg	Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 56 (5.36%)	1 / 60 (1.67%)	1 / 61 (1.64%)
number of deaths (all causes)	1	0	0
number of deaths resulting from adverse events		0	0
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 56 (1.79%)	0 / 60 (0.00%)	0 / 61 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	1 / 56 (1.79%)	0 / 60 (0.00%)	0 / 61 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			
subjects affected / exposed	0 / 56 (0.00%)	1 / 60 (1.67%)	0 / 61 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ventricular septal defect			

subjects affected / exposed	1 / 56 (1.79%)	0 / 60 (0.00%)	0 / 61 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Cerebral haemorrhage			
subjects affected / exposed	1 / 56 (1.79%)	0 / 60 (0.00%)	0 / 61 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Gastrointestinal disorders			
Dysphagia			
subjects affected / exposed	1 / 56 (1.79%)	0 / 60 (0.00%)	0 / 61 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Knee deformity			
subjects affected / exposed	0 / 56 (0.00%)	0 / 60 (0.00%)	1 / 61 (1.64%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 2 %

<b>Non-serious adverse events</b>	LND101001 5mg	LND101001 25 mg	Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	21 / 56 (37.50%)	20 / 60 (33.33%)	20 / 61 (32.79%)
Investigations			
Blood cholesterol increased			
subjects affected / exposed	2 / 56 (3.57%)	0 / 60 (0.00%)	0 / 61 (0.00%)
occurrences (all)	2	0	0
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 56 (0.00%)	0 / 60 (0.00%)	2 / 61 (3.28%)
occurrences (all)	0	0	2
Vascular disorders			
Hypertension			

subjects affected / exposed occurrences (all)	3 / 56 (5.36%) 4	2 / 60 (3.33%) 2	0 / 61 (0.00%) 0
Cardiac disorders Bradycardia subjects affected / exposed occurrences (all)	0 / 56 (0.00%) 0	2 / 60 (3.33%) 2	0 / 61 (0.00%) 0
Nervous system disorders Headache subjects affected / exposed occurrences (all)  Dizziness subjects affected / exposed occurrences (all)	2 / 56 (3.57%) 2  0 / 56 (0.00%) 0	2 / 60 (3.33%) 3  2 / 60 (3.33%) 2	1 / 61 (1.64%) 1  2 / 61 (3.28%) 4
Gastrointestinal disorders Nausea subjects affected / exposed occurrences (all)  Diarrhoea subjects affected / exposed occurrences (all)	2 / 56 (3.57%) 2  0 / 56 (0.00%) 0	3 / 60 (5.00%) 3  2 / 60 (3.33%) 2	0 / 61 (0.00%) 0  1 / 61 (1.64%) 1
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	2 / 56 (3.57%) 2	0 / 60 (0.00%) 0	1 / 61 (1.64%) 1
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all)  Urinary tract infection subjects affected / exposed occurrences (all)  Upper respiratory tract infection subjects affected / exposed occurrences (all)	2 / 56 (3.57%) 2  0 / 56 (0.00%) 0  0 / 56 (0.00%) 0	1 / 60 (1.67%) 1  1 / 60 (1.67%) 1  0 / 60 (0.00%) 0	2 / 61 (3.28%) 2  3 / 61 (4.92%) 3  2 / 61 (3.28%) 2

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
22 January 2015	Protocol was amended to include following substantial changes – <ul style="list-style-type: none"><li>• Sponsor changed from fully owned subsidiary (Lupin Atlantis Holdings SA, Switzerland) to its parent company (Lupin Limited, India)</li><li>• EU Legal representative changed from Lupin (Europe) Limited to Hormosan Pharma GmbH</li></ul>

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported