Clinical trial results:
A Long-Term Open-Label Extension Study for Subjects Completing a Phase 3 Efficacy and Safety Study of Lesinurad Monotherapy in Subjects with Gout

Summary

EudraCT number	2012-002956-18
Trial protocol	DE BE
Global end of trial date	29 April 2014

Results information

Result version number	v1 (current)
This version publication date	14 December 2016
First version publication date	17 July 2015

Trial information

Trial identification

Sponsor protocol code	RDEA594-305

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01650246
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Ardea Biosciences, Inc.
Sponsor organisation address	9390 Towne Centre Drive, San Diego, United States, 92121
Public contact	Maple Fung, Ardea Biosciences, Inc., mfung@ardeabio.com
Scientific contact	Maple Fung, MD, Ardea Biosciences, Inc., mfung@ardeabio.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 August 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	29 April 2014
Global end of trial reached?	Yes
Global end of trial date	29 April 2014
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To determine the long-term efficacy and safety of lesinurad monotherapy.

Protection of trial subjects:

This study was conducted in accordance with the protocol, International Conference on Harmonisation (ICH) E6 Good Clinical Practice (GCP), the Declaration of Helsinki (2008), and all other applicable regulatory requirements.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	05 September 2012
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	United States: 101
Country: Number of subjects enrolled	Belgium: 9
Country: Number of subjects enrolled	South Africa: 16
Country: Number of subjects enrolled	Canada: 6
Country: Number of subjects enrolled	Germany: 6
Country: Number of subjects enrolled	New Zealand: 3
Country: Number of subjects enrolled	Australia: 2
Worldwide total number of subjects	143
EEA total number of subjects	15

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)	111
From 65 to 84 years	32
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects who completed the double-blind treatment period in Study RDEA594-303 and met the eligibility criteria and provided informed consent.

Pre-assignment

Screening details:

There was no screening for this study. Subjects who meet the eligibility requirements and provide informed consent were enrolled in this extension 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	lesinurad 400 mg

Arm description:

lesinurad 400 mg qd

Arm type	Experimental
Investigational medicinal product name	lesinurad (RDEA594)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet, Tablet
Routes of administration	Oral use, Oral use

Dosage and administration details:

Tablet for oral use.

Number of subjects in period 1	lesinurad 400 mg
Started	143
Completed	0
Not completed	143
Adverse event, serious fatal	1
Consent withdrawn by subject	26
Adverse event, non-fatal	23
Lost to follow-up	5
Sponsor terminated study	53
Protocol deviation	5
Lack of efficacy	30

Baseline characteristics

Reporting groups	
Reporting group title	lesinurad 400 mg
Reporting group description: lesinurad 400 mg qd	

Reporting group values	lesinurad 400 mg	Total	
Number of subjects	143	143	
Age categorical Units: Subjects			
From 65-84 years	111	111	
85 years and over	32	32	
Age Continuous | Units: years			
arithmetic mean	55.1		
standard deviation	± 12	-	
Gender, Male/Female Units: Participants			
Male	132	132	
Female	11	11	
Region of Enrollment Units: Subjects			
Australia	2	2	
Belgium	9	9	
Canada	6	6	
Germany	6	6	
New Zealand	3	3	
South Africa	16	16	
United States	101	101	
lesinurad 400 mg Units: Subjects			

Age continuous Units: years			
arithmetic mean	55.1		
standard deviation	± 12	-	

End points

End points reporting groups

Reporting group title	lesinurad 400 mg
Reporting group description: lesinurad 400 mg qd	

Primary: Proportion of subjects with an sUA level that is < 6.0 mg/dL

End point title	Proportion of subjects with an sUA level that is < 6.0 mg/dL[1]
End point description:	
End point type	Primary
End point timeframe: Month 1	

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 is a long-term, uncontrolled, open-label, safety extension study. No statistical analyses were planned.

End point values	lesinurad 400 mg			
Subject group type	Reporting group			
Number of subjects analysed	134			
Units: Number				
Number	68			

Statistical analyses

No statistical analyses for this end point

Primary: Incidence of TEAEs

End point title	Incidence of TEAEs[2]
End point description:	
End point type	Primary
End point timeframe: Up to approximately 2 years	

Notes:

[2] - 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 is a long-term, uncontrolled, open-label, safety extension study. No statistical analyses were planned.

End point values	lesinurad 400 mg			
Subject group type	Reporting group			
Number of subjects analysed	143			
Units: Number				
Number	105			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were assessed from the time the subject provided informed consent through the duration of the study.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	14.0

Reporting groups

Reporting group title	lesinurad 400 mg

Reporting group description:

lesinurad 400 mg qd

Serious adverse events	lesinurad 400 mg		
Total subjects affected by serious adverse events			
subjects affected / exposed	15 / 143 (10.49%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events	0		
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	1 / 143 (0.70%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Atrioventricular block complete			
subjects affected / exposed	1 / 143 (0.70%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Coronary artery disease			
subjects affected / exposed	1 / 143 (0.70%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Myocardial infarction			
subjects affected / exposed	1 / 143 (0.70%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Nervous system disorders			
Transient ischaemic attack			
subjects affected / exposed	1 / 143 (0.70%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Death			
subjects affected / exposed	1 / 143 (0.70%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Gastrointestinal disorders			
Pancreatitis			
subjects affected / exposed	1 / 143 (0.70%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Depression			
subjects affected / exposed	1 / 143 (0.70%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Schizoaffective disorder			
subjects affected / exposed	1 / 143 (0.70%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	3 / 143 (2.10%)		
occurrences causally related to treatment / all	3 / 3		
deaths causally related to treatment / all	0 / 0		
Renal failure acute			
subjects affected / exposed	1 / 143 (0.70%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Renal impairment			

subjects affected / exposed	1 / 143 (0.70%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Facet joint syndrome			
subjects affected / exposed	1 / 143 (0.70%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Bursitis infective			
subjects affected / exposed	1 / 143 (0.70%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis salmonella			
subjects affected / exposed	1 / 143 (0.70%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Gout			
subjects affected / exposed	1 / 143 (0.70%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 0.02 %

Non-serious adverse events	lesinurad 400 mg		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	73 / 143 (51.05%)		
Investigations			
Blood creatine phosphokinase increased			
subjects affected / exposed	4 / 143 (2.80%)		
occurrences (all)	4		
Blood creatinine increased			

subjects affected / exposed	16 / 143 (11.19%)		
occurrences (all)	20		
Vascular disorders			
Hypertension			
subjects affected / exposed	10 / 143 (6.99%)		
occurrences (all)	10		
Nervous system disorders			
Headache			
subjects affected / exposed	6 / 143 (4.20%)		
occurrences (all)	8		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	4 / 143 (2.80%)		
occurrences (all)	4		
Pyrexia			
subjects affected / exposed	3 / 143 (2.10%)		
occurrences (all)	3		
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	3 / 143 (2.10%)		
occurrences (all)	3		
Gastrooesophageal reflux disease			
subjects affected / exposed	3 / 143 (2.10%)		
occurrences (all)	3		
Vomiting			
subjects affected / exposed	4 / 143 (2.80%)		
occurrences (all)	7		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	4 / 143 (2.80%)		
occurrences (all)	5		
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	3 / 143 (2.10%)		
occurrences (all)	3		
Renal impairment			

subjects affected / exposed	4 / 143 (2.80%)		
occurrences (all)	4		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	6 / 143 (4.20%)		
occurrences (all)	6		
Back pain			
subjects affected / exposed	7 / 143 (4.90%)		
occurrences (all)	8		
Flank pain			
subjects affected / exposed	3 / 143 (2.10%)		
occurrences (all)	4		
Pain in extremity			
subjects affected / exposed	3 / 143 (2.10%)		
occurrences (all)	4		
Infections and infestations			
Bronchitis			
subjects affected / exposed	5 / 143 (3.50%)		
occurrences (all)	5		
Gastroenteritis			
subjects affected / exposed	7 / 143 (4.90%)		
occurrences (all)	8		
Influenza			
subjects affected / exposed	3 / 143 (2.10%)		
occurrences (all)	3		
Nasopharyngitis			
subjects affected / exposed	4 / 143 (2.80%)		
occurrences (all)	5		
Sinusitis			
subjects affected / exposed	4 / 143 (2.80%)		
occurrences (all)	5		
Upper respiratory tract infection			
subjects affected / exposed	14 / 143 (9.79%)		
occurrences (all)	15		
Urinary tract infection			

subjects affected / exposed occurrences (all)	7 / 143 (4.90%) 8		
Metabolism and nutrition disorders Hyperlipidaemia subjects affected / exposed occurrences (all)	 3 / 143 (2.10%) 3		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
20 June 2013	This amendment expanded guidance on subject hydration and to expand the management algorithm if a subject experiences an elevated serum creatinine or kidney stone.
20 December 2013	This amendment was an as an Urgent Safety Measure to restrict continued participation to only those subjects benefiting from lesinurad treatment and to require urine urine alkalinization in all subjects to maintain urine pH above 6.5.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported