



Clinical trial results:

A Phase 3 Randomized, Double-Blind, Multicenter, Placebo-Controlled Study to Assess the Efficacy and Safety of Lesinurad Monotherapy Compared to Placebo in Subjects with Gout and an Intolerance or Contraindication to a Xanthine Oxidase Inhibitor.

Summary

EudraCT number	2011-003756-39
Trial protocol	BE DE
Global end of trial date	23 October 2013

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	RDEA594-303
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Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Ardea Biosciences, Inc.
Sponsor organisation address	9390 Towne Centre Dr, San Diego, United States, 92121
Public contact	Nihar Bhakta, Ardea Biosciences, Inc., US 858-652-6522, nbhakta@ardeabio.com
Scientific contact	Nihar Bhakta, MD, Ardea Biosciences, Inc., US 858-652-6671, nbhakta@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	31 October 2013
Is this the analysis of the primary completion data?	Yes
Primary completion date	23 October 2013
Global end of trial reached?	Yes
Global end of trial date	23 October 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine the efficacy of lesinurad monotherapy at Month 6 compared to placebo.

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	03 February 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: 157
Country: Number of subjects enrolled	Belgium: 9
Country: Number of subjects enrolled	Canada: 11
Country: Number of subjects enrolled	Germany: 7
Country: Number of subjects enrolled	New Zealand: 5
Country: Number of subjects enrolled	Australia: 2
Country: Number of subjects enrolled	South Africa: 23
Worldwide total number of subjects	214
EEA total number of subjects	16

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)	167
From 65 to 84 years	47
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Screening procedures to determine subject eligibility were performed within approximately 28 days prior to the first dose of randomized study medication (lesinurad or placebo) on Day 1. Subjects had to have an sUA level \geq 6.5 mg/dL (387 μ mol/L) at the Screening and Day -7 Visits for study eligibility.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	lesinurad 400 mg

Arm description:

lesinurad 400 mg

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

Dosage and administration details:

400 mg

Arm title	Placebo
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Arm description: -

Arm type	Placebo Comparator
No investigational medicinal product assigned in this arm	

Number of subjects in period 1	lesinurad 400 mg	Placebo
Started	107	107
Completed	84	94
Not completed	23	13
Consent withdrawn by subject	11	7
Adverse event, non-fatal	7	3
Gout flare	2	-
Lost to follow-up	1	2
Protocol deviation	2	1

Baseline characteristics

Reporting groups

Reporting group title	lesinurad 400 mg
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Reporting group description:

lesinurad 400 mg

Reporting group title	Placebo
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Reporting group description: -

Reporting group values	lesinurad 400 mg	Placebo	Total
Number of subjects	107	107	214
Age categorical			
Units: Subjects			
<65 years	87	80	167
>=65 years	20	27	47
Age Continuous			
Units: Years			
arithmetic mean	53.6	55.3	
standard deviation	± 12.5	± 12	-
Gender, Male/Female			
Units: Participants			
Male	98	97	195
Female	9	10	19
Region of Enrollment			
Units: Subjects			
Australia	1	1	2
Belgium	5	4	9
Canada	5	6	11
Germany	5	2	7
New Zealand	3	2	5
South Africa	12	11	23
United States	76	81	157

End points

End points reporting groups

Reporting group title	lesinurad 400 mg
Reporting group description:	lesinurad 400 mg
Reporting group title	Placebo
Reporting group description:	-

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

End point title	Number of subjects with an sUA level that is < 6.0 mg/dL
End point description:	
End point type	Primary
End point timeframe:	6 months

End point values	lesinurad 400 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	107	107		
Units: Number of Subjects	32	2		

Statistical analyses

Statistical analysis title	sUA level that is < 6.0 mg/dL
Comparison groups	lesinurad 400 mg v Placebo
Number of subjects included in analysis	214
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	0.28
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.19
upper limit	0.37

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
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Dictionary used

Dictionary name	MedDRA
Dictionary version	14.0

Reporting groups

Reporting group title	lesinurad 400 mg
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Reporting group description:

lesinurad 400 mg

Reporting group title	Placebo
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Reporting group description: -

Serious adverse events	lesinurad 400 mg	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	9 / 107 (8.41%)	4 / 107 (3.74%)	
number of deaths (all causes)	1	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Ovarian epithelial cancer			
subjects affected / exposed	1 / 107 (0.93%)	0 / 107 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Coronary artery disease			
subjects affected / exposed	0 / 107 (0.00%)	1 / 107 (0.93%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericardial effusion			
subjects affected / exposed	0 / 107 (0.00%)	1 / 107 (0.93%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			

Carpal tunnel syndrome			
subjects affected / exposed	1 / 107 (0.93%)	0 / 107 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Death			
subjects affected / exposed	1 / 107 (0.93%)	0 / 107 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Renal and urinary disorders			
Calculus ureteric			
subjects affected / exposed	1 / 107 (0.93%)	0 / 107 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal failure			
subjects affected / exposed	2 / 107 (1.87%)	0 / 107 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal failure acute			
subjects affected / exposed	2 / 107 (1.87%)	0 / 107 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal impairment			
subjects affected / exposed	1 / 107 (0.93%)	0 / 107 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Diverticulitis			
subjects affected / exposed	0 / 107 (0.00%)	1 / 107 (0.93%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			

subjects affected / exposed	0 / 107 (0.00%)	1 / 107 (0.93%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Gout			
subjects affected / exposed	1 / 107 (0.93%)	1 / 107 (0.93%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	lesinurad 400 mg	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	39 / 107 (36.45%)	8 / 107 (7.48%)	
Investigations			
Blood creatinine increased			
subjects affected / exposed	9 / 107 (8.41%)	0 / 107 (0.00%)	
occurrences (all)	10	0	
General disorders and administration site conditions			
Oedema peripheral			
subjects affected / exposed	3 / 107 (2.80%)	0 / 107 (0.00%)	
occurrences (all)	4	0	
Pyrexia			
subjects affected / exposed	3 / 107 (2.80%)	0 / 107 (0.00%)	
occurrences (all)	3	0	
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	6 / 107 (5.61%)	0 / 107 (0.00%)	
occurrences (all)	6	0	
Diarrhoea			
subjects affected / exposed	10 / 107 (9.35%)	6 / 107 (5.61%)	
occurrences (all)	10	6	
Respiratory, thoracic and mediastinal disorders			
Cough			

subjects affected / exposed occurrences (all)	4 / 107 (3.74%) 4	1 / 107 (0.93%) 1	
Renal and urinary disorders Renal impairment subjects affected / exposed occurrences (all)	4 / 107 (3.74%) 5	0 / 107 (0.00%) 0	
Musculoskeletal and connective tissue disorders Musculoskeletal stiffness subjects affected / exposed occurrences (all)	3 / 107 (2.80%) 3	0 / 107 (0.00%) 0	
Infections and infestations Bronchitis subjects affected / exposed occurrences (all)	5 / 107 (4.67%) 5	2 / 107 (1.87%) 2	
Metabolism and nutrition disorders Hyperkalaemia subjects affected / exposed occurrences (all)	3 / 107 (2.80%) 5	0 / 107 (0.00%) 0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
06 July 2012	This amendment addressed comments from the FDA and clarified procedures and process for study conduct.
17 June 2013	This amendment expanded guidance on subject hydration and expanded the management algorithm if a subject experiences an elevated serum creatinine or kidney stones.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported