



Clinical trial results:

A Phase 3 Randomized, Double-Blind, Multicenter, Placebo-Controlled, Combination Study to Evaluate the Efficacy and Safety of Lesinurad and Allopurinol Compared to Allopurinol Alone in Subjects with Gout who have had an Inadequate Hypouricemic Response to Standard of Care Allopurinol

Summary

EudraCT number	2011-003767-29
Trial protocol	DE BE PL ES
Global end of trial date	03 July 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	RDEA594-302
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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, MD, Ardea Biosciences, Inc., US 858-652-6671, 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	20 July 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	03 July 2014
Global end of trial reached?	Yes
Global end of trial date	03 July 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine the efficacy of lesinurad by Month 6 when used in combination with allopurinol compared to allopurinol 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	16 December 2011
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: 309
Country: Number of subjects enrolled	Canada: 25
Country: Number of subjects enrolled	Belgium: 4
Country: Number of subjects enrolled	Germany: 25
Country: Number of subjects enrolled	Spain: 8
Country: Number of subjects enrolled	Poland: 22
Country: Number of subjects enrolled	Switzerland: 1
Country: Number of subjects enrolled	Ukraine: 74
Country: Number of subjects enrolled	New Zealand: 26
Country: Number of subjects enrolled	Australia: 17
Country: Number of subjects enrolled	South Africa: 99
Worldwide total number of subjects	610
EEA total number of subjects	59

Notes:

Subjects enrolled per age group

In utero	0
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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)	544
From 65 to 84 years	66
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 Day 1.

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 200 mg + allopurinol

Arm description:

lesinurad 200 mg qd plus allopurinol

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:

200 mg

Arm title	lesinurad 400 mg + allopurinol
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Arm description: -

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 + allopurinol
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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 200 mg + allopurinol	lesinurad 400 mg + allopurinol	Placebo + allopurinol
Started	204	200	206
Completed	163	150	158
Not completed	41	50	48
Adverse event, serious fatal	-	1	-
Consent withdrawn by subject	16	13	11
Adverse event, non-fatal	4	12	9
Gout flare	3	-	2
Lost to follow-up	5	7	11
Sponsor terminated study	5	2	3
Protocol deviation	8	15	12

Baseline characteristics

Reporting groups

Reporting group title	lesinurad 200 mg + allopurinol
Reporting group description:	lesinurad 200 mg qd plus allopurinol
Reporting group title	lesinurad 400 mg + allopurinol
Reporting group description: -	
Reporting group title	Placebo + allopurinol
Reporting group description: -	

Reporting group values	lesinurad 200 mg + allopurinol	lesinurad 400 mg + allopurinol	Placebo + allopurinol
Number of subjects	204	200	206
Age categorical			
Units: Subjects			
<65	184	175	185
>=65	20	25	21
Age Continuous			
Units: years			
arithmetic mean	51	51.3	51.4
standard deviation	± 11.1	± 11.1	± 10.6
Gender, Male/Female			
Units: Participants			
Male	197	194	196
Female	7	6	10
Region of Enrollment			
Units: Subjects			
Australia	4	9	4
Belgium	1	1	2
Canada	7	6	12
Germany	9	8	8
New Zealand	12	7	7
Poland	5	11	6
South Africa	30	36	33
Spain	2	4	2
Switzerland	1	0	0
Ukraine	25	24	25
United States	108	94	107

Reporting group values	Total		
Number of subjects	610		
Age categorical			
Units: Subjects			
<65	544		
>=65	66		
Age Continuous			
Units: years			
arithmetic mean			

standard deviation	-		
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Gender, Male/Female			
Units: Participants			
Male	587		
Female	23		
Region of Enrollment			
Units: Subjects			
Australia	17		
Belgium	4		
Canada	25		
Germany	25		
New Zealand	26		
Poland	22		
South Africa	99		
Spain	8		
Switzerland	1		
Ukraine	74		
United States	309		

End points

End points reporting groups

Reporting group title	lesinurad 200 mg + allopurinol
Reporting group description:	lesinurad 200 mg qd plus allopurinol
Reporting group title	lesinurad 400 mg + allopurinol
Reporting group description:	-
Reporting group title	Placebo + allopurinol
Reporting group description:	-

Primary: Number of Subjects with sUA < 6.0 mg/dL

End point title	Number of Subjects with sUA < 6.0 mg/dL
End point description:	
End point type	Primary
End point timeframe:	6 months, analysis after all subjects complete 12 months

End point values	lesinurad 200 mg + allopurinol	lesinurad 400 mg + allopurinol	Placebo + allopurinol	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	204	200	206	
Units: Number of Subjects	113	33	48	

Statistical analyses

Statistical analysis title	Number of Subjects with sUA < 6.0 mg/dL
Statistical analysis description:	The primary endpoint for this study was the proportion of subjects with sUA < 6.0 mg/dL by Month 6.
Comparison groups	Placebo + allopurinol v lesinurad 200 mg + allopurinol
Number of subjects included in analysis	410
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.0001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	0.32
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.23
upper limit	0.41

Statistical analysis title	Number of Subjects with sUA < 6.0 mg/dL
Comparison groups	lesinurad 400 mg + allopurinol v Placebo + allopurinol
Number of subjects included in analysis	406
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.0001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	0.43
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.34
upper limit	0.52

Secondary: Gout flares

End point title	Gout flares
End point description:	
Mean rate of gout flares requiring treatment for the 6-month period from the end of Month 6 to the end of Month 12.	
End point type	Secondary
End point timeframe:	
12 Months	

End point values	lesinurad 200 mg + allopurinol	lesinurad 400 mg + allopurinol	Placebo + allopurinol	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	204	200	206	
Units: number of gout flares				
arithmetic mean (standard deviation)	0.7 (± 1.4)	0.8 (± 1.7)	0.9 (± 1.8)	

Statistical analyses

Statistical analysis title	Gout flares
Statistical analysis description:	
Mean rate of gout flares requiring treatment for the 6-month period from the end of Month 6 to the end of Month 12.	
Comparison groups	lesinurad 200 mg + allopurinol v Placebo + allopurinol

Number of subjects included in analysis	410
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.5716
Method	Negative Binomial Regression
Parameter estimate	Risk ratio (RR)
Point estimate	0.88
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.57
upper limit	1.37

Statistical analysis title	Gout flares
Comparison groups	lesinurad 400 mg + allopurinol v Placebo + allopurinol
Number of subjects included in analysis	406
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.7454
Method	Negative Binomial Regression
Parameter estimate	Risk ratio (RR)
Point estimate	0.93
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.6
upper limit	1.45

Secondary: Tophus

End point title	Tophus
End point description:	
Proportion of subjects with ≥ 1 target tophus at Baseline who experience complete resolution of at least 1 target tophus by Month 12	
End point type	Secondary
End point timeframe:	
12 months	

End point values	lesinurad 200 mg + allopurinol	lesinurad 400 mg + allopurinol	Placebo + allopurinol	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	35	29	38	
Units: Number of subjects	11	8	11	

Statistical analyses

Statistical analysis title	Tophus
Comparison groups	lesinurad 400 mg + allopurinol v Placebo + allopurinol
Number of subjects included in analysis	67
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.6301
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	-0.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.29
upper limit	0.17

Statistical analysis title	Tophus
Statistical analysis description:	
Proportion of subjects with greater than or equal 1 target tophus at Baseline who experience complete resolution of at least 1 target tophus by Month 12.	
Comparison groups	lesinurad 200 mg + allopurinol v Placebo + allopurinol
Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.8466
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	-0.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.24
upper limit	0.2

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 200 mg + allopurinol
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Reporting group description: -

Reporting group title	Placebo + allopurinol
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Reporting group description: -

Reporting group title	lesinurad 400 mg + allopurinol
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Reporting group description: -

Serious adverse events	lesinurad 200 mg + allopurinol	Placebo + allopurinol	lesinurad 400 mg + allopurinol
Total subjects affected by serious adverse events			
subjects affected / exposed	9 / 204 (4.41%)	8 / 206 (3.88%)	19 / 200 (9.50%)
number of deaths (all causes)	0	0	2
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	0 / 204 (0.00%)	0 / 206 (0.00%)	1 / 200 (0.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric cancer			
subjects affected / exposed	0 / 204 (0.00%)	0 / 206 (0.00%)	1 / 200 (0.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Ovarian adenoma			
subjects affected / exposed	1 / 204 (0.49%)	0 / 206 (0.00%)	0 / 200 (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
Pancreatic neuroendocrine tumour			

subjects affected / exposed	0 / 204 (0.00%)	1 / 206 (0.49%)	0 / 200 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Parathyroid tumour benign			
subjects affected / exposed	1 / 204 (0.49%)	0 / 206 (0.00%)	0 / 200 (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
Prostate cancer			
subjects affected / exposed	0 / 204 (0.00%)	0 / 206 (0.00%)	1 / 200 (0.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypertensive crisis			
subjects affected / exposed	0 / 204 (0.00%)	0 / 206 (0.00%)	1 / 200 (0.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Adverse drug reaction			
subjects affected / exposed	1 / 204 (0.49%)	0 / 206 (0.00%)	0 / 200 (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
Non-cardiac chest pain			
subjects affected / exposed	1 / 204 (0.49%)	0 / 206 (0.00%)	0 / 200 (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
Respiratory, thoracic and mediastinal disorders			
Pulmonary oedema			
subjects affected / exposed	0 / 204 (0.00%)	0 / 206 (0.00%)	1 / 200 (0.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Psychiatric disorders			
Depression			

subjects affected / exposed	1 / 204 (0.49%)	0 / 206 (0.00%)	0 / 200 (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
Dissociative disorder			
subjects affected / exposed	0 / 204 (0.00%)	0 / 206 (0.00%)	1 / 200 (0.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Femur fracture			
subjects affected / exposed	0 / 204 (0.00%)	1 / 206 (0.49%)	0 / 200 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Multiple drug overdose			
subjects affected / exposed	1 / 204 (0.49%)	0 / 206 (0.00%)	0 / 200 (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
Multiple injuries			
subjects affected / exposed	1 / 204 (0.49%)	0 / 206 (0.00%)	0 / 200 (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			
Atrial fibrillation			
subjects affected / exposed	1 / 204 (0.49%)	0 / 206 (0.00%)	0 / 200 (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
Coronary artery disease			
subjects affected / exposed	0 / 204 (0.00%)	0 / 206 (0.00%)	1 / 200 (0.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intracardiac thrombus			
subjects affected / exposed	0 / 204 (0.00%)	0 / 206 (0.00%)	1 / 200 (0.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Myocardial infarction			
subjects affected / exposed	0 / 204 (0.00%)	0 / 206 (0.00%)	3 / 200 (1.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Subarachnoid haemorrhage			
subjects affected / exposed	0 / 204 (0.00%)	1 / 206 (0.49%)	0 / 200 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Duodenal ulcer haemorrhage			
subjects affected / exposed	0 / 204 (0.00%)	1 / 206 (0.49%)	1 / 200 (0.50%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal haemorrhage			
subjects affected / exposed	1 / 204 (0.49%)	0 / 206 (0.00%)	0 / 200 (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
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	0 / 204 (0.00%)	0 / 206 (0.00%)	2 / 200 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal failure acute			
subjects affected / exposed	0 / 204 (0.00%)	1 / 206 (0.49%)	1 / 200 (0.50%)
occurrences causally related to treatment / all	0 / 0	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal impairment			
subjects affected / exposed	0 / 204 (0.00%)	0 / 206 (0.00%)	1 / 200 (0.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Arthralgia			

subjects affected / exposed	1 / 204 (0.49%)	0 / 206 (0.00%)	0 / 200 (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
Back pain			
subjects affected / exposed	1 / 204 (0.49%)	0 / 206 (0.00%)	0 / 200 (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
Flank pain			
subjects affected / exposed	1 / 204 (0.49%)	0 / 206 (0.00%)	0 / 200 (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
Intervertebral disc degeneration			
subjects affected / exposed	0 / 204 (0.00%)	0 / 206 (0.00%)	1 / 200 (0.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoarthritis			
subjects affected / exposed	0 / 204 (0.00%)	0 / 206 (0.00%)	2 / 200 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Abscess limb			
subjects affected / exposed	0 / 204 (0.00%)	1 / 206 (0.49%)	0 / 200 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis			
subjects affected / exposed	0 / 204 (0.00%)	1 / 206 (0.49%)	0 / 200 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchopneumonia			
subjects affected / exposed	0 / 204 (0.00%)	0 / 206 (0.00%)	1 / 200 (0.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			

subjects affected / exposed	0 / 204 (0.00%)	0 / 206 (0.00%)	1 / 200 (0.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis			
subjects affected / exposed	0 / 204 (0.00%)	1 / 206 (0.49%)	0 / 200 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Empyema			
subjects affected / exposed	1 / 204 (0.49%)	0 / 206 (0.00%)	0 / 200 (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
Pneumonia			
subjects affected / exposed	2 / 204 (0.98%)	0 / 206 (0.00%)	0 / 200 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis chronic			
subjects affected / exposed	0 / 204 (0.00%)	0 / 206 (0.00%)	1 / 200 (0.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinobronchitis			
subjects affected / exposed	1 / 204 (0.49%)	0 / 206 (0.00%)	0 / 200 (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
Metabolism and nutrition disorders			
Gout			
subjects affected / exposed	0 / 204 (0.00%)	0 / 206 (0.00%)	2 / 200 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	3 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	lesinurad 200 mg + allopurinol	Placebo + allopurinol	lesinurad 400 mg + allopurinol
Total subjects affected by non-serious adverse events subjects affected / exposed	85 / 204 (41.67%)	60 / 206 (29.13%)	82 / 200 (41.00%)
Investigations Blood creatinine increased subjects affected / exposed occurrences (all)	8 / 204 (3.92%) 9	7 / 206 (3.40%) 7	19 / 200 (9.50%) 24
Injury, poisoning and procedural complications Joint sprain subjects affected / exposed occurrences (all)	9 / 204 (4.41%) 9	4 / 206 (1.94%) 4	2 / 200 (1.00%) 2
Vascular disorders Hypertension subjects affected / exposed occurrences (all)	17 / 204 (8.33%) 17	10 / 206 (4.85%) 10	16 / 200 (8.00%) 16
Nervous system disorders Headache subjects affected / exposed occurrences (all)	10 / 204 (4.90%) 11	8 / 206 (3.88%) 8	12 / 200 (6.00%) 13
Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all) Gastrooesophageal reflux disease subjects affected / exposed occurrences (all)	10 / 204 (4.90%) 13 10 / 204 (4.90%) 10	7 / 206 (3.40%) 8 1 / 206 (0.49%) 1	14 / 200 (7.00%) 21 4 / 200 (2.00%) 4
Respiratory, thoracic and mediastinal disorders Oropharyngeal pain subjects affected / exposed occurrences (all)	5 / 204 (2.45%) 5	0 / 206 (0.00%) 0	1 / 200 (0.50%) 1
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all)	24 / 204 (11.76%) 24	9 / 206 (4.37%) 14	6 / 200 (3.00%) 7
Infections and infestations			

Bronchitis			
subjects affected / exposed	9 / 204 (4.41%)	4 / 206 (1.94%)	4 / 200 (2.00%)
occurrences (all)	9	5	4
Influenza			
subjects affected / exposed	14 / 204 (6.86%)	4 / 206 (1.94%)	8 / 200 (4.00%)
occurrences (all)	17	4	9
Upper respiratory tract infection			
subjects affected / exposed	14 / 204 (6.86%)	21 / 206 (10.19%)	30 / 200 (15.00%)
occurrences (all)	16	23	39

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
28 August 2012	This amendment addressed comments from the US FDA and incorporated newly acquired information regarding the inherent inter-day variability of serum urate to the screening serum urate eligibility criteria.
20 June 2013	This amendment expanded the guidance on subject hydration and expanded the management algorithm if a subject experiences an elevated serum creatinine or kidney stone.
24 December 2013	This amendment clarified the risks associated with lesinurad in the monotherapy setting and emphasized the requirement for subjects to concomitantly take lesinurad with a xanthine oxidase inhibitor.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported