Clinical trial results:
A Phase 3 Randomized, Double-Blind, Multicenter, Placebo-Controlled, Combination Study to Evaluate the Efficacy and Safety of Lesinurad and Febuxostat Compared to Febuxostat Alone at Lowering Serum Uric Acid and Resolving Tophi in Subjects with Tophaceous Gout

Summary

EudraCT number	2011-003768-55
Trial protocol	PL ES
Global end of trial date	17 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	RDEA594-304

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	Maple Fung, MD, Ardea Biosciences, Inc., US 858-652-6721, mfung@ardeabio.com
Scientific contact	Maple Fung, MD, Ardea Biosciences, Inc., US 858-652-6721, 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	24 June 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	17 April 2014
Global end of trial reached?	Yes
Global end of trial date	17 April 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 febuxostat compared to febuxostat 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	23 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: 244
Country: Number of subjects enrolled	Canada: 17
Country: Number of subjects enrolled	Poland: 32
Country: Number of subjects enrolled	Switzerland: 2
Country: Number of subjects enrolled	New Zealand: 13
Country: Number of subjects enrolled	Australia: 16
Worldwide total number of subjects	324
EEA total number of subjects	32

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)	268
From 65 to 84 years	56
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Screening procedures to determine subject eligibility were performed within approximately 35 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	Investigator, Subject

Arms

Are arms mutually exclusive?	Yes
Arm title	lesinurad 200 mg + febuxostat

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:

200 mg

Arm title	lesinurad 400 mg + febuxostat

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 + febuxostat

Arm description: -

Arm type	Placebo Comparator

No investigational medicinal product assigned in this arm

Number of subjects in period 1	lesinurad 200 mg + febuxostat	lesinurad 400 mg + febuxostat	Placebo + febuxostat
Started	106	109	109
Completed	79	84	87
Not completed	27	25	22
Adverse event, serious fatal	1	1	-
Consent withdrawn by subject	3	4	3
Adverse event, non-fatal	7	6	4
Lost to follow-up	5	1	5
Gout Flare	-	3	1
Protocol deviation	11	10	9

Baseline characteristics

Reporting groups	
Reporting group title	lesinurad 200 mg + febuxostat
Reporting group description: -	
Reporting group title	lesinurad 400 mg + febuxostat
Reporting group description: -	
Reporting group title	Placebo + febuxostat
Reporting group description: -	

Reporting group values	lesinurad 200 mg + febuxostat	lesinurad 400 mg + febuxostat	Placebo + febuxostat
Number of subjects	106	109	109
Age categorical Units: Subjects			
<65	89	90	89
>=65	17	19	20
Age Continuous | Units: years			
arithmetic mean	54.2	53.3	54.6
standard deviation	± 11	± 11.2	± 10.9
Gender, Male/Female Units: Participants			
Male	100	102	107
Female	6	7	2
Region of Enrollment Units: Subjects			
Australia	6	6	4
Canada	9	2	6
New Zealand	2	6	5
Poland	8	10	14
Switzerland	0	1	1
United States	81	84	79

Reporting group values	Total		
Number of subjects	324		
Age categorical Units: Subjects			
<65	268		
>=65	56		
Age Continuous | Units: years			
arithmetic mean			
standard deviation	-		
Gender, Male/Female Units: Participants			
Male	309		
Female	15		

Region of Enrollment Units: Subjects			
Australia	16		
Canada	17		
New Zealand	13		
Poland	32		
Switzerland	2		
United States	244		

End points

End points reporting groups	
Reporting group title	lesinurad 200 mg + febuxostat
Reporting group description: -	
Reporting group title	lesinurad 400 mg + febuxostat
Reporting group description: -	
Reporting group title	Placebo + febuxostat
Reporting group description: -	

Primary: Number of subjects with an sUA level that is < 5.0 mg/dL	
End point title	Number of subjects with an sUA level that is < 5.0 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 + febuxostat	lesinurad 400 mg + febuxostat	Placebo + febuxostat	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	106	109	109	
Units: Number of Subjects	60	83	51	

Statistical analyses

Statistical analysis title	sUA level that is < 5.0 mg/dL
Comparison groups	lesinurad 200 mg + febuxostat v Placebo + febuxostat
Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.1298
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.03
upper limit	0.23

Statistical analysis title	sUA level that is < 5.0 mg/dL
Comparison groups	lesinurad 400 mg + febuxostat v Placebo + febuxostat
Number of subjects included in analysis	218
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.0001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	0.29
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.17
upper limit	0.42

Secondary: Complete Resolution of at Least One Target Tophus	
End point title	Complete Resolution of at Least One Target Tophus
End point description: Proportion of subjects 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 + febuxostat	lesinurad 400 mg + febuxostat	Placebo + febuxostat	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	106	109	109	
Units: Subjects				
number (not applicable)	27	33	23	

Statistical analyses

Statistical analysis title	Complete Resolution Target Tophus
Comparison groups	lesinurad 200 mg + febuxostat v Placebo + febuxostat

Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.4453
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	0.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.07
upper limit	0.16

Statistical analysis title	Complete Resolution Target Tophus
Comparison groups	lesinurad 400 mg + febuxostat v Placebo + febuxostat
Number of subjects included in analysis	218
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.1149
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	0.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.02
upper limit	0.21

Secondary: Complete or Partial Response of at Least One Tophus	
End point title	Complete or Partial Response of at Least One Tophus
End point description:	
Proportion of subjects with a best tophus response on at least 1 target tophus of complete or partial resolution by Month 12.	
End point type	Secondary
End point timeframe:	
12 Months	

End point values	lesinurad 200 mg + febuxostat	lesinurad 400 mg + febuxostat	Placebo + febuxostat	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	106	109	109	
Units: Subjects	52	56	50	

Statistical analyses

Statistical analysis title	Complete or Partial Response of Tophus
Comparison groups	lesinurad 200 mg + febuxostat v Placebo + febuxostat
Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.645
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	0.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.1
upper limit	0.17

Statistical analysis title	Complete or Partial Response Tophus
Comparison groups	lesinurad 400 mg + febuxostat v Placebo + febuxostat
Number of subjects included in analysis	218
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.4118
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	0.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.08
upper limit	0.19

Secondary: Quality of Life

End point title	Quality of Life

End point description:

Proportion of subjects with an improvement from Baseline in Health Assessment Questionnaire - Disability Index (HAQ-DI) of at least 0.25 at Month 12

End point type	Secondary

End point timeframe:

12 Months

End point values	lesinurad 200 mg + febuxostat	lesinurad 400 mg + febuxostat	Placebo + febuxostat	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	77	78	82	
Units: Number of Subjects	34	26	42	

Statistical analyses

Statistical analysis title	Quality of Life
Comparison groups	lesinurad 200 mg + febuxostat v Placebo + febuxostat
Number of subjects included in analysis	159
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.3034
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	-0.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.24
upper limit	0.07

Statistical analysis title	Quality of Life
Comparison groups	lesinurad 400 mg + febuxostat v Placebo + febuxostat
Number of subjects included in analysis	160
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.021
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	-0.19
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.34
upper limit	-0.04

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 200 mg + febuxostat
Reporting group description: -	
Reporting group title	Placebo + febuxostat
Reporting group description: -	
Reporting group title	lesinurad 400 mg + febuxostat
Reporting group description: -	

Serious adverse events	lesinurad 200 mg + febuxostat	Placebo + febuxostat	lesinurad 400 mg + febuxostat
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 106 (5.66%)	10 / 109 (9.17%)	9 / 109 (8.26%)
number of deaths (all causes)	1	0	1
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Prostate cancer			
subjects affected / exposed	0 / 106 (0.00%)	1 / 109 (0.92%)	0 / 109 (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
Injury, poisoning and procedural complications			
Laceration			
subjects affected / exposed	1 / 106 (0.94%)	0 / 109 (0.00%)	0 / 109 (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
Subdural haematoma			
subjects affected / exposed	0 / 106 (0.00%)	1 / 109 (0.92%)	0 / 109 (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

Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 106 (0.00%)	0 / 109 (0.00%)	1 / 109 (0.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina pectoris			
subjects affected / exposed	0 / 106 (0.00%)	0 / 109 (0.00%)	1 / 109 (0.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arrhythmia			
subjects affected / exposed	0 / 106 (0.00%)	1 / 109 (0.92%)	0 / 109 (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
Atrial fibrillation			
subjects affected / exposed	1 / 106 (0.94%)	0 / 109 (0.00%)	0 / 109 (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 failure acute			
subjects affected / exposed	0 / 106 (0.00%)	0 / 109 (0.00%)	1 / 109 (0.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure congestive			
subjects affected / exposed	0 / 106 (0.00%)	0 / 109 (0.00%)	1 / 109 (0.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Coronary artery disease			
subjects affected / exposed	1 / 106 (0.94%)	0 / 109 (0.00%)	1 / 109 (0.92%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulseless electrical activity			
subjects affected / exposed	1 / 106 (0.94%)	0 / 109 (0.00%)	0 / 109 (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
General disorders and administration			

site conditions			
Non-cardiac chest pain			
subjects affected / exposed	0 / 106 (0.00%)	1 / 109 (0.92%)	0 / 109 (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
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 106 (0.00%)	1 / 109 (0.92%)	1 / 109 (0.92%)
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 disorders			
Gastritis			
subjects affected / exposed	1 / 106 (0.94%)	0 / 109 (0.00%)	0 / 109 (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
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	0 / 106 (0.00%)	0 / 109 (0.00%)	1 / 109 (0.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 106 (0.00%)	1 / 109 (0.92%)	0 / 109 (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
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	0 / 106 (0.00%)	1 / 109 (0.92%)	0 / 109 (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
Renal failure acute			
subjects affected / exposed	0 / 106 (0.00%)	1 / 109 (0.92%)	1 / 109 (0.92%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal failure chronic			

subjects affected / exposed	0 / 106 (0.00%)	0 / 109 (0.00%)	1 / 109 (0.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Joint contracture			
subjects affected / exposed	0 / 106 (0.00%)	1 / 109 (0.92%)	0 / 109 (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
Osteoarthritis			
subjects affected / exposed	0 / 106 (0.00%)	1 / 109 (0.92%)	0 / 109 (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
Spinal column stenosis			
subjects affected / exposed	0 / 106 (0.00%)	0 / 109 (0.00%)	1 / 109 (0.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Pneumonia			
subjects affected / exposed	0 / 106 (0.00%)	1 / 109 (0.92%)	0 / 109 (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
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 106 (0.00%)	0 / 109 (0.00%)	1 / 109 (0.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gout			
subjects affected / exposed	0 / 106 (0.00%)	0 / 109 (0.00%)	1 / 109 (0.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Type 2 diabetes mellitus			
subjects affected / exposed	1 / 106 (0.94%)	0 / 109 (0.00%)	0 / 109 (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

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

Non-serious adverse events	lesinurad 200 mg + febuxostat	Placebo + febuxostat	lesinurad 400 mg + febuxostat
Total subjects affected by non-serious adverse events			
subjects affected / exposed	50 / 106 (47.17%)	34 / 109 (31.19%)	59 / 109 (54.13%)
Investigations			
Blood creatine phosphokinase increased			
subjects affected / exposed	6 / 106 (5.66%)	3 / 109 (2.75%)	4 / 109 (3.67%)
occurrences (all)	8	3	4
Blood creatinine increased			
subjects affected / exposed	7 / 106 (6.60%)	3 / 109 (2.75%)	8 / 109 (7.34%)
occurrences (all)	7	3	11
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	2 / 106 (1.89%)	3 / 109 (2.75%)	7 / 109 (6.42%)
occurrences (all)	2	3	9
Excoriation			
subjects affected / exposed	3 / 106 (2.83%)	0 / 109 (0.00%)	2 / 109 (1.83%)
occurrences (all)	3	0	2
Joint sprain			
subjects affected / exposed	4 / 106 (3.77%)	2 / 109 (1.83%)	6 / 109 (5.50%)
occurrences (all)	4	2	6
Laceration			
subjects affected / exposed	3 / 106 (2.83%)	4 / 109 (3.67%)	8 / 109 (7.34%)
occurrences (all)	3	5	12
Vascular disorders			
Hypertension			
subjects affected / exposed	6 / 106 (5.66%)	8 / 109 (7.34%)	12 / 109 (11.01%)
occurrences (all)	6	8	13
Nervous system disorders			
Headache			

subjects affected / exposed	10 / 106 (9.43%)	8 / 109 (7.34%)	6 / 109 (5.50%)
occurrences (all)	11	12	7
General disorders and administration site conditions			
Non-cardiac chest pain			
subjects affected / exposed	1 / 106 (0.94%)	0 / 109 (0.00%)	3 / 109 (2.75%)
occurrences (all)	1	0	4
Pyrexia			
subjects affected / exposed	1 / 106 (0.94%)	4 / 109 (3.67%)	7 / 109 (6.42%)
occurrences (all)	1	4	7
Gastrointestinal disorders			
Dental caries			
subjects affected / exposed	0 / 106 (0.00%)	0 / 109 (0.00%)	3 / 109 (2.75%)
occurrences (all)	0	0	3
Toothache			
subjects affected / exposed	1 / 106 (0.94%)	0 / 109 (0.00%)	3 / 109 (2.75%)
occurrences (all)	1	0	3
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	4 / 106 (3.77%)	3 / 109 (2.75%)	9 / 109 (8.26%)
occurrences (all)	4	3	9
Sinus congestion			
subjects affected / exposed	4 / 106 (3.77%)	0 / 109 (0.00%)	0 / 109 (0.00%)
occurrences (all)	4	0	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	8 / 106 (7.55%)	5 / 109 (4.59%)	6 / 109 (5.50%)
occurrences (all)	9	6	7
Pain in extremity			
subjects affected / exposed	6 / 106 (5.66%)	4 / 109 (3.67%)	9 / 109 (8.26%)
occurrences (all)	9	4	9
Infections and infestations			
Influenza			
subjects affected / exposed	6 / 106 (5.66%)	2 / 109 (1.83%)	2 / 109 (1.83%)
occurrences (all)	6	2	4
Nasopharyngitis			

subjects affected / exposed occurrences (all)	10 / 106 (9.43%) 10	9 / 109 (8.26%) 12	15 / 109 (13.76%) 15
Metabolism and nutrition disorders Type 2 diabetes mellitus subjects affected / exposed occurrences (all)	4 / 106 (3.77%) 4	1 / 109 (0.92%) 1	1 / 109 (0.92%) 1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
09 December 2011	This amendment clarified the dosing recommendations for febuxostat when the dose has been interrupted due to potential toxicity.
20 July 2012	This amendment addressed comments received from the US FDA and reduced the complexity of the screening serum urate eligibility criteria.
14 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.
02 January 2014	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