Clinical trial results:
Randomized, Double-Blind, Multicenter, Placebo-Controlled, Combination Study to Evaluate the Safety, Efficacy and Potential Pharmacokinetic Interaction of RDEA594 and Allopurinol in Gout Patients with an Inadequate Hypouricemic Response with Standard Doses of Allopurinol

Summary

EudraCT number	2009-014660-19
Trial protocol	GB ES PL
Global end of trial date	12 August 2016

Results information

Result version number	v1 (current)
This version publication date	29 December 2017
First version publication date	29 December 2017

Trial information

Trial identification

Sponsor protocol code	RDEA594-203

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01001338
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Ardea Biosciences, Inc.
Sponsor organisation address	9390 Towne Centre Dr., San Diego, United States,
Public contact	Nihar Bhakta, Ardea Biosciences, Inc., nbhakta@ardeabio.com
Scientific contact	Nihar Bhakta, MD, Ardea Biosciences, Inc., 1 8586526671, 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	12 August 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	07 July 2016
Global end of trial reached?	Yes
Global end of trial date	12 August 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To compare the percent reduction from baseline in serum urate levels following 4 weeks of continuous treatment of RDEA594 in combination with allopurinol to allopurinol alone in subjects with documented inadequate hypouricemic response.

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	01 October 2009
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	Canada: 28
Country: Number of subjects enrolled	Georgia: 32
Country: Number of subjects enrolled	Poland: 25
Country: Number of subjects enrolled	Spain: 2
Country: Number of subjects enrolled	Ukraine: 40
Country: Number of subjects enrolled	United Kingdom: 3
Country: Number of subjects enrolled	United States: 78
Worldwide total number of subjects	208
EEA total number of subjects	30

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)	17
From 65 to 84 years	191
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Subjects who completed the Main Period could enter the optional Double-Blind Extension (DBE) Period. Subjects who completed the DBE Period could enter the optional OLE Period, with the Week 44 visit of the DBE Period serving as the Month 0 visit of the OLE Period.

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	Main Period Cohort 1: Lesinurad 200 mg

Arm description:

Lesinurad 200 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:

200 mg

Arm title	Main Period Cohort 2: 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	Main Period Cohort 3: Lesinurad 600 mg

Arm description:

Lesinurad 600 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:
600 mg

Arm title	Main Period: Pooled Placebo

Arm description:
Pooled placebo.

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

Dosage and administration details:
N/A

Number of subjects in period 1	Main Period Cohort 1: Lesinurad 200 mg	Main Period Cohort 2: Lesinurad 400 mg	Main Period Cohort 3: Lesinurad 600 mg
Started	46	42	48
Completed	41	40	42
Not completed	5	2	6
Consent withdrawn by subject	3	-	2
Adverse event, non-fatal	-	1	2
Prolonged QTc intervals	1	-	-
Day 27 dose at home	1	-	-
Lost to follow-up	-	1	-
Protocol deviation	-	-	2

Number of subjects in period 1	Main Period: Pooled Placebo
Started	72
Completed	66
Not completed	6
Consent withdrawn by subject	3
Adverse event, non-fatal	1
Prolonged QTc intervals	-
Day 27 dose at home	-
Lost to follow-up	1
Protocol deviation	1

Baseline characteristics

Reporting groups	
Reporting group title	Main Period Cohort 1: Lesinurad 200 mg
Reporting group description:	
Lesinurad 200 mg	
Reporting group title	Main Period Cohort 2: Lesinurad 400 mg
Reporting group description:	
Lesinurad 400 mg	
Reporting group title	Main Period Cohort 3: Lesinurad 600 mg
Reporting group description:	
Lesinurad 600 mg	
Reporting group title	Main Period: Pooled Placebo
Reporting group description:	
Pooled placebo.	

Reporting group values	Main Period Cohort 1: Lesinurad 200 mg	Main Period Cohort 2: Lesinurad 400 mg	Main Period Cohort 3: Lesinurad 600 mg
Number of subjects	46	42	48
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)	39	39	45
From 65-84 years	7	3	3
85 years and over	0	0	0
Age Continuous			
Units: Years			
arithmetic mean	52.9	50.7	48.4
standard deviation	± 10.11	± 10.38	± 11.03
Sex/Gender, Customized			
Units: Subjects			
Male|	44	41	48
Female|	2	1	0

Reporting group values	Main Period: Pooled Placebo	Total	
Number of subjects	72	208	
Age categorical			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	

Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	68	191	
From 65-84 years	4	17	
85 years and over	0	0	
Age Continuous			
Units: Years			
arithmetic mean	51.1		
standard deviation	± 9.21	-	
Sex/Gender, Customized			
Units: Subjects			
Male|	71	204	
Female|	1	4	

End points

End points reporting groups

Reporting group title	Main Period Cohort 1: Lesinurad 200 mg
Reporting group description:	
Lesinurad 200 mg	
Reporting group title	Main Period Cohort 2: Lesinurad 400 mg
Reporting group description:	
Lesinurad 400 mg	
Reporting group title	Main Period Cohort 3: Lesinurad 600 mg
Reporting group description:	
Lesinurad 600 mg	
Reporting group title	Main Period: Pooled Placebo
Reporting group description:	
Pooled placebo.	
Subject analysis set title	Cohort 1: Lesinurad 200 mg qd + Allopurinol 300 mg qd
Subject analysis set type	Full analysis
Subject analysis set description:	
RDEA594 (Lesinurad) 200 mg qd for 28 days. (N at Baseline = 46)	
Subject analysis set title	Cohort 2: Lesinurad 400 mg qd + Allopurinol 300 mg qd
Subject analysis set type	Full analysis
Subject analysis set description:	
RDEA594 200 mg qd for 7 days followed by 400 mg qd for 21 days. (N at Baseline = 42)	
Subject analysis set title	Cohort 3: Lesinurad 600 mg + Allopurinol 300 mg qd
Subject analysis set type	Full analysis
Subject analysis set description:	
RDEA594 200 mg qd for 7 days followed by 400 mg qd for 7 days followed by 600 mg qd for 14 days. (N at Baseline = 48)	
Subject analysis set title	Pooled Placebo
Subject analysis set type	Full analysis
Subject analysis set description:	
Pooled place72 (N at Baseline = 72)	
Subject analysis set title	Cohort 1: Lesinurad 200 mg qd + Allopurinol 300 mg qd
Subject analysis set type	Full analysis
Subject analysis set description:	
RDEA594 200 mg qd for 28 days	
Subject analysis set title	Cohort 2: Lesinurad 400 mg qd + Allopurinol 300 mg qd
Subject analysis set type	Full analysis
Subject analysis set description:	
RDEA594 200 mg qd for 7 days followed by 400 mg qd for 21 days	
Subject analysis set title	Cohort 3: Lesinurad 600 mg + Allopurinol 300 mg qd
Subject analysis set type	Full analysis
Subject analysis set description:	
RDEA594 200 mg qd for 7 days followed by 400 mg qd for 7 days followed by 600 mg qd for 14 days.	
Subject analysis set title	Pooled Placebo
Subject analysis set type	Full analysis
Subject analysis set description:	
Pooled placebo	
Subject analysis set title	Cohort 1: Lesinurad 200 mg qd + Allopurinol 300 mg qd

Subject analysis set type	Full analysis
Subject analysis set description:	
RDEA594 200 mg qd for 28 days.	
Subject analysis set title	Cohort 2: Lesinurad 400 mg qd + Allopurinol 300 mg qd
Subject analysis set type	Full analysis
Subject analysis set description:	
RDEA594 200 mg qd for 7 days followed by 400 mg qd for 21 days.	
Subject analysis set title	Total RDEA594
Subject analysis set type	Full analysis
Subject analysis set description:	
Participants in the Double-Blind Extension remained on their randomized treatment (RDEA594 or placebo) plus allopurinol.	
Subject analysis set title	Pooled Placebo
Subject analysis set type	Full analysis
Subject analysis set description:	
Participants in the Double-Blind Extension remained on their randomized treatment (RDEA594 or placebo) plus allopurinol.	
Subject analysis set title	Cohort 1: Lesinurad 200 mg qd + Allopurinol 300 mg qd
Subject analysis set type	Full analysis
Subject analysis set description:	
Participants in the Double-Blind Extension remained on their randomized treatment (RDEA594 or placebo) plus allopurinol.	
Subject analysis set title	Cohort 2: Lesinurad 400 mg qd + Allopurinol 300 mg qd
Subject analysis set type	Full analysis
Subject analysis set description:	
Participants in the Double-Blind Extension remained on their randomized treatment (RDEA594 or placebo) plus allopurinol.	
Subject analysis set title	Cohort 3: Lesinurad 600 mg + Allopurinol 300 mg qd
Subject analysis set type	Full analysis
Subject analysis set description:	
Participants in the Double-Blind Extension remained on their randomized treatment (RDEA594 or placebo) plus allopurinol.	
Subject analysis set title	ALLO-only
Subject analysis set type	Full analysis
Subject analysis set description:	
Subjects originally randomized to receive placebo plus allopurinol whose sUA values were <6.0 mg/dL continued on allopurinol alone in the OLE Period.	
Subject analysis set title	ALLO-switch
Subject analysis set type	Full analysis
Subject analysis set description:	
Among subjects who continued on allopurinol alone, those whose sUA values later increased to ≥6.0 mg/dL in the OLE Period began dosing with lesinurad (starting at 200 mg and escalating to a maximum of 600 mg qd as necessary using 6.0 mg/dL as the target sUA level) in combination with their current dose of allopurinol.	
Subject analysis set title	PBO-switch
Subject analysis set type	Full analysis
Subject analysis set description:	
Subjects originally randomized to receive placebo plus allopurinol whose sUA values were ≥6.0 mg/dL at Week 44 of the DBE Period began dosing with lesinurad (starting at 200 mg and escalating to a maximum of 600 mg qd as necessary using 6.0 mg/dL as the target sUA level) in combination with their current dose of allopurinol.	
Subject analysis set title	Lesinurad
Subject analysis set type	Full analysis
Subject analysis set description:	
Subjects randomized to lesinurad in combination with allopurinol in the Main and DBE Periods began taking open-label lesinurad at the dose level they were taking at the end of the DBE Period (200, 400,	

or 600 mg qd) in combination with the dose of allopurinol they were taking at the end of the DBE Period.

Subject analysis set title	Total Lesinurad
Subject analysis set type	Full analysis
Subject analysis set description:	
Total Lesinurad	

Primary: Percent reduction from Baseline in serum urate (sUA) following 4 weeks of treatment (Main Period).

End point title	Percent reduction from Baseline in serum urate (sUA) following 4 weeks of treatment (Main Period).
End point description:	
The percent reduction from Baseline in sUA levels following 4 weeks of continuous treatment with lesinurad in combination with allopurinol compared to allopurinol alone (the placebo group) in participants with documented inadequate hypouricemic response with standard doses of allopurinol.	
End point type	Primary
End point timeframe:	
4 Weeks	

End point values	Cohort 1: Lesinurad 200 mg qd + Allopurinol 300 mg qd	Cohort 2: Lesinurad 400 mg qd + Allopurinol 300 mg qd	Cohort 3: Lesinurad 600 mg + Allopurinol 300 mg qd	Pooled Placebo
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	40	40	41	72
Units: Percent (%) Change				
arithmetic mean (standard deviation)	-16.12 (± 18.89)	-22.07 (± 21.59)	-30.35 (± 14.03)	2.63 (± 21.12)

Statistical analyses

Statistical analysis title	Cohort 1 vs. Placebo
Comparison groups	Cohort 1: Lesinurad 200 mg qd + Allopurinol 300 mg qd v Pooled Placebo
Number of subjects included in analysis	112
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Point estimate	-23.62
Confidence interval	
level	95 %
sides	2-sided
lower limit	-38.42
upper limit	-8.83

Statistical analysis title	Cohort 2 vs. Placebo
Comparison groups	Cohort 2: Lesinurad 400 mg qd + Allopurinol 300 mg qd v Pooled Placebo
Number of subjects included in analysis	112
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Point estimate	-23.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-30.71
upper limit	-17.09

Statistical analysis title	Cohort 3 vs. Placebo
Comparison groups	Cohort 3: Lesinurad 600 mg + Allopurinol 300 mg qd v Pooled Placebo
Number of subjects included in analysis	113
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Point estimate	-29.25
Confidence interval	
level	95 %
sides	2-sided
lower limit	-36.08
upper limit	-22.41

Secondary: Percentage of participants whose sUA level was < 6.0 mg/dL at Day 28 by treatment group in all participants and in participants who have an sUA ≥ 6.0 mg/dL at the Baseline visit (Main Period).

End point title	Percentage of participants whose sUA level was < 6.0 mg/dL at Day 28 by treatment group in all participants and in participants who have an sUA ≥ 6.0 mg/dL at the Baseline visit (Main Period).

End point description:

End point type	Secondary

End point timeframe:

4 Weeks

End point values	Pooled Placebo	Cohort 1: Lesinurad 200 mg qd + Allopurinol 300 mg qd	Cohort 2: Lesinurad 400 mg qd + Allopurinol 300 mg qd	Cohort 3: Lesinurad 600 mg + Allopurinol 300 mg qd
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	64	40	39	40
Units: Percent (%) of Participants				
Day 28	16	29	28	33

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants whose sUA level was < 5.0 mg/dL at Day 28 by treatment group in all participants and in participants who have an sUA ≥ 6.0 mg/dL at the Baseline visit (Main Period).

End point title	Percentage of participants whose sUA level was < 5.0 mg/dL at Day 28 by treatment group in all participants and in participants who have an sUA ≥ 6.0 mg/dL at the Baseline visit (Main Period).

End point description:

End point type	Secondary

End point timeframe:

4 Weeks

End point values	Pooled Placebo	Cohort 1: Lesinurad 200 mg qd + Allopurinol 300 mg qd	Cohort 2: Lesinurad 400 mg qd + Allopurinol 300 mg qd	Cohort 3: Lesinurad 600 mg + Allopurinol 300 mg qd
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	64	40	39	40
Units: Percent (%) of Participants				
Day 28	4	13	14	23

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants whose sUA level was < 4.0 mg/dL at Day 28 by treatment group in all participants and in participants who have an sUA ≥ 6.0 mg/dL at the Baseline visit (Main Period).

End point title	Percentage of participants whose sUA level was < 4.0 mg/dL at Day 28 by treatment group in all participants and in participants who have an sUA ≥ 6.0 mg/dL at the Baseline visit (Main Period).

End point description:

End point type	Secondary

End point timeframe:

4 Weeks

End point values	Pooled Placebo	Cohort 1: Lesinurad 200 mg qd + Allopurinol 300 mg qd	Cohort 2: Lesinurad 400 mg qd + Allopurinol 300 mg qd	Cohort 3: Lesinurad 600 mg + Allopurinol 300 mg qd
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	64	40	39	40
Units: Percent (%) of Participants				
Day 28	1	4	6	7

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute reduction from Baseline in sUA levels at each visit. (Main Period)

End point title	Absolute reduction from Baseline in sUA levels at each visit. (Main Period)

End point description:

End point type	Secondary

End point timeframe:

4 Weeks

End point values	Pooled Placebo	Cohort 1: Lesinurad 200 mg qd + Allopurinol 300 mg qd	Cohort 2: Lesinurad 400 mg qd + Allopurinol 300 mg qd	Cohort 3: Lesinurad 600 mg + Allopurinol 300 mg qd
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	72	46	42	48
Units: mg/dL				
arithmetic mean (standard deviation)				
Baseline|	6.70 (± 1.29)	6.37 (± 1.27)	6.89 (± 1.37)	7.30 (± 1.53)
Day 7|	-0.05 (± 1.07)	-1.12 (± 1.08)	-1.12 (± 1.36)	-1.54 (± 1.45)
Day 14|	-0.19 (± 1.13)	-0.81 (± 1.16)	-1.30 (± 1.45)	-1.88 (± 1.51)
Day 21|	0.06 (± 1.50)	-0.93 (± 1.18)	-1.29 (± 1.63)	-1.89 (± 1.82)
Day 27|	0.01 (± 1.14)	-1.19 (± 1.47)	-1.59 (± 1.53)	-2.29 (± 1.28)
Day 28|	-0.10 (± 1.09)	-1.00 (± 1.31)	-1.38 (± 1.40)	-2.11 (± 1.45)

Statistical analyses

No statistical analyses for this end point

Secondary: Percent reduction from Baseline in sUA levels at each visit. (Main Period).

End point title	Percent reduction from Baseline in sUA levels at each visit. (Main Period).

End point description:

End point type	Secondary

End point timeframe:

4 Weeks

End point values	Pooled Placebo	Cohort 1: Lesinurad 200 mg qd + Allopurinol 300 mg qd	Cohort 2: Lesinurad 400 mg qd + Allopurinol 300 mg qd	Cohort 3: Lesinurad 600 mg + Allopurinol 300 mg qd
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	72	46	42	48
Units: Percent (%) Reduction in sUA				
arithmetic mean (standard deviation)				
Day 7|	2.15 (± 25.80)	-16.15 (± 14.62)	-15.66 (± 18.78)	-19.09 (± 17.37)
Day 14|	-0.06 (± 22.73)	-10.94 (± 15.28)	-17.63 (± 20.49)	-24.22 (± 16.27)
Day 21|	4.28 (± 30.86)	-12.73 (± 15.58)	-17.90 (± 23.94)	-23.19 (± 27.88)
Day 27|	2.63 (± 21.12)	-16.12 (± 18.89)	-22.07 (± 21.59)	-30.35 (± 14.03)
Day 28|	1.07 (± 21.51)	-13.57 (± 17.31)	-19.53 (± 20.74)	-27.86 (± 20.45)

Statistical analyses

No statistical analyses for this end point

Secondary: Percent change in 24-hour urine urate excretion from Baseline to Day 28. (Main Period)

End point title	Percent change in 24-hour urine urate excretion from Baseline to Day 28. (Main Period)

End point description:

End point type	Secondary

End point timeframe:

4 Weeks

End point values	Pooled Placebo	Cohort 1: Lesinurad 200 mg qd + Allopurinol 300 mg qd	Cohort 2: Lesinurad 400 mg qd + Allopurinol 300 mg qd	Cohort 3: Lesinurad 600 mg + Allopurinol 300 mg qd
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	72	46	42	48
Units: mg/24hr				
arithmetic mean (standard deviation)	6.7 (± 60.88)	22.3 (± 52.19)	33.5 (± 107.18)	38.3 (± 88.62)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants who experienced a gout flare (Main Period)

End point title	Percentage of participants who experienced a gout flare (Main Period)

End point description:

End point type	Secondary

End point timeframe:

4 Weeks

End point values	Pooled Placebo	Cohort 1: Lesinurad 200 mg qd + Allopurinol 300 mg qd	Cohort 2: Lesinurad 400 mg qd + Allopurinol 300 mg qd	Cohort 3: Lesinurad 600 mg + Allopurinol 300 mg qd
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	72	46	42	48
Units: Percent (%) of Participants	15	10	13	15

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants whose sUA level decreased to or is

maintained at < 6.0 mg/dL at Week 44. (Double-Blind Extension Period)	
End point title	Percentage of participants whose sUA level decreased to or is maintained at < 6.0 mg/dL at Week 44. (Double-Blind Extension Period)

End point description:

End point type	Secondary

End point timeframe:

44 Weeks

End point values	Total RDEA594	Pooled Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	61	34		
Units: Percent (%) of Participants				
Week 44 Extension	51	25		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants whose sUA level decreased to or is maintained at < 5.0 mg/dL at Week 44. (Double-Blind Extension Period)	
End point title	Percentage of participants whose sUA level decreased to or is maintained at < 5.0 mg/dL at Week 44. (Double-Blind Extension Period)

End point description:

End point type	Secondary

End point timeframe:

44 Weeks

End point values	Total RDEA594	Pooled Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	61	34		
Units: Percent (%) of Participants				
Week 44 - Extension	41	9		

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute reduction from Baseline in sUA levels at each visit (Double-Blind Extension)

End point title	Absolute reduction from Baseline in sUA levels at each visit (Double-Blind Extension)

End point description:

End point type	Secondary

End point timeframe:

44 Weeks

End point values	Pooled Placebo	Cohort 1: Lesinurad 200 mg qd + Allopurinol 300 mg qd	Cohort 2: Lesinurad 400 mg qd + Allopurinol 300 mg qd	Cohort 3: Lesinurad 600 mg + Allopurinol 300 mg qd
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	48	18	15	45
Units: mg/dL				
arithmetic mean (standard deviation)				
Baseline|	7.79 (± 1.675)	6.59 (± 1.333)	7.57 (± 2.611)	7.52 (± 1.708)
Week 2 - Extension|	-0.83 (± 1.926)	-1.13 (± 1.627)	-2.07 (± 2.033)	-1.59 (± 1.936)
Week 4 - Extension|	-1.51 (± 1.843)	-0.94 (± 1.664)	-1.56 (± 1.699)	-1.72 (± 2.162)
Week 6 - Extension|	-1.12 (± 1.823)	-1.91 (± 1.797)	-2.27 (± 2.822)	-1.76 (± 1.824)
Week 8 - Extension|	-1.12 (± 1.674)	-1.80 (± 1.905)	-2.29 (± 3.159)	-1.69 (± 2.049)
Week 10 - Extension|	-1.21 (± 1.823)	-1.60 (± 0)	-2.80 (± 0)	-2.20 (± 2.286)
Week 12 - Extension|	-1.38 (± 1.786)	-1.95 (± 1.635)	-2.74 (± 2.651)	-1.68 (± 2.564)
Week 14 - Extension|	-1.04 (± 1.494)	0 (± 0)	0 (± 0)	-1.00 (± 2.047)
Week 16 - Extension|	-1.61 (± 2.064)	-2.18 (± 1.834)	-2.21 (± 2.581)	-2.11 (± 2.535)
Week 18 - Extension|	-1.37 (± 1.405)	-0.60 (± 0)	.50 (± 0)	-2.06 (± 2.238)
Week 20 - Extension|	-1.40 (± 1.998)	-2.31 (± 1.591)	-2.48 (± 3.131)	-1.93 (± 2.150)
Week 22 - Extension|	-1.53 (± 1.688)	0 (± 0)	-4.17 (± 3.580)	-0.75 (± 2.836)
Week 24 - Extension|	-2.50 (± 0)	0 (± 0)	0 (± 0)	0 (± 0)
Week 28 - Extension|	-1.33 (± 1.922)	-2.03 (± 1.493)	-2.71 (± 2.695)	-2.12 (± 1.840)
Week 36 - Extension|	-2.06 (± 1.655)	-2.03 (± 2.147)	-2.68 (± 2.898)	-2.04 (± 2.042)
Week 44 - Extension|	-2.10 (± 1.710)	-2.31 (± 1.639)	-2.55 (± 3.052)	-2.03 (± 2.154)

Statistical analyses

No statistical analyses for this end point

Secondary: Percent reduction from Baseline in sUA levels at each visit (Double-Blind Extension)

End point title	Percent reduction from Baseline in sUA levels at each visit (Double-Blind Extension)

End point description:

End point type	Secondary

End point timeframe:

44 Weeks

End point values	Pooled Placebo	Cohort 1: Lesinurad 200 mg qd + Allopurinol 300 mg qd	Cohort 2: Lesinurad 400 mg qd + Allopurinol 300 mg qd	Cohort 3: Lesinurad 600 mg + Allopurinol 300 mg qd
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	48	18	15	45
Units: Percent (%) of Participants				
arithmetic mean (standard deviation)				
Baseline|	7.79 (± 1.675)	6.59 (± 1.333)	7.57 (± 2.611)	7.52 (± 1.708)
Week 2 - Extension|	-7.75 (± 24.484)	-15.85 (± 21.576)	-25.12 (± 17.303)	-17.70 (± 21.909)
Week 4 - Extension|	-9.67 (± 18.734)	-21.17 (± 20.475)	-19.16 (± 18.955)	-17.74 (± 20.824)
Week 6 - Extension|	-11.60 (± 19.573)	-25.56 (± 21.483)	-23.14 (± 23.962)	-20.97 (± 19.995)
Week 8 - Extension|	-11.82 (± 17.999)	-24.14 (± 22.498)	-23.04 (± 29.376)	-18.77 (± 25.88)
Week 10 - Extension|	-13.05 (± 20.267)	-25.40 (± 0)	-41.18 (± 0)	-25.49 (± 33.216)
Week 12 - Extension|	-15.48 (± 18.189)	-26.25 (± 19.959)	-31.30 (± 20.792)	-18.25 (± 35.377)
Week 14 - Extension|	-11.65 (± 34.933)	0 (± 0)	0 (± 0)	-11.65 (± 34.933)
Week 16 - Extension|	-17.55 (± 21.420)	-29.49 (± 20.642)	-24.27 (± 25.706)	-24.06 (± 35.250)
Week 18 - Extension|	-17.83 (± 17.100)	-11.32 (± 0)	7.04 (± 0)	-24.84 (± 31.399)
Week 20 - Extension|	15.63 (± 21.872)	-31.76 (± 17.488)	-25.28 (± 30.392)	-22.97 (± 27.814)
Week 22 - Extension|	-19.64 (± 20.032)	-19.64 (± 20.032)	0 (± 0)	-46.47 (± 25.079)
Week 24 - Extension|	-29.41 (± 0)	0 (± 0)	0 (± 0)	0 (± 0)
Week 28 - Extension|	-1.33 (± 1.922)	-27.99 (± 18.002)	-30.52 (± 24.583)	-26.32 (± 26.541)
Week 36 - Extension|	-25.24 (± 17.434)	-26.18 (± 29.565)	-30.56 (± 23.603)	-26.31 (± 26.460)
Week 44 - Extension|	-25.68 (± 16.126)	-31.59 (± 18.047)	-27.37 (± 28.450)	-25.66 (± 30.065)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants who experienced a gout flare (Double-Blind Extension)

End point title	Percentage of participants who experienced a gout flare (Double-Blind Extension)

End point description:

End point type	Secondary

End point timeframe:

4 Weeks

End point values	Pooled Placebo	Cohort 1: Lesinurad 200 mg qd + Allopurinol 300 mg qd	Cohort 2: Lesinurad 400 mg qd + Allopurinol 300 mg qd	Cohort 3: Lesinurad 600 mg + Allopurinol 300 mg qd
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	48	18	15	45
Units: Percent (%) of Participants	19	4	4	29

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants whose sUA level decreased to or is maintained at < 6.0 mg/dL at Month 36. (Open-Label Extension Period)

End point title	Percentage of participants whose sUA level decreased to or is maintained at < 6.0 mg/dL at Month 36. (Open-Label Extension Period)

End point description:

End point type	Secondary

End point timeframe:

Up to 60 Months

End point values	ALLO-only	ALLO-switch	PBO-switch	Lesinurad
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	4	3	12	28
Units: Percent (%) of Participants				
Month 36 - OLE Extension	4	2	9	27

End point values	Total Lesinurad			
Subject group type	Subject analysis set			
Number of subjects analysed	43			
Units: Percent (%) of Participants				
Month 36 - OLE Extension	38			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants whose sUA level decreased to or is maintained at < 5.0 mg/dL at Month 36. (Open-Label Extension Period)

End point title	Percentage of participants whose sUA level decreased to or is maintained at < 5.0 mg/dL at Month 36. (Open-Label Extension Period)

End point description:

End point type	Secondary

End point timeframe:

Up to 60 Months

End point values	ALLO-only	ALLO-switch	PBO-switch	Lesinurad
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	4	3	12	28
Units: Percent (%) of Participants				
Month 36 - OLE Extension	4	2	9	25

End point values	Total Lesinurad			
Subject group type	Subject analysis set			
Number of subjects analysed	43			
Units: Percent (%) of Participants				
Month 36 - OLE Extension	36			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent reduction from Baseline in sUA levels at each visit (Open-Label Extension Period).

End point title	Percent reduction from Baseline in sUA levels at each visit (Open-Label Extension Period).

End point description:

End point type	Secondary

End point timeframe:

Up to 60 Months

End point values	ALLO-only	ALLO-switch	PBO-switch	Lesinurad
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	8	5	20	54
Units: Percent (%)				
arithmetic mean (standard deviation)				
Baseline - OLE Extension	4.29 (± 0.853)	5.04 (± 0.699)	6.16 (± 1.225)	4.92 (± 1.477)
Month 2 - OLE Extension	2.05 (± 3.065)	-5.57 (± 24.901)	-20.24 (± 19.323)	0.61 (± 35.536)
Month 4 - OLE Extension	3.01 (± 13.001)	-5.52 (± 22.037)	-14.18 (± 24.297)	-1.13 (± 36.777)
Month 6 - OLE Extension|	0.06 (± 16.962)	-7.66 (± 25.335)	-23.13 (± 9.942)	-3.69 (± 32.608)
Month 9 - OLE Extension	6.13 (± 16.282)	20.02 (± 49.012)	-26.38 (± 17.833)	-1.55 (± 27.492)
Month 12 - OLE Extension	3.57 (± 15.923)	-0.45 (± 31.900)	-16.02 (± 32.121)	-1.75 (± 28.975)
Month 15 - OLE Extension	20.95 (± 47.880)	-39.05 (± 15.549)	-21.12 (± 39.352)	-3.31 (± 30.808)
Month 18 - OLE Extension	2.94 (± 14.276)	-3.90 (± 23.734)	-25.95 (± 16.229)	1.64 (± 27.272)
Month 21 - OLE Extension	3.30 (± 6.092)	-10.45 (± 3.900)	-9.74 (± 30.567)	-3.51 (± 29.581)
Month 24 - OLE Extension	4.17 (± 9.420)	-25.59 (± 30.147)	-12.00 (± 43.066)	-6.56 (± 30.364)
Month 27 - OLE Extension	-1.04 (± 6.635)	-16.17 (± 19.180)	-30.04 (± 19.773)	-1.37 (± 32.387)
Month 30 - OLE Extension	7.64 (± 10.486)	9.50 (± 65.700)	-27.28 (± 25.489)	-8.50 (± 27.604)
Month 32 - OLE Extension	6.22 (± 13.247)	-24.53 (± 0)	-25.98 (± 26.936)	-5.51 (± 36.135)
Month 33 - OLE Extension	0.00 (± 0)	-15.69 (± 0)	-28.93 (± 29.062)	-7.08 (± 22.807)
Month 34 - OLE Extension	7.94 (± 4.490)	-18.34 (± 11.426)	-27.52 (± 18.439)	-9.57 (± 25.251)
Month 36 - OLE Extension	-2.01 (± 5.490)	6.41 (± 19.146)	-23.07 (± 25.086)	-11.61 (± 24.349)
Month 38 - OLE Extension	3.50 (± 5.166)	-8.80 (± 20.195)	-21.04 (± 32.691)	-8.01 (± 19.273)
Month 40 - OLE Extension	5.31 (± 15.925)	-26.90 (± 19.391)	-17.91 (± 27.938)	2.08 (± 31.297)
Month 42 - OLE Extension	2.00 (± 6.558)	-5.31 (± 20.237)	-26.35 (± 21.386)	-2.62 (± 33.778)
Month 44 - OLE Extension	-4.04 (± 12.042)	21.64 (± 41.488)	-15.75 (± 24.242)	-3.86 (± 28.528)

Month 46 - OLE Extension	13.27 (± 22.891)	-17.35 (± 28.156)	-19.24 (± 32.838)	2.62 (± 29.863)
Month 48 - OLE Extension	-5.76 (± 13.184)	-12.82 (± 0)	-26.63 (± 25.675)	2.57 (± 28.594)
Month 50 - OLE Extension	-3.29 (± 5.998)	-37.18 (± 41.701)	-24.88 (± 29.375)	0.66 (± 37.373)
Month 52 - OLE Extension	-16.7 (± 0)	-25.04 (± 17.278)	-7.60 (± 50.400)	8.35 (± 43.554)
Month 54 - OLE Extension	0 (± 0)	-23.08 (± 14.505)	-17.81 (± 23.967)	13.78 (± 35.494)
Month 56 - OLE Extension	0 (± 0)	-22.40 (± 9.919)	-32.88 (± 23.681)	1.74 (± 21.235)
Month 58 - OLE Extension	0 (± 0)	-2.56 (± 0)	-9.62 (± 36.096)	3.35 (± 25.674)
Month 60 - OLE Extension	0 (± 0)	0 (± 0)	-36.77 (± 6.084)	3.13 (± 14.530)
Month 62 - OLE Extension	0 (± 0)	0 (± 0)	57.14 (± 0)	48.38 (± 65.750)
Follow-Up - OLE Extension	29.33 (± 57.288)	9.26 (± 16.155)	25.46 (± 36.841)	44.58 (± 38.853)

End point values	Total Lesinurad			
Subject group type	Subject analysis set			
Number of subjects analysed	79			
Units: Percent (%)				
arithmetic mean (standard deviation)				
Baseline - OLE Extension	5.24 (± 1.470)			
Month 2 - OLE Extension	-5.01 (± 32.589)			
Month 4 - OLE Extension	-4.60 (± 33.490)			
Month 6 - OLE Extension|	-8.69 (± 29.247)			
Month 9 - OLE Extension	-5.85 (± 29.801)			
Month 12 - OLE Extension	-5.07 (± 30.134)			
Month 15 - OLE Extension	-9.25 (± 33.729)			
Month 18 - OLE Extension	-5.41 (± 27.268)			
Month 21 - OLE Extension	-5.47 (± 29.215)			
Month 24 - OLE Extension	-8.89 (± 33.561)			
Month 27 - OLE Extension	-8.99 (± 31.404)			
Month 30 - OLE Extension	-12.23 (± 30.720)			
Month 32 - OLE Extension	-12.25 (± 33.348)			
Month 33 - OLE Extension	-13.41 (± 25.725)			
Month 34 - OLE Extension	-14.93 (± 23.319)			
Month 36 - OLE Extension	-13.55 (± 24.905)			

Month 38 - OLE Extension	-11.65 (± 23.821)			
Month 40 - OLE Extension	-5.59 (± 31.054)			
Month 42 - OLE Extension	-8.91 (± 31.442)			
Month 44 - OLE Extension	-5.69 (± 28.447)			
Month 46 - OLE Extension	-4.36 (± 31.478)			
Month 48 - OLE Extension	-5.97 (± 30.093)			
Month 50 - OLE Extension	-7.83 (± 37.149)			
Month 52 - OLE Extension	1.98 (± 44.594)			
Month 54 - OLE Extension	3.89 (± 35.097)			
Month 56 - OLE Extension	-10.37 (± 26.221)			
Month 58 - OLE Extension	-0.05 (± 27.008)			
Month 60 - OLE Extension	-4.85 (± 21.243)			
Month 62 - OLE Extension	51.30 (± 46.767)			
Follow-Up - OLE Extension	38.14 (± 38.502)			

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute reduction from Baseline in sUA levels at each visit (Open-Label Extension Period).

End point title	Absolute reduction from Baseline in sUA levels at each visit (Open-Label Extension Period).
End point description:	
End point type	Secondary
End point timeframe: Up to 60 Months	

End point values	ALLO-only	ALLO-switch	PBO-switch	Lesinurad
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	8	5	20	54
Units: mg/dL				
arithmetic mean (standard deviation)				
Baseline - OLE Extension	4.29 (± 0.853)	5.04 (± 0.699)	6.16 (± 1.225)	4.92 (± 1.477)
Month 2 - OLE Extension	0.10 (± 0.163)	-0.38 (± 1.190)	-1.25 (± 1.331)	-0.22 (± 1.877)

Month 4 - OLE Extension	0.07 (± 0.610)	-0.40 (± 1.037)	-0.89 (± 1.486)	-0.35 (± 1.933)
Month 6 - OLE Extension	-0.10 (± 0.852)	-0.50 (± 1.317)	-1.44 (± 0.683)	-0.36 (± 1.619)
Month 9 - OLE Extension	0.16 (± 0.842)	0.76 (± 2.110)	-1.65 (± 1.231)	-0.26 (± 1.555)
Month 12 - OLE Extension	0.10 (± 0.543)	-0.04 (± 1.635)	-0.90 (± 1.991)	-0.27 (± 1.702)
Month 15 - OLE Extension	0.68 (± 1.590)	-1.90 (± 0.917)	-1.37 (± 2.177)	-0.35 (± 1.672)
Month 18 - OLE Extension	0.10 (± 0.548)	-0.30 (± 1.058)	-1.56 (± 1.027)	-0.06 (± 1.562)
Month 21 - OLE Extension	0.13 (± 0.222)	-0.50 (± 0.283)	-0.64 (± 1.813)	-0.38 (± 1.770)
Month 24 - OLE Extension	0.17 (± 0.377)	-1.23 (± 1.570)	-0.93 (± 2.433)	-0.56 (± 1.660)
Month 27 - OLE Extension	-0.05 (± 0.252)	-0.87 (± 0.971)	-1.83 (± 1.177)	-0.24 (± 1.668)
Month 30 - OLE Extension	0.30 (± 0.408)	0.13 (± 2.779)	-1.61 (± 1.620)	-0.52 (± 1.411)
Month 32 - OLE Extension	0.27 (± 0.551)	-1.30 (± 0)	-1.58 (± 1.579)	-0.48 (± 1.814)
Month 33 - OLE Extension	0.00 (± 0)	-0.80 (± 0)	-1.74 (± 1.745)	-0.39 (± 1.159)
Month 34 - OLE Extension	0.30 (± 0.141)	-0.90 (± 0.707)	-1.60 (± 1.111)	-0.62 (± 1.424)
Month 36 - OLE Extension	-0.08 (± 0.206)	0.27 (± 0.929)	-1.33 (± 1.559)	-0.67 (± 1.535)
Month 38 - OLE Extension	0.13 (± 0.208)	-0.43 (± 1.041)	-1.35 (± 1.978)	-0.45 (± 1.133)
Month 40 - OLE Extension	0.20 (± 0.656)	-1.33 (± 1.041)	-1.00 (± 1.860)	0.00 (± 1.514)
Month 42 - OLE Extension|	0.07 (± 0.252)	-0.30 (± 1.058)	-1.66 (± 1.360)	-0.26 (± 1.606)
Month 44 - OLE Extension	-0.17 (± 0.503)	1.15 (± 2.051)	-1.02 (± 1.522)	-0.27 (± 1.505)
Month 46 - OLE Extension	0.53 (± 0.945)	-0.90 (± 1.414)	-1.22 (± 2.013)	0.04 (± 1.485)
Month 48 - OLE Extension	-0.23 (± 0.551)	-0.50 (± 0)	-1.70 (± 1.559)	0.11 (± 1.510)
Month 50 - OLE Extension	-0.13 (± 0.252)	-1.85 (± 2.192)	-1.53 (± 1.764)	-0.06 (± 1.771)
Month 52 - OLE Extension	-0.70 (± 0)	-1.20 (± 0.990)	-0.67 (± 2.595)	0.33 (± 1.956)
Month 54 - OLE Extension	0 (± 0)	-1.10 (± 0.849)	-1.11 (± 1.415)	0.60 (± 1.720)
Month 56 - OLE Extension	0 (± 0)	-1.05 (± 0.636)	-2.13 (± 1.619)	0.03 (± 0.934)
Month 58 - OLE Extension	0 (± 0)	-0.10 (± 0)	-0.75 (± 2.278)	-0.15 (± 1.918)
Month 60 - OLE Extension	0 (± 0)	0 (± 0)	-2.40 (± 0.141)	0.16 (± 0.635)
Month 62 - OLE Extension	0 (± 0)	0 (± 0)	3.20 (± 0)	1.90 (± 2.546)
Follow-Up - OLE Extension	1.03 (± 2.290)	0.42 (± 0.760)	1.38 (± 2.232)	1.96 (± 1.616)

End point values	Total Lesinurad			

Subject group type	Subject analysis set			
Number of subjects analysed	79			
Units: mg/dL				
arithmetic mean (standard deviation)				
Baseline - OLE Extension	5.24 (± 1.470)			
Month 2 - OLE Extension	-0.49 (± 1.760)			
Month 4 - OLE Extension	-0.49 (± 1.785)			
Month 6 - OLE Extension	-0.63 (± 1.619)			
Month 9 - OLE Extension	-0.51 (± 1.651)			
Month 12 - OLE Extension	-0.41 (± 1.768)			
Month 15 - OLE Extension	-0.67 (± 1.834)			
Month 18 - OLE Extension	-0.44 (± 1.554)			
Month 21 - OLE Extension	-0.46 (± 1.739)			
Month 24 - OLE Extension	-0.69 (± 1.850)			
Month 27 - OLE Extension	-0.65 (± 1.659)			
Month 30 - OLE Extension	-0.76 (± 1.603)			
Month 32 - OLE Extension	-0.83 (± 1.726)			
Month 33 - OLE Extension	-0.77 (± 1.430)			
Month 34 - OLE Extension	-0.90 (± 1.322)			
Month 36 - OLE Extension	-0.79 (± 1.539)			
Month 38 - OLE Extension	-0.69 (± 1.431)			
Month 40 - OLE Extension	-0.37 (± 1.640)			
Month 42 - OLE Extension|	-0.62 (± 1.605)			
Month 44 - OLE Extension	-0.40 (± 1.568)			
Month 46 - OLE Extension	-0.35 (± 1.694)			
Month 48 - OLE Extension	-0.41 (± 1.690)			
Month 50 - OLE Extension	-0.53 (± 1.876)			
Month 52 - OLE Extension	-0.04 (± 2.124)			
Month 54 - OLE Extension	0.08 (± 1.768)			
Month 56 - OLE Extension	-0.69 (± 1.486)			
Month 58 - OLE Extension	-0.29 (± 1.890)			
Month 60 - OLE Extension	-0.35 (± 1.218)			
Month 62 - OLE Extension	2.33 (± 1.950)			
Follow-Up - OLE Extension	1.73 (± 1.736)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants who experienced a gout flare (Open-Label Extension)

End point title	Percentage of participants who experienced a gout flare (Open-Label Extension)

End point description:

End point type	Secondary

End point timeframe:

Up to 60 months.

End point values	ALLO-only	ALLO-switch	PBO-switch	Lesinurad
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	8	5	20	54
Units: Percent (%) of Participants	2	2	11	18

End point values	Total Lesinurad			
Subject group type	Subject analysis set			
Number of subjects analysed	79			
Units: Percent (%) of Participants	31			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Main Period: 4 Weeks;
Double-Blind Extension Period: 44 Weeks;
Open-Label Extension Period: Up to 60 Months.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	12.0

Reporting groups

Reporting group title	Main Period Cohort 2: Lesinurad 400 mg
Reporting group description:	
Lesinurad 400 mg	
Reporting group title	Main Period Cohort 1: Lesinurad 200 mg
Reporting group description:	
Lesinurad 200 mg	
Reporting group title	Main Period: Pooled Placebo
Reporting group description:	
Pooled placebo	
Reporting group title	Main Period Cohort 3: Lesinurad 600 mg
Reporting group description:	
Lesinurad 600 mg	
Reporting group title	Double-Blind Extension Period: Lesinurad 200 mg
Reporting group description:	
Lesinurad 200 mg	
Reporting group title	Double-Blind Extension Period: Lesinurad 400 mg
Reporting group description:	
Lesinurad 400 mg	
Reporting group title	Double-Blind Extension Period: Lesinurad 600 mg
Reporting group description:	
Lesinurad 600 mg	
Reporting group title	Double-Blind Extension Period: Pooled Placebo
Reporting group description:	
Pooled Placebo	
Reporting group title	Open-Label Extension Period: Pooled Lesinurad
Reporting group description:	
Pooled Lesinurad	
Reporting group title	Open-Label Extension Period: ALLO-only
Reporting group description:	
ALLO-only	

Serious adverse events	Main Period Cohort 2: Lesinurad 400 mg	Main Period Cohort 1: Lesinurad 200 mg	Main Period: Pooled Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 72 (0.00%)
number of deaths (all causes)	0	0	0

number of deaths resulting from adverse events	0	0	0
Investigations			
WEIGHT INCREASED			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 72 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
THYROID CANCER METASTATIC			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 72 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
MUSCLE RUPTURE			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 72 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
ACUTE MYOCARDIAL INFARCTION			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 72 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ANGINA PECTORIS			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 72 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MYOCARDIAL INFARCTION			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 72 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
CAUDA EQUINA SYNDROME			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 72 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

CEREBRAL ARTERY EMBOLISM			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 72 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
GASTROINTESTINAL HAEMORRHAGE			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 72 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
COSTOCHONDRITIS			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 72 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
OSTEOARTHRITIS			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 72 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
BURSITIS INFECTIVE			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 72 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
DIABETIC KETOACIDOSIS			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 72 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
OBESITY			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 72 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Main Period Cohort 3: Lesinurad 600 mg	Double-Blind Extension Period: Lesinurad 200 mg	Double-Blind Extension Period: Lesinurad 400 mg

Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 48 (0.00%)	1 / 78 (1.28%)	1 / 60 (1.67%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Investigations			
WEIGHT INCREASED			
subjects affected / exposed	0 / 48 (0.00%)	0 / 78 (0.00%)	0 / 60 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
THYROID CANCER METASTATIC			
subjects affected / exposed	0 / 48 (0.00%)	0 / 78 (0.00%)	0 / 60 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
MUSCLE RUPTURE			
subjects affected / exposed	0 / 48 (0.00%)	0 / 78 (0.00%)	0 / 60 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
ACUTE MYOCARDIAL INFARCTION			
subjects affected / exposed	0 / 48 (0.00%)	0 / 78 (0.00%)	0 / 60 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ANGINA PECTORIS			
subjects affected / exposed	0 / 48 (0.00%)	0 / 78 (0.00%)	1 / 60 (1.67%)
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 / 48 (0.00%)	0 / 78 (0.00%)	0 / 60 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
CAUDA EQUINA SYNDROME			

subjects affected / exposed	0 / 48 (0.00%)	0 / 78 (0.00%)	0 / 60 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CEREBRAL ARTERY EMBOLISM			
subjects affected / exposed	0 / 48 (0.00%)	0 / 78 (0.00%)	0 / 60 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
GASTROINTESTINAL HAEMORRHAGE			
subjects affected / exposed	0 / 48 (0.00%)	0 / 78 (0.00%)	0 / 60 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
COSTOCHONDRITIS			
subjects affected / exposed	0 / 48 (0.00%)	0 / 78 (0.00%)	0 / 60 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
OSTEOARTHRITIS			
subjects affected / exposed	0 / 48 (0.00%)	0 / 78 (0.00%)	0 / 60 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
BURSITIS INFECTIVE			
subjects affected / exposed	0 / 48 (0.00%)	1 / 78 (1.28%)	0 / 60 (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			
DIABETIC KETOACIDOSIS			
subjects affected / exposed	0 / 48 (0.00%)	0 / 78 (0.00%)	0 / 60 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
OBESITY			

subjects affected / exposed	0 / 48 (0.00%)	0 / 78 (0.00%)	0 / 60 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Double-Blind Extension Period: Lesinurad 600 mg	Double-Blind Extension Period: Pooled Placebo	Open-Label Extension Period: Pooled Lesinurad
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 45 (2.22%)	0 / 48 (0.00%)	7 / 79 (8.86%)
number of deaths (all causes)	1	0	0
number of deaths resulting from adverse events	0	0	0
Investigations			
WEIGHT INCREASED			
subjects affected / exposed	0 / 45 (0.00%)	0 / 48 (0.00%)	1 / 79 (1.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
THYROID CANCER METASTATIC			
subjects affected / exposed	0 / 45 (0.00%)	0 / 48 (0.00%)	1 / 79 (1.27%)
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			
MUSCLE RUPTURE			
subjects affected / exposed	0 / 45 (0.00%)	0 / 48 (0.00%)	1 / 79 (1.27%)
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 disorders			
ACUTE MYOCARDIAL INFARCTION			
subjects affected / exposed	0 / 45 (0.00%)	0 / 48 (0.00%)	1 / 79 (1.27%)
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 / 45 (0.00%)	0 / 48 (0.00%)	0 / 79 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MYOCARDIAL INFARCTION			

subjects affected / exposed	0 / 45 (0.00%)	0 / 48 (0.00%)	1 / 79 (1.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
CAUDA EQUINA SYNDROME			
subjects affected / exposed	0 / 45 (0.00%)	0 / 48 (0.00%)	1 / 79 (1.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CEREBRAL ARTERY EMBOLISM			
subjects affected / exposed	1 / 45 (2.22%)	0 / 48 (0.00%)	0 / 79 (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
Gastrointestinal disorders			
GASTROINTESTINAL HAEMORRHAGE			
subjects affected / exposed	0 / 45 (0.00%)	0 / 48 (0.00%)	1 / 79 (1.27%)
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			
COSTOCHONDRITIS			
subjects affected / exposed	0 / 45 (0.00%)	0 / 48 (0.00%)	1 / 79 (1.27%)
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 / 45 (0.00%)	0 / 48 (0.00%)	1 / 79 (1.27%)
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			
BURSITIS INFECTIVE			
subjects affected / exposed	0 / 45 (0.00%)	0 / 48 (0.00%)	0 / 79 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
DIABETIC KETOACIDOSIS			

subjects affected / exposed	0 / 45 (0.00%)	0 / 48 (0.00%)	1 / 79 (1.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
OBESITY			
subjects affected / exposed	0 / 45 (0.00%)	0 / 48 (0.00%)	0 / 79 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Open-Label Extension Period: ALLO-only		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 8 (12.50%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Investigations			
WEIGHT INCREASED			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
THYROID CANCER METASTATIC			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
MUSCLE RUPTURE			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
ACUTE MYOCARDIAL INFARCTION			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
ANGINA PECTORIS			

subjects affected / exposed	0 / 8 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
MYOCARDIAL INFARCTION			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
CAUDA EQUINA SYNDROME			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
CEREBRAL ARTERY EMBOLISM			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
GASTROINTESTINAL HAEMORRHAGE			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
COSTOCHONDRITIS			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
OSTEOARTHRITIS			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
BURSITIS INFECTIVE			

subjects affected / exposed	0 / 8 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
DIABETIC KETOACIDOSIS			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
OBESITY			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Main Period Cohort 2: Lesinurad 400 mg	Main Period Cohort 1: Lesinurad 200 mg	Main Period: Pooled Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	20 / 42 (47.62%)	23 / 46 (50.00%)	35 / 72 (48.61%)
Vascular disorders			
HYPERTENSION			
subjects affected / exposed	0 / 42 (0.00%)	1 / 46 (2.17%)	0 / 72 (0.00%)
occurrences (all)	0	2	0
HYPERTENSIVE CRISIS			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
VARICOSE VEIN			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
Surgical and medical procedures			
KNEE ARTHROPLASTY			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
ASTHENIA			

subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
FATIGUE			
subjects affected / exposed	1 / 42 (2.38%)	0 / 46 (0.00%)	2 / 72 (2.78%)
occurrences (all)	2	0	3
GASTROENTERITIS			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
INFLAMMATION			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
INFLUENZA LIKE ILLNESS			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
OEDEMA PERIPHERAL			
subjects affected / exposed	0 / 42 (0.00%)	1 / 46 (2.17%)	1 / 72 (1.39%)
occurrences (all)	0	2	2
SWELLING			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
SERUM SICKNESS			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
EPIDIDYMAL CYST			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
ERECTILE DYSFUNCTION			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
COUGH			
subjects affected / exposed	0 / 42 (0.00%)	1 / 46 (2.17%)	1 / 72 (1.39%)
occurrences (all)	0	2	1
EPISTAXIS			

subjects affected / exposed	1 / 42 (2.38%)	0 / 46 (0.00%)	0 / 72 (0.00%)
occurrences (all)	2	0	0
NASAL CONGESTION			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
OROPHARYNGEAL PAIN			
subjects affected / exposed	0 / 42 (0.00%)	1 / 46 (2.17%)	0 / 72 (0.00%)
occurrences (all)	0	1	0
SINUS CONGESTION			
subjects affected / exposed	1 / 42 (2.38%)	2 / 46 (4.35%)	0 / 72 (0.00%)
occurrences (all)	1	3	0
SLEEP APNOEA SYNDROME			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
UPPER RESPIRATORY TRACT CONGESTION			
subjects affected / exposed	0 / 42 (0.00%)	1 / 46 (2.17%)	0 / 72 (0.00%)
occurrences (all)	0	2	0
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
ANXIETY			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
DEPRESSION			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
INSOMNIA			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
Investigations			
ALANINE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
ASPARTATE AMINOTRANSFERASE			

INCREASED			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
BLOOD AMYLASE INCREASED			
subjects affected / exposed	1 / 42 (2.38%)	0 / 46 (0.00%)	0 / 72 (0.00%)
occurrences (all)	2	0	0
BLOOD CREATINE PHOSPHOKINASE ABNORMAL			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
BLOOD CREATINE PHOSPHOKINASE INCREASED			
subjects affected / exposed	1 / 42 (2.38%)	1 / 46 (2.17%)	1 / 72 (1.39%)
occurrences (all)	2	1	1
BLOOD CREATININE INCREASED			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
BLOOD GLUCOSE INCREASED			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
BLOOD PRESSURE INCREASED			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
BLOOD UREA INCREASED			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
CREATININE RENAL CLEARANCE DECREASED			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
ELECTROCARDIOGRAM QT PROLONGED			
subjects affected / exposed	0 / 42 (0.00%)	1 / 46 (2.17%)	0 / 72 (0.00%)
occurrences (all)	0	1	0
ELECTROCARDIOGRAM ST SEGMENT DEPRESSION			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
GAMMA-GLUTAMYLTRANSFERASE			

INCREASED			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
LIPASE INCREASED			
subjects affected / exposed	2 / 42 (4.76%)	0 / 46 (0.00%)	1 / 72 (1.39%)
occurrences (all)	2	0	1
Injury, poisoning and procedural complications			
CONTUSION			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
EXPOSURE TO TOXIC AGENT			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
JOINT SPRAIN			
subjects affected / exposed	1 / 42 (2.38%)	1 / 46 (2.17%)	0 / 72 (0.00%)
occurrences (all)	2	2	0
MOUTH INJURY			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
MUSCLE INJURY			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
MUSCLE RUPTURE			
subjects affected / exposed	0 / 42 (0.00%)	1 / 46 (2.17%)	0 / 72 (0.00%)
occurrences (all)	0	1	0
MUSCLE STRAIN			
subjects affected / exposed	1 / 42 (2.38%)	0 / 46 (0.00%)	1 / 72 (1.39%)
occurrences (all)	2	0	2
POST-TRAUMATIC PAIN			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
PROCEDURAL PAIN			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
SKIN LACERATION			

subjects affected / exposed	1 / 42 (2.38%)	1 / 46 (2.17%)	0 / 72 (0.00%)
occurrences (all)	1	2	0
SOFT TISSUE INJURY			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
ATRIAL FIBRILLATION			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
CORONARY ARTERY DISEASE			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
CARPAL TUNNEL SYNDROME			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
DIZZINESS			
subjects affected / exposed	0 / 42 (0.00%)	1 / 46 (2.17%)	0 / 72 (0.00%)
occurrences (all)	0	1	0
HEADACHE			
subjects affected / exposed	2 / 42 (4.76%)	4 / 46 (8.70%)	1 / 72 (1.39%)
occurrences (all)	4	6	1
HYPOREFLEXIA			
subjects affected / exposed	1 / 42 (2.38%)	0 / 46 (0.00%)	0 / 72 (0.00%)
occurrences (all)	2	0	0
PARAESTHESIA			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
PRESYNCOPE			
subjects affected / exposed	0 / 42 (0.00%)	1 / 46 (2.17%)	0 / 72 (0.00%)
occurrences (all)	0	1	0
RESTLESS LEGS SYNDROME			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			

ANAEMIA			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
EOSINOPHILIA			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
LEUKOPENIA			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
NEUTROPENIA			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
CATARACT			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
SCLERAL PIGMENTATION			
subjects affected / exposed	0 / 42 (0.00%)	1 / 46 (2.17%)	0 / 72 (0.00%)
occurrences (all)	0	2	0
Gastrointestinal disorders			
ABDOMINAL DISCOMFORT			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
ABDOMINAL PAIN			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
ABDOMINAL PAIN UPPER			
subjects affected / exposed	1 / 42 (2.38%)	0 / 46 (0.00%)	0 / 72 (0.00%)
occurrences (all)	2	0	0
CONSTIPATION			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	1 / 72 (1.39%)
occurrences (all)	0	0	2
DIARRHOEA			
subjects affected / exposed	1 / 42 (2.38%)	2 / 46 (4.35%)	4 / 72 (5.56%)
occurrences (all)	1	3	4
DRY MOUTH			

subjects affected / exposed	0 / 42 (0.00%)	1 / 46 (2.17%)	1 / 72 (1.39%)
occurrences (all)	0	3	2
DUODENITIS			
subjects affected / exposed	1 / 42 (2.38%)	0 / 46 (0.00%)	0 / 72 (0.00%)
occurrences (all)	2	0	0
DYSPEPSIA			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	1 / 72 (1.39%)
occurrences (all)	0	0	2
FLATULENCE			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	1 / 72 (1.39%)
occurrences (all)	0	0	2
GASTRITIS			
subjects affected / exposed	1 / 42 (2.38%)	0 / 46 (0.00%)	0 / 72 (0.00%)
occurrences (all)	1	0	0
GASTROENTERITIS VIRAL			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
GASTROOESOPHAGEAL REFLUX DISEASE			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
HERNIA			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
HIATUS HERNIA			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
NAUSEA			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	2 / 72 (2.78%)
occurrences (all)	0	0	3
PYREXIA			
subjects affected / exposed	0 / 42 (0.00%)	1 / 46 (2.17%)	0 / 72 (0.00%)
occurrences (all)	0	1	0
VOMITING			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0

Hepatobiliary disorders			
HEPATIC STEATOSIS			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
HYPERBILIRUBINAEMIA			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
LIVER DISORDER			
subjects affected / exposed	1 / 42 (2.38%)	0 / 46 (0.00%)	0 / 72 (0.00%)
occurrences (all)	1	0	0
Skin and subcutaneous tissue disorders			
DERMATITIS			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
DERMATITIS CONTACT			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	1 / 72 (1.39%)
occurrences (all)	0	0	1
ECZEMA			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
ERYTHEMA			
subjects affected / exposed	0 / 42 (0.00%)	1 / 46 (2.17%)	0 / 72 (0.00%)
occurrences (all)	0	2	0
TINEA CRURIS			
subjects affected / exposed	1 / 42 (2.38%)	0 / 46 (0.00%)	0 / 72 (0.00%)
occurrences (all)	2	0	0
URTICARIA			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
VITILIGO			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
CALCULUS URINARY			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
HAEMATURIA			

subjects affected / exposed	1 / 42 (2.38%)	0 / 46 (0.00%)	3 / 72 (4.17%)
occurrences (all)	2	0	3
NEPHROLITHIASIS			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
PROTEINURIA			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
PYURIA			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
RENAL FAILURE CHRONIC			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
Endocrine disorders			
HYPERPARATHYROIDISM			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
HYPOTHYROIDISM			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
ARTHRALGIA			
subjects affected / exposed	1 / 42 (2.38%)	3 / 46 (6.52%)	4 / 72 (5.56%)
occurrences (all)	1	11	9
BACK PAIN			
subjects affected / exposed	1 / 42 (2.38%)	0 / 46 (0.00%)	3 / 72 (4.17%)
occurrences (all)	1	0	4
FLANK PAIN			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
JOINT SWELLING			
subjects affected / exposed	0 / 42 (0.00%)	1 / 46 (2.17%)	0 / 72 (0.00%)
occurrences (all)	0	1	0
MUSCULOSKELETAL PAIN			

subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
MUSCULOSKELETAL STIFFNESS			
subjects affected / exposed	0 / 42 (0.00%)	1 / 46 (2.17%)	1 / 72 (1.39%)
occurrences (all)	0	1	2
MYALGIA			
subjects affected / exposed	1 / 42 (2.38%)	1 / 46 (2.17%)	2 / 72 (2.78%)
occurrences (all)	2	1	3
NECK PAIN			
subjects affected / exposed	1 / 42 (2.38%)	1 / 46 (2.17%)	0 / 72 (0.00%)
occurrences (all)	2	2	0
NODULE ON EXTREMITY			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
OSTEOARTHRITIS			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
PAIN IN EXTREMITY			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
SYNOVIAL CYST			
subjects affected / exposed	0 / 42 (0.00%)	1 / 46 (2.17%)	0 / 72 (0.00%)
occurrences (all)	0	2	0
TENDON DISORDER			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
TENDONITIS			
subjects affected / exposed	0 / 42 (0.00%)	2 / 46 (4.35%)	0 / 72 (0.00%)
occurrences (all)	0	4	0
Infections and infestations			
BRONCHITIS			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
EAR INFECTION			
subjects affected / exposed	1 / 42 (2.38%)	0 / 46 (0.00%)	0 / 72 (0.00%)
occurrences (all)	2	0	0

INFLUENZA			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
NASOPHARYNGITIS			
subjects affected / exposed	0 / 42 (0.00%)	4 / 46 (8.70%)	1 / 72 (1.39%)
occurrences (all)	0	7	1
ORAL HERPES			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
PHARYNGITIS			
subjects affected / exposed	0 / 42 (0.00%)	1 / 46 (2.17%)	1 / 72 (1.39%)
occurrences (all)	0	2	2
POST PROCEDURAL INFECTION			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
RESPIRATORY TRACT INFECTION			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
SINUSITIS			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
TONSILLITIS			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
TOOTH INFECTION			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
TRACHEITIS			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
URINARY TRACT INFECTION			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
VIRAL INFECTION			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0

VIRAL UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
DEHYDRATION			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
DIABETES MELLITUS			
subjects affected / exposed	1 / 42 (2.38%)	0 / 46 (0.00%)	0 / 72 (0.00%)
occurrences (all)	2	0	0
GOUT			
subjects affected / exposed	13 / 42 (30.95%)	11 / 46 (23.91%)	16 / 72 (22.22%)
occurrences (all)	30	29	22
HYPERCHOLESTEROLAEMIA			
subjects affected / exposed	0 / 42 (0.00%)	1 / 46 (2.17%)	0 / 72 (0.00%)
occurrences (all)	0	2	0
HYPERGLYCAEMIA			
subjects affected / exposed	1 / 42 (2.38%)	0 / 46 (0.00%)	1 / 72 (1.39%)
occurrences (all)	2	0	1
HYPERLIPIDAEMIA			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
HYPERTRIGLYCERIDAEMIA			
subjects affected / exposed	0 / 42 (0.00%)	1 / 46 (2.17%)	0 / 72 (0.00%)
occurrences (all)	0	2	0
TYPE 2 DIABETES MELLITUS			
subjects affected / exposed	0 / 42 (0.00%)	0 / 46 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Main Period Cohort 3: Lesinurad 600 mg	Double-Blind Extension Period: Lesinurad 200 mg	Double-Blind Extension Period: Lesinurad 400 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	26 / 48 (54.17%)	44 / 78 (56.41%)	26 / 60 (43.33%)
Vascular disorders			
HYPERTENSION			
subjects affected / exposed	1 / 48 (2.08%)	4 / 78 (5.13%)	2 / 60 (3.33%)
occurrences (all)	1	4	2

HYPERTENSIVE CRISIS			
subjects affected / exposed	1 / 48 (2.08%)	0 / 78 (0.00%)	0 / 60 (0.00%)
occurrences (all)	1	0	0
VARICOSE VEIN			
subjects affected / exposed	0 / 48 (0.00%)	0 / 78 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
Surgical and medical procedures			
KNEE ARTHROPLASTY			
subjects affected / exposed	0 / 48 (0.00%)	0 / 78 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
ASTHENIA			
subjects affected / exposed	0 / 48 (0.00%)	0 / 78 (0.00%)	1 / 60 (1.67%)
occurrences (all)	0	0	1
FATIGUE			
subjects affected / exposed	0 / 48 (0.00%)	0 / 78 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
GASTROENTERITIS			
subjects affected / exposed	0 / 48 (0.00%)	0 / 78 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
INFLAMMATION			
subjects affected / exposed	0 / 48 (0.00%)	0 / 78 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
INFLUENZA LIKE ILLNESS			
subjects affected / exposed	0 / 48 (0.00%)	1 / 78 (1.28%)	0 / 60 (0.00%)
occurrences (all)	0	1	0
OEDEMA PERIPHERAL			
subjects affected / exposed	0 / 48 (0.00%)	0 / 78 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
SWELLING			
subjects affected / exposed	1 / 48 (2.08%)	0 / 78 (0.00%)	0 / 60 (0.00%)
occurrences (all)	1	0	0
Immune system disorders			
SERUM SICKNESS			
subjects affected / exposed	0 / 48 (0.00%)	0 / 78 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0

Reproductive system and breast disorders			
EPIDIDYMAL CYST			
subjects affected / exposed	0 / 48 (0.00%)	0 / 78 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
ERECTILE DYSFUNCTION			
subjects affected / exposed	0 / 48 (0.00%)	0 / 78 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
COUGH			
subjects affected / exposed	0 / 48 (0.00%)	1 / 78 (1.28%)	1 / 60 (1.67%)
occurrences (all)	0	1	1
EPISTAXIS			
subjects affected / exposed	0 / 48 (0.00%)	0 / 78 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
NASAL CONGESTION			
subjects affected / exposed	1 / 48 (2.08%)	1 / 78 (1.28%)	0 / 60 (0.00%)
occurrences (all)	3	1	0
OROPHARYNGEAL PAIN			
subjects affected / exposed	0 / 48 (0.00%)	0 / 78 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
SINUS CONGESTION			
subjects affected / exposed	1 / 48 (2.08%)	0 / 78 (0.00%)	0 / 60 (0.00%)
occurrences (all)	1	0	0
SLEEP APNOEA SYNDROME			
subjects affected / exposed	0 / 48 (0.00%)	0 / 78 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
UPPER RESPIRATORY TRACT CONGESTION			
subjects affected / exposed	0 / 48 (0.00%)	0 / 78 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	2 / 48 (4.17%)	5 / 78 (6.41%)	3 / 60 (5.00%)
occurrences (all)	3	6	3
Psychiatric disorders			

ANXIETY			
subjects affected / exposed	0 / 48 (0.00%)	0 / 78 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
DEPRESSION			
subjects affected / exposed	0 / 48 (0.00%)	1 / 78 (1.28%)	0 / 60 (0.00%)
occurrences (all)	0	1	0
INSOMNIA			
subjects affected / exposed	0 / 48 (0.00%)	0 / 78 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
Investigations			
ALANINE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	0 / 48 (0.00%)	0 / 78 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
ASPARTATE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	0 / 48 (0.00%)	0 / 78 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
BLOOD AMYLASE INCREASED			
subjects affected / exposed	0 / 48 (0.00%)	0 / 78 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
BLOOD CREATINE PHOSPHOKINASE ABNORMAL			
subjects affected / exposed	1 / 48 (2.08%)	0 / 78 (0.00%)	0 / 60 (0.00%)
occurrences (all)	3	0	0
BLOOD CREATINE PHOSPHOKINASE INCREASED			
subjects affected / exposed	1 / 48 (2.08%)	2 / 78 (2.56%)	2 / 60 (3.33%)
occurrences (all)	2	2	2
BLOOD CREATININE INCREASED			
subjects affected / exposed	1 / 48 (2.08%)	2 / 78 (2.56%)	2 / 60 (3.33%)
occurrences (all)	1	3	2
BLOOD GLUCOSE INCREASED			
subjects affected / exposed	0 / 48 (0.00%)	0 / 78 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
BLOOD PRESSURE INCREASED			
subjects affected / exposed	0 / 48 (0.00%)	0 / 78 (0.00%)	1 / 60 (1.67%)
occurrences (all)	0	0	1

BLOOD UREA INCREASED			
subjects affected / exposed	1 / 48 (2.08%)	0 / 78 (0.00%)	0 / 60 (0.00%)
occurrences (all)	1	0	0
CREATININE RENAL CLEARANCE DECREASED			
subjects affected / exposed	0 / 48 (0.00%)	0 / 78 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
ELECTROCARDIOGRAM QT PROLONGED			
subjects affected / exposed	0 / 48 (0.00%)	0 / 78 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
ELECTROCARDIOGRAM ST SEGMENT DEPRESSION			
subjects affected / exposed	0 / 48 (0.00%)	0 / 78 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
GAMMA-GLUTAMYLTRANSFERASE INCREASED			
subjects affected / exposed	0 / 48 (0.00%)	2 / 78 (2.56%)	0 / 60 (0.00%)
occurrences (all)	0	2	0
LIPASE INCREASED			
subjects affected / exposed	0 / 48 (0.00%)	0 / 78 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
CONTUSION			
subjects affected / exposed	0 / 48 (0.00%)	0 / 78 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
EXPOSURE TO TOXIC AGENT			
subjects affected / exposed	0 / 48 (0.00%)	0 / 78 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
JOINT SPRAIN			
subjects affected / exposed	0 / 48 (0.00%)	3 / 78 (3.85%)	0 / 60 (0.00%)
occurrences (all)	0	3	0
MOUTH INJURY			
subjects affected / exposed	0 / 48 (0.00%)	0 / 78 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
MUSCLE INJURY			
subjects affected / exposed	0 / 48 (0.00%)	0 / 78 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0

MUSCLE RUPTURE			
subjects affected / exposed	0 / 48 (0.00%)	1 / 78 (1.28%)	0 / 60 (0.00%)
occurrences (all)	0	1	0
MUSCLE STRAIN			
subjects affected / exposed	0 / 48 (0.00%)	0 / 78 (0.00%)	1 / 60 (1.67%)
occurrences (all)	0	0	1
POST-TRAUMATIC PAIN			
subjects affected / exposed	0 / 48 (0.00%)	0 / 78 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
PROCEDURAL PAIN			
subjects affected / exposed	0 / 48 (0.00%)	0 / 78 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
SKIN LACERATION			
subjects affected / exposed	0 / 48 (0.00%)	1 / 78 (1.28%)	0 / 60 (0.00%)
occurrences (all)	0	1	0
SOFT TISSUE INJURY			
subjects affected / exposed	1 / 48 (2.08%)	0 / 78 (0.00%)	0 / 60 (0.00%)
occurrences (all)	2	0	0
Cardiac disorders			
ATRIAL FIBRILLATION			
subjects affected / exposed	0 / 48 (0.00%)	0 / 78 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
CORONARY ARTERY DISEASE			
subjects affected / exposed	0 / 48 (0.00%)	0 / 78 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
CARPAL TUNNEL SYNDROME			
subjects affected / exposed	0 / 48 (0.00%)	0 / 78 (0.00%)	1 / 60 (1.67%)
occurrences (all)	0	0	1
DIZZINESS			
subjects affected / exposed	2 / 48 (4.17%)	0 / 78 (0.00%)	0 / 60 (0.00%)
occurrences (all)	4	0	0
HEADACHE			
subjects affected / exposed	1 / 48 (2.08%)	2 / 78 (2.56%)	1 / 60 (1.67%)
occurrences (all)	1	2	1
HYPOREFLEXIA			

subjects affected / exposed	0 / 48 (0.00%)	0 / 78 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
PARAESTHESIA			
subjects affected / exposed	0 / 48 (0.00%)	0 / 78 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
PRESYNCOPE			
subjects affected / exposed	0 / 48 (0.00%)	0 / 78 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
RESTLESS LEGS SYNDROME			
subjects affected / exposed	0 / 48 (0.00%)	0 / 78 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	0 / 48 (0.00%)	0 / 78 (0.00%)	1 / 60 (1.67%)
occurrences (all)	0	0	1
EOSINOPHILIA			
subjects affected / exposed	1 / 48 (2.08%)	0 / 78 (0.00%)	0 / 60 (0.00%)
occurrences (all)	3	0	0
LEUKOPENIA			
subjects affected / exposed	1 / 48 (2.08%)	0 / 78 (0.00%)	0 / 60 (0.00%)
occurrences (all)	2	0	0
NEUTROPENIA			
subjects affected / exposed	1 / 48 (2.08%)	0 / 78 (0.00%)	0 / 60 (0.00%)
occurrences (all)	1	0	0
Eye disorders			
CATARACT			
subjects affected / exposed	0 / 48 (0.00%)	0 / 78 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
SCLERAL PIGMENTATION			
subjects affected / exposed	0 / 48 (0.00%)	0 / 78 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
ABDOMINAL DISCOMFORT			
subjects affected / exposed	1 / 48 (2.08%)	1 / 78 (1.28%)	1 / 60 (1.67%)
occurrences (all)	2	1	1
ABDOMINAL PAIN			

subjects affected / exposed	0 / 48 (0.00%)	0 / 78 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
ABDOMINAL PAIN UPPER			
subjects affected / exposed	0 / 48 (0.00%)	0 / 78 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
CONSTIPATION			
subjects affected / exposed	0 / 48 (0.00%)	0 / 78 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
DIARRHOEA			
subjects affected / exposed	0 / 48 (0.00%)	1 / 78 (1.28%)	0 / 60 (0.00%)
occurrences (all)	0	1	0
DRY MOUTH			
subjects affected / exposed	0 / 48 (0.00%)	0 / 78 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
DUODENITIS			
subjects affected / exposed	0 / 48 (0.00%)	0 / 78 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
DYSPEPSIA			
subjects affected / exposed	1 / 48 (2.08%)	1 / 78 (1.28%)	0 / 60 (0.00%)
occurrences (all)	2	1	0
FLATULENCE			
subjects affected / exposed	0 / 48 (0.00%)	0 / 78 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
GASTRITIS			
subjects affected / exposed	0 / 48 (0.00%)	0 / 78 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
GASTROENTERITIS VIRAL			
subjects affected / exposed	0 / 48 (0.00%)	2 / 78 (2.56%)	1 / 60 (1.67%)
occurrences (all)	0	2	1
GASTROOESOPHAGEAL REFLUX DISEASE			
subjects affected / exposed	0 / 48 (0.00%)	0 / 78 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
HERNIA			
subjects affected / exposed	0 / 48 (0.00%)	0 / 78 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0

HIATUS HERNIA			
subjects affected / exposed	0 / 48 (0.00%)	0 / 78 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
NAUSEA			
subjects affected / exposed	0 / 48 (0.00%)	0 / 78 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
PYREXIA			
subjects affected / exposed	0 / 48 (0.00%)	0 / 78 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
VOMITING			
subjects affected / exposed	1 / 48 (2.08%)	0 / 78 (0.00%)	0 / 60 (0.00%)
occurrences (all)	2	0	0
Hepatobiliary disorders			
HEPATIC STEATOSIS			
subjects affected / exposed	0 / 48 (0.00%)	0 / 78 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
HYPERBILIRUBINAEMIA			
subjects affected / exposed	0 / 48 (0.00%)	0 / 78 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
LIVER DISORDER			
subjects affected / exposed	0 / 48 (0.00%)	0 / 78 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
DERMATITIS			
subjects affected / exposed	1 / 48 (2.08%)	0 / 78 (0.00%)	1 / 60 (1.67%)
occurrences (all)	2	0	1
DERMATITIS CONTACT			
subjects affected / exposed	0 / 48 (0.00%)	0 / 78 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
ECZEMA			
subjects affected / exposed	1 / 48 (2.08%)	1 / 78 (1.28%)	0 / 60 (0.00%)
occurrences (all)	2	1	0
ERYTHEMA			
subjects affected / exposed	0 / 48 (0.00%)	0 / 78 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
TINEA CRURIS			

subjects affected / exposed	0 / 48 (0.00%)	0 / 78 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
URTICARIA			
subjects affected / exposed	2 / 48 (4.17%)	0 / 78 (0.00%)	0 / 60 (0.00%)
occurrences (all)	4	0	0
VITILIGO			
subjects affected / exposed	0 / 48 (0.00%)	0 / 78 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
CALCULUS URINARY			
subjects affected / exposed	0 / 48 (0.00%)	0 / 78 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
HAEMATURIA			
subjects affected / exposed	0 / 48 (0.00%)	0 / 78 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
NEPHROLITHIASIS			
subjects affected / exposed	0 / 48 (0.00%)	1 / 78 (1.28%)	0 / 60 (0.00%)
occurrences (all)	0	1	0
PROTEINURIA			
subjects affected / exposed	0 / 48 (0.00%)	1 / 78 (1.28%)	0 / 60 (0.00%)
occurrences (all)	0	1	0
PYURIA			
subjects affected / exposed	1 / 48 (2.08%)	0 / 78 (0.00%)	0 / 60 (0.00%)
occurrences (all)	2	0	0
RENAL FAILURE CHRONIC			
subjects affected / exposed	0 / 48 (0.00%)	0 / 78 (0.00%)	1 / 60 (1.67%)
occurrences (all)	0	0	1
Endocrine disorders			
HYPERPARATHYROIDISM			
subjects affected / exposed	0 / 48 (0.00%)	0 / 78 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
HYPOTHYROIDISM			
subjects affected / exposed	0 / 48 (0.00%)	0 / 78 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			

ARTHRALGIA			
subjects affected / exposed	2 / 48 (4.17%)	1 / 78 (1.28%)	0 / 60 (0.00%)
occurrences (all)	3	2	0
BACK PAIN			
subjects affected / exposed	0 / 48 (0.00%)	0 / 78 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
FLANK PAIN			
subjects affected / exposed	0 / 48 (0.00%)	0 / 78 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
JOINT SWELLING			
subjects affected / exposed	0 / 48 (0.00%)	0 / 78 (0.00%)	1 / 60 (1.67%)
occurrences (all)	0	0	1
MUSCULOSKELETAL PAIN			
subjects affected / exposed	0 / 48 (0.00%)	0 / 78 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
MUSCULOSKELETAL STIFFNESS			
subjects affected / exposed	0 / 48 (0.00%)	0 / 78 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
MYALGIA			
subjects affected / exposed	0 / 48 (0.00%)	2 / 78 (2.56%)	0 / 60 (0.00%)
occurrences (all)	0	2	0
NECK PAIN			
subjects affected / exposed	0 / 48 (0.00%)	1 / 78 (1.28%)	0 / 60 (0.00%)
occurrences (all)	0	1	0
NODULE ON EXTREMITY			
subjects affected / exposed	0 / 48 (0.00%)	0 / 78 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
OSTEOARTHRITIS			
subjects affected / exposed	0 / 48 (0.00%)	1 / 78 (1.28%)	0 / 60 (0.00%)
occurrences (all)	0	1	0
PAIN IN EXTREMITY			
subjects affected / exposed	1 / 48 (2.08%)	1 / 78 (1.28%)	0 / 60 (0.00%)
occurrences (all)	2	1	0
SYNOVIAL CYST			
subjects affected / exposed	0 / 48 (0.00%)	1 / 78 (1.28%)	0 / 60 (0.00%)
occurrences (all)	0	2	0

TENDON DISORDER			
subjects affected / exposed	0 / 48 (0.00%)	0 / 78 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
TENDONITIS			
subjects affected / exposed	1 / 48 (2.08%)	0 / 78 (0.00%)	0 / 60 (0.00%)
occurrences (all)	2	0	0
Infections and infestations			
BRONCHITIS			
subjects affected / exposed	0 / 48 (0.00%)	0 / 78 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
EAR INFECTION			
subjects affected / exposed	0 / 48 (0.00%)	0 / 78 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
INFLUENZA			
subjects affected / exposed	0 / 48 (0.00%)	0 / 78 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
NASOPHARYNGITIS			
subjects affected / exposed	1 / 48 (2.08%)	1 / 78 (1.28%)	0 / 60 (0.00%)
occurrences (all)	1	1	0
ORAL HERPES			
subjects affected / exposed	0 / 48 (0.00%)	0 / 78 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
PHARYNGITIS			
subjects affected / exposed	0 / 48 (0.00%)	0 / 78 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
POST PROCEDURAL INFECTION			
subjects affected / exposed	0 / 48 (0.00%)	0 / 78 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
RESPIRATORY TRACT INFECTION			
subjects affected / exposed	0 / 48 (0.00%)	0 / 78 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
SINUSITIS			
subjects affected / exposed	0 / 48 (0.00%)	1 / 78 (1.28%)	0 / 60 (0.00%)
occurrences (all)	0	1	0
TONSILLITIS			

subjects affected / exposed	1 / 48 (2.08%)	0 / 78 (0.00%)	0 / 60 (0.00%)
occurrences (all)	2	0	0
TOOTH INFECTION			
subjects affected / exposed	1 / 48 (2.08%)	1 / 78 (1.28%)	0 / 60 (0.00%)
occurrences (all)	2	1	0
TRACHEITIS			
subjects affected / exposed	0 / 48 (0.00%)	0 / 78 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
URINARY TRACT INFECTION			
subjects affected / exposed	0 / 48 (0.00%)	0 / 78 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
VIRAL INFECTION			
subjects affected / exposed	0 / 48 (0.00%)	0 / 78 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
VIRAL UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	0 / 48 (0.00%)	0 / 78 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
DEHYDRATION			
subjects affected / exposed	0 / 48 (0.00%)	0 / 78 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
DIABETES MELLITUS			
subjects affected / exposed	0 / 48 (0.00%)	2 / 78 (2.56%)	0 / 60 (0.00%)
occurrences (all)	0	2	0
GOUT			
subjects affected / exposed	17 / 48 (35.42%)	25 / 78 (32.05%)	14 / 60 (23.33%)
occurrences (all)	43	42	20
HYPERCHOLESTEROLAEMIA			
subjects affected / exposed	0 / 48 (0.00%)	0 / 78 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
HYPERGLYCAEMIA			
subjects affected / exposed	0 / 48 (0.00%)	0 / 78 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
HYPERLIPIDAEMIA			

subjects affected / exposed	0 / 48 (0.00%)	0 / 78 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
HYPERTRIGLYCERIDAEMIA			
subjects affected / exposed	0 / 48 (0.00%)	0 / 78 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
TYPE 2 DIABETES MELLITUS			
subjects affected / exposed	1 / 48 (2.08%)	2 / 78 (2.56%)	2 / 60 (3.33%)
occurrences (all)	1	2	2

Non-serious adverse events	Double-Blind Extension Period: Lesinurad 600 mg	Double-Blind Extension Period: Pooled Placebo	Open-Label Extension Period: Pooled Lesinurad
Total subjects affected by non-serious adverse events			
subjects affected / exposed	26 / 45 (57.78%)	35 / 48 (72.92%)	60 / 79 (75.95%)
Vascular disorders			
HYPERTENSION			
subjects affected / exposed	2 / 45 (4.44%)	1 / 48 (2.08%)	9 / 79 (11.39%)
occurrences (all)	2	1	9
HYPERTENSIVE CRISIS			
subjects affected / exposed	0 / 45 (0.00%)	0 / 48 (0.00%)	0 / 79 (0.00%)
occurrences (all)	0	0	0
VARICOSE VEIN			
subjects affected / exposed	0 / 45 (0.00%)	0 / 48 (0.00%)	0 / 79 (0.00%)
occurrences (all)	0	0	0
Surgical and medical procedures			
KNEE ARTHROPLASTY			
subjects affected / exposed	1 / 45 (2.22%)	0 / 48 (0.00%)	0 / 79 (0.00%)
occurrences (all)	1	0	0
General disorders and administration site conditions			
ASTHENIA			
subjects affected / exposed	0 / 45 (0.00%)	1 / 48 (2.08%)	1 / 79 (1.27%)
occurrences (all)	0	1	1
FATIGUE			
subjects affected / exposed	0 / 45 (0.00%)	1 / 48 (2.08%)	3 / 79 (3.80%)
occurrences (all)	0	1	4
GASTROENTERITIS			
subjects affected / exposed	0 / 45 (0.00%)	1 / 48 (2.08%)	1 / 79 (1.27%)
occurrences (all)	0	1	1

INFLAMMATION			
subjects affected / exposed	1 / 45 (2.22%)	0 / 48 (0.00%)	0 / 79 (0.00%)
occurrences (all)	1	0	0
INFLUENZA LIKE ILLNESS			
subjects affected / exposed	0 / 45 (0.00%)	0 / 48 (0.00%)	3 / 79 (3.80%)
occurrences (all)	0	0	7
OEDEMA PERIPHERAL			
subjects affected / exposed	0 / 45 (0.00%)	0 / 48 (0.00%)	2 / 79 (2.53%)
occurrences (all)	0	0	2
SWELLING			
subjects affected / exposed	0 / 45 (0.00%)	0 / 48 (0.00%)	0 / 79 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
SERUM SICKNESS			
subjects affected / exposed	1 / 45 (2.22%)	0 / 48 (0.00%)	0 / 79 (0.00%)
occurrences (all)	1	0	0
Reproductive system and breast disorders			
EPIDIDYMAL CYST			
subjects affected / exposed	0 / 45 (0.00%)	1 / 48 (2.08%)	0 / 79 (0.00%)
occurrences (all)	0	1	0
ERECTILE DYSFUNCTION			
subjects affected / exposed	0 / 45 (0.00%)	0 / 48 (0.00%)	2 / 79 (2.53%)
occurrences (all)	0	0	2
Respiratory, thoracic and mediastinal disorders			
COUGH			
subjects affected / exposed	0 / 45 (0.00%)	1 / 48 (2.08%)	0 / 79 (0.00%)
occurrences (all)	0	1	0
EPISTAXIS			
subjects affected / exposed	0 / 45 (0.00%)	0 / 48 (0.00%)	2 / 79 (2.53%)
occurrences (all)	0	0	2
NASAL CONGESTION			
subjects affected / exposed	0 / 45 (0.00%)	1 / 48 (2.08%)	0 / 79 (0.00%)
occurrences (all)	0	1	0
OROPHARYNGEAL PAIN			
subjects affected / exposed	0 / 45 (0.00%)	0 / 48 (0.00%)	1 / 79 (1.27%)
occurrences (all)	0	0	1

SINUS CONGESTION			
subjects affected / exposed	1 / 45 (2.22%)	0 / 48 (0.00%)	1 / 79 (1.27%)
occurrences (all)	1	0	1
SLEEP APNOEA SYNDROME			
subjects affected / exposed	0 / 45 (0.00%)	0 / 48 (0.00%)	2 / 79 (2.53%)
occurrences (all)	0	0	2
UPPER RESPIRATORY TRACT CONGESTION			
subjects affected / exposed	0 / 45 (0.00%)	0 / 48 (0.00%)	0 / 79 (0.00%)
occurrences (all)	0	0	0
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	0 / 45 (0.00%)	2 / 48 (4.17%)	9 / 79 (11.39%)
occurrences (all)	0	2	18
Psychiatric disorders			
ANXIETY			
subjects affected / exposed	0 / 45 (0.00%)	0 / 48 (0.00%)	3 / 79 (3.80%)
occurrences (all)	0	0	3
DEPRESSION			
subjects affected / exposed	0 / 45 (0.00%)	0 / 48 (0.00%)	2 / 79 (2.53%)
occurrences (all)	0	0	2
INSOMNIA			
subjects affected / exposed	0 / 45 (0.00%)	0 / 48 (0.00%)	2 / 79 (2.53%)
occurrences (all)	0	0	3
Investigations			
ALANINE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	0 / 45 (0.00%)	0 / 48 (0.00%)	4 / 79 (5.06%)
occurrences (all)	0	0	5
ASPARTATE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	1 / 45 (2.22%)	0 / 48 (0.00%)	4 / 79 (5.06%)
occurrences (all)	1	0	4
BLOOD AMYLASE INCREASED			
subjects affected / exposed	0 / 45 (0.00%)	0 / 48 (0.00%)	1 / 79 (1.27%)
occurrences (all)	0	0	1
BLOOD CREATINE PHOSPHOKINASE ABNORMAL			

subjects affected / exposed	0 / 45 (0.00%)	0 / 48 (0.00%)	0 / 79 (0.00%)
occurrences (all)	0	0	0
BLOOD CREATINE PHOSPHOKINASE INCREASED			
subjects affected / exposed	0 / 45 (0.00%)	3 / 48 (6.25%)	5 / 79 (6.33%)
occurrences (all)	0	4	5
BLOOD CREATININE INCREASED			
subjects affected / exposed	3 / 45 (6.67%)	1 / 48 (2.08%)	12 / 79 (15.19%)
occurrences (all)	3	1	15
BLOOD GLUCOSE INCREASED			
subjects affected / exposed	0 / 45 (0.00%)	0 / 48 (0.00%)	1 / 79 (1.27%)
occurrences (all)	0	0	1
BLOOD PRESSURE INCREASED			
subjects affected / exposed	0 / 45 (0.00%)	1 / 48 (2.08%)	0 / 79 (0.00%)
occurrences (all)	0	1	0
BLOOD UREA INCREASED			
subjects affected / exposed	0 / 45 (0.00%)	0 / 48 (0.00%)	1 / 79 (1.27%)
occurrences (all)	0	0	1
CREATININE RENAL CLEARANCE DECREASED			
subjects affected / exposed	2 / 45 (4.44%)	0 / 48 (0.00%)	0 / 79 (0.00%)
occurrences (all)	2	0	0
ELECTROCARDIOGRAM QT PROLONGED			
subjects affected / exposed	0 / 45 (0.00%)	0 / 48 (0.00%)	0 / 79 (0.00%)
occurrences (all)	0	0	0
ELECTROCARDIOGRAM ST SEGMENT DEPRESSION			
subjects affected / exposed	0 / 45 (0.00%)	1 / 48 (2.08%)	0 / 79 (0.00%)
occurrences (all)	0	3	0
GAMMA-GLUTAMYLTRANSFERASE INCREASED			
subjects affected / exposed	0 / 45 (0.00%)	1 / 48 (2.08%)	3 / 79 (3.80%)
occurrences (all)	0	1	3
LIPASE INCREASED			
subjects affected / exposed	0 / 45 (0.00%)	0 / 48 (0.00%)	1 / 79 (1.27%)
occurrences (all)	0	0	1
Injury, poisoning and procedural complications			

CONTUSION			
subjects affected / exposed	0 / 45 (0.00%)	2 / 48 (4.17%)	4 / 79 (5.06%)
occurrences (all)	0	2	7
EXPOSURE TO TOXIC AGENT			
subjects affected / exposed	0 / 45 (0.00%)	0 / 48 (0.00%)	0 / 79 (0.00%)
occurrences (all)	0	0	0
JOINT SPRAIN			
subjects affected / exposed	0 / 45 (0.00%)	0 / 48 (0.00%)	4 / 79 (5.06%)
occurrences (all)	0	0	4
MOUTH INJURY			
subjects affected / exposed	0 / 45 (0.00%)	0 / 48 (0.00%)	2 / 79 (2.53%)
occurrences (all)	0	0	2
MUSCLE INJURY			
subjects affected / exposed	0 / 45 (0.00%)	0 / 48 (0.00%)	1 / 79 (1.27%)
occurrences (all)	0	0	1
MUSCLE RUPTURE			
subjects affected / exposed	0 / 45 (0.00%)	0 / 48 (0.00%)	0 / 79 (0.00%)
occurrences (all)	0	0	0
MUSCLE STRAIN			
subjects affected / exposed	0 / 45 (0.00%)	0 / 48 (0.00%)	5 / 79 (6.33%)
occurrences (all)	0	0	7
POST-TRAUMATIC PAIN			
subjects affected / exposed	1 / 45 (2.22%)	0 / 48 (0.00%)	0 / 79 (0.00%)
occurrences (all)	1	0	0
PROCEDURAL PAIN			
subjects affected / exposed	0 / 45 (0.00%)	0 / 48 (0.00%)	2 / 79 (2.53%)
occurrences (all)	0	0	2
SKIN LACERATION			
subjects affected / exposed	0 / 45 (0.00%)	0 / 48 (0.00%)	0 / 79 (0.00%)
occurrences (all)	0	0	0
SOFT TISSUE INJURY			
subjects affected / exposed	0 / 45 (0.00%)	0 / 48 (0.00%)	0 / 79 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
ATRIAL FIBRILLATION			

subjects affected / exposed	1 / 45 (2.22%)	0 / 48 (0.00%)	2 / 79 (2.53%)
occurrences (all)	1	0	2
CORONARY ARTERY DISEASE			
subjects affected / exposed	0 / 45 (0.00%)	0 / 48 (0.00%)	2 / 79 (2.53%)
occurrences (all)	0	0	2
Nervous system disorders			
CARPAL TUNNEL SYNDROME			
subjects affected / exposed	0 / 45 (0.00%)	1 / 48 (2.08%)	1 / 79 (1.27%)
occurrences (all)	0	1	2
DIZZINESS			
subjects affected / exposed	0 / 45 (0.00%)	0 / 48 (0.00%)	4 / 79 (5.06%)
occurrences (all)	0	0	4
HEADACHE			
subjects affected / exposed	0 / 45 (0.00%)	2 / 48 (4.17%)	1 / 79 (1.27%)
occurrences (all)	0	3	1
HYPOREFLEXIA			
subjects affected / exposed	0 / 45 (0.00%)	0 / 48 (0.00%)	0 / 79 (0.00%)
occurrences (all)	0	0	0
PARAESTHESIA			
subjects affected / exposed	0 / 45 (0.00%)	0 / 48 (0.00%)	3 / 79 (3.80%)
occurrences (all)	0	0	3
PRESYNCOPE			
subjects affected / exposed	0 / 45 (0.00%)	0 / 48 (0.00%)	0 / 79 (0.00%)
occurrences (all)	0	0	0
RESTLESS LEGS SYNDROME			
subjects affected / exposed	0 / 45 (0.00%)	0 / 48 (0.00%)	0 / 79 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	0 / 45 (0.00%)	0 / 48 (0.00%)	2 / 79 (2.53%)
occurrences (all)	0	0	2
EOSINOPHILIA			
subjects affected / exposed	1 / 45 (2.22%)	0 / 48 (0.00%)	0 / 79 (0.00%)
occurrences (all)	1	0	0
LEUKOPENIA			

subjects affected / exposed	0 / 45 (0.00%)	0 / 48 (0.00%)	0 / 79 (0.00%)
occurrences (all)	0	0	0
NEUTROPENIA			
subjects affected / exposed	0 / 45 (0.00%)	0 / 48 (0.00%)	0 / 79 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
CATARACT			
subjects affected / exposed	0 / 45 (0.00%)	0 / 48 (0.00%)	2 / 79 (2.53%)
occurrences (all)	0	0	2
SCLERAL PIGMENTATION			
subjects affected / exposed	0 / 45 (0.00%)	0 / 48 (0.00%)	0 / 79 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
ABDOMINAL DISCOMFORT			
subjects affected / exposed	0 / 45 (0.00%)	0 / 48 (0.00%)	1 / 79 (1.27%)
occurrences (all)	0	0	2
ABDOMINAL PAIN			
subjects affected / exposed	0 / 45 (0.00%)	1 / 48 (2.08%)	1 / 79 (1.27%)
occurrences (all)	0	1	1
ABDOMINAL PAIN UPPER			
subjects affected / exposed	0 / 45 (0.00%)	0 / 48 (0.00%)	1 / 79 (1.27%)
occurrences (all)	0	0	1
CONSTIPATION			
subjects affected / exposed	0 / 45 (0.00%)	0 / 48 (0.00%)	3 / 79 (3.80%)
occurrences (all)	0	0	3
DIARRHOEA			
subjects affected / exposed	2 / 45 (4.44%)	1 / 48 (2.08%)	1 / 79 (1.27%)
occurrences (all)	2	1	1
DRY MOUTH			
subjects affected / exposed	0 / 45 (0.00%)	0 / 48 (0.00%)	0 / 79 (0.00%)
occurrences (all)	0	0	0
DUODENITIS			
subjects affected / exposed	0 / 45 (0.00%)	0 / 48 (0.00%)	0 / 79 (0.00%)
occurrences (all)	0	0	0
DYSPEPSIA			

subjects affected / exposed	0 / 45 (0.00%)	1 / 48 (2.08%)	0 / 79 (0.00%)
occurrences (all)	0	2	0
FLATULENCE			
subjects affected / exposed	0 / 45 (0.00%)	1 / 48 (2.08%)	0 / 79 (0.00%)
occurrences (all)	0	1	0
GASTRITIS			
subjects affected / exposed	1 / 45 (2.22%)	1 / 48 (2.08%)	1 / 79 (1.27%)
occurrences (all)	1	1	1
GASTROENTERITIS VIRAL			
subjects affected / exposed	0 / 45 (0.00%)	0 / 48 (0.00%)	2 / 79 (2.53%)
occurrences (all)	0	0	2
GASTROOESOPHAGEAL REFLUX DISEASE			
subjects affected / exposed	0 / 45 (0.00%)	0 / 48 (0.00%)	2 / 79 (2.53%)
occurrences (all)	0	0	2
HERNIA			
subjects affected / exposed	0 / 45 (0.00%)	1 / 48 (2.08%)	0 / 79 (0.00%)
occurrences (all)	0	1	0
HIATUS HERNIA			
subjects affected / exposed	0 / 45 (0.00%)	0 / 48 (0.00%)	0 / 79 (0.00%)
occurrences (all)	0	0	0
NAUSEA			
subjects affected / exposed	0 / 45 (0.00%)	0 / 48 (0.00%)	2 / 79 (2.53%)
occurrences (all)	0	0	2
PYREXIA			
subjects affected / exposed	0 / 45 (0.00%)	0 / 48 (0.00%)	0 / 79 (0.00%)
occurrences (all)	0	0	0
VOMITING			
subjects affected / exposed	0 / 45 (0.00%)	0 / 48 (0.00%)	0 / 79 (0.00%)
occurrences (all)	0	0	0
Hepatobiliary disorders			
HEPATIC STEATOSIS			
subjects affected / exposed	0 / 45 (0.00%)	0 / 48 (0.00%)	2 / 79 (2.53%)
occurrences (all)	0	0	2
HYPERBILIRUBINAEMIA			

subjects affected / exposed	1 / 45 (2.22%)	0 / 48 (0.00%)	0 / 79 (0.00%)
occurrences (all)	1	0	0
LIVER DISORDER			
subjects affected / exposed	0 / 45 (0.00%)	0 / 48 (0.00%)	0 / 79 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
DERMATITIS			
subjects affected / exposed	0 / 45 (0.00%)	0 / 48 (0.00%)	0 / 79 (0.00%)
occurrences (all)	0	0	0
DERMATITIS CONTACT			
subjects affected / exposed	2 / 45 (4.44%)	1 / 48 (2.08%)	1 / 79 (1.27%)
occurrences (all)	3	1	1
ECZEMA			
subjects affected / exposed	0 / 45 (0.00%)	0 / 48 (0.00%)	1 / 79 (1.27%)
occurrences (all)	0	0	1
ERYTHEMA			
subjects affected / exposed	0 / 45 (0.00%)	0 / 48 (0.00%)	0 / 79 (0.00%)
occurrences (all)	0	0	0
TINEA CRURIS			
subjects affected / exposed	0 / 45 (0.00%)	0 / 48 (0.00%)	0 / 79 (0.00%)
occurrences (all)	0	0	0
URTICARIA			
subjects affected / exposed	0 / 45 (0.00%)	0 / 48 (0.00%)	0 / 79 (0.00%)
occurrences (all)	0	0	0
VITILIGO			
subjects affected / exposed	0 / 45 (0.00%)	0 / 48 (0.00%)	0 / 79 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
CALCULUS URINARY			
subjects affected / exposed	0 / 45 (0.00%)	0 / 48 (0.00%)	2 / 79 (2.53%)
occurrences (all)	0	0	2
HAEMATURIA			
subjects affected / exposed	0 / 45 (0.00%)	1 / 48 (2.08%)	3 / 79 (3.80%)
occurrences (all)	0	2	4
NEPHROLITHIASIS			

subjects affected / exposed	0 / 45 (0.00%)	1 / 48 (2.08%)	3 / 79 (3.80%)
occurrences (all)	0	1	3
PROTEINURIA			
subjects affected / exposed	0 / 45 (0.00%)	1 / 48 (2.08%)	0 / 79 (0.00%)
occurrences (all)	0	1	0
PYURIA			
subjects affected / exposed	0 / 45 (0.00%)	0 / 48 (0.00%)	0 / 79 (0.00%)
occurrences (all)	0	0	0
RENAL FAILURE CHRONIC			
subjects affected / exposed	0 / 45 (0.00%)	0 / 48 (0.00%)	2 / 79 (2.53%)
occurrences (all)	0	0	2
Endocrine disorders			
HYPERPARATHYROIDISM			
subjects affected / exposed	1 / 45 (2.22%)	0 / 48 (0.00%)	0 / 79 (0.00%)
occurrences (all)	1	0	0
HYPOTHYROIDISM			
subjects affected / exposed	0 / 45 (0.00%)	0 / 48 (0.00%)	3 / 79 (3.80%)
occurrences (all)	0	0	3
Musculoskeletal and connective tissue disorders			
ARTHRALGIA			
subjects affected / exposed	1 / 45 (2.22%)	2 / 48 (4.17%)	2 / 79 (2.53%)
occurrences (all)	1	2	2
BACK PAIN			
subjects affected / exposed	1 / 45 (2.22%)	2 / 48 (4.17%)	8 / 79 (10.13%)
occurrences (all)	1	3	8
FLANK PAIN			
subjects affected / exposed	1 / 45 (2.22%)	0 / 48 (0.00%)	1 / 79 (1.27%)
occurrences (all)	1	0	1
JOINT SWELLING			
subjects affected / exposed	0 / 45 (0.00%)	0 / 48 (0.00%)	1 / 79 (1.27%)
occurrences (all)	0	0	2
MUSCULOSKELETAL PAIN			
subjects affected / exposed	2 / 45 (4.44%)	0 / 48 (0.00%)	1 / 79 (1.27%)
occurrences (all)	2	0	1
MUSCULOSKELETAL STIFFNESS			

subjects affected / exposed	0 / 45 (0.00%)	1 / 48 (2.08%)	0 / 79 (0.00%)
occurrences (all)	0	1	0
MYALGIA			
subjects affected / exposed	0 / 45 (0.00%)	0 / 48 (0.00%)	3 / 79 (3.80%)
occurrences (all)	0	0	4
NECK PAIN			
subjects affected / exposed	0 / 45 (0.00%)	0 / 48 (0.00%)	0 / 79 (0.00%)
occurrences (all)	0	0	0
NODULE ON EXTREMITY			
subjects affected / exposed	0 / 45 (0.00%)	0 / 48 (0.00%)	0 / 79 (0.00%)
occurrences (all)	0	0	0
OSTEOARTHRITIS			
subjects affected / exposed	1 / 45 (2.22%)	1 / 48 (2.08%)	3 / 79 (3.80%)
occurrences (all)	1	1	3
PAIN IN EXTREMITY			
subjects affected / exposed	0 / 45 (0.00%)	0 / 48 (0.00%)	7 / 79 (8.86%)
occurrences (all)	0	0	7
SYNOVIAL CYST			
subjects affected / exposed	0 / 45 (0.00%)	0 / 48 (0.00%)	0 / 79 (0.00%)
occurrences (all)	0	0	0
TENDON DISORDER			
subjects affected / exposed	0 / 45 (0.00%)	0 / 48 (0.00%)	1 / 79 (1.27%)
occurrences (all)	0	0	1
TENDONITIS			
subjects affected / exposed	0 / 45 (0.00%)	0 / 48 (0.00%)	2 / 79 (2.53%)
occurrences (all)	0	0	2
Infections and infestations			
BRONCHITIS			
subjects affected / exposed	0 / 45 (0.00%)	1 / 48 (2.08%)	5 / 79 (6.33%)
occurrences (all)	0	1	5
EAR INFECTION			
subjects affected / exposed	0 / 45 (0.00%)	0 / 48 (0.00%)	0 / 79 (0.00%)
occurrences (all)	0	0	0
INFLUENZA			
subjects affected / exposed	0 / 45 (0.00%)	1 / 48 (2.08%)	2 / 79 (2.53%)
occurrences (all)	0	1	2

NASOPHARYNGITIS			
subjects affected / exposed	0 / 45 (0.00%)	2 / 48 (4.17%)	4 / 79 (5.06%)
occurrences (all)	0	3	5
ORAL HERPES			
subjects affected / exposed	0 / 45 (0.00%)	1 / 48 (2.08%)	0 / 79 (0.00%)
occurrences (all)	0	1	0
PHARYNGITIS			
subjects affected / exposed	0 / 45 (0.00%)	1 / 48 (2.08%)	1 / 79 (1.27%)
occurrences (all)	0	1	1
POST PROCEDURAL INFECTION			
subjects affected / exposed	1 / 45 (2.22%)	0 / 48 (0.00%)	0 / 79 (0.00%)
occurrences (all)	1	0	0
RESPIRATORY TRACT INFECTION			
subjects affected / exposed	0 / 45 (0.00%)	0 / 48 (0.00%)	2 / 79 (2.53%)
occurrences (all)	0	0	2
SINUSITIS			
subjects affected / exposed	2 / 45 (4.44%)	0 / 48 (0.00%)	2 / 79 (2.53%)
occurrences (all)	2	0	2
TONSILLITIS			
subjects affected / exposed	0 / 45 (0.00%)	0 / 48 (0.00%)	2 / 79 (2.53%)
occurrences (all)	0	0	2
TOOTH INFECTION			
subjects affected / exposed	1 / 45 (2.22%)	0 / 48 (0.00%)	2 / 79 (2.53%)
occurrences (all)	1	0	2
TRACHEITIS			
subjects affected / exposed	1 / 45 (2.22%)	1 / 48 (2.08%)	0 / 79 (0.00%)
occurrences (all)	1	1	0
URINARY TRACT INFECTION			
subjects affected / exposed	0 / 45 (0.00%)	2 / 48 (4.17%)	0 / 79 (0.00%)
occurrences (all)	0	2	0
VIRAL INFECTION			
subjects affected / exposed	0 / 45 (0.00%)	1 / 48 (2.08%)	0 / 79 (0.00%)
occurrences (all)	0	1	0
VIRAL UPPER RESPIRATORY TRACT INFECTION			

subjects affected / exposed	1 / 45 (2.22%)	1 / 48 (2.08%)	0 / 79 (0.00%)
occurrences (all)	1	1	0
Metabolism and nutrition disorders			
DEHYDRATION			
subjects affected / exposed	0 / 45 (0.00%)	0 / 48 (0.00%)	2 / 79 (2.53%)
occurrences (all)	0	0	2
DIABETES MELLITUS			
subjects affected / exposed	0 / 45 (0.00%)	0 / 48 (0.00%)	0 / 79 (0.00%)
occurrences (all)	0	0	0
GOUT			
subjects affected / exposed	16 / 45 (35.56%)	19 / 48 (39.58%)	31 / 79 (39.24%)
occurrences (all)	39	37	99
HYPERCHOLESTEROLAEMIA			
subjects affected / exposed	0 / 45 (0.00%)	0 / 48 (0.00%)	2 / 79 (2.53%)
occurrences (all)	0	0	2
HYPERGLYCAEMIA			
subjects affected / exposed	0 / 45 (0.00%)	1 / 48 (2.08%)	2 / 79 (2.53%)
occurrences (all)	0	1	2
HYPERLIPIDAEMIA			
subjects affected / exposed	0 / 45 (0.00%)	0 / 48 (0.00%)	2 / 79 (2.53%)
occurrences (all)	0	0	2
HYPERTRIGLYCERIDAEMIA			
subjects affected / exposed	1 / 45 (2.22%)	1 / 48 (2.08%)	3 / 79 (3.80%)
occurrences (all)	1	1	3
TYPE 2 DIABETES MELLITUS			
subjects affected / exposed	1 / 45 (2.22%)	1 / 48 (2.08%)	5 / 79 (6.33%)
occurrences (all)	1	1	6

Non-serious adverse events	Open-Label Extension Period: ALLO-only		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 8 (75.00%)		
Vascular disorders			
HYPERTENSION			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
HYPERTENSIVE CRISIS			

subjects affected / exposed occurrences (all) VARICOSE VEIN subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0 1 / 8 (12.50%) 1		
Surgical and medical procedures KNEE ARTHROPLASTY subjects affected / exposed occurrences (all)	 0 / 8 (0.00%) 0		
General disorders and administration site conditions ASTHENIA subjects affected / exposed occurrences (all) FATIGUE subjects affected / exposed occurrences (all) GASTROENTERITIS subjects affected / exposed occurrences (all) INFLAMMATION subjects affected / exposed occurrences (all) INFLUENZA LIKE ILLNESS subjects affected / exposed occurrences (all) OEDEMA PERIPHERAL subjects affected / exposed occurrences (all) SWELLING subjects affected / exposed occurrences (all)	 0 / 8 (0.00%) 0 0 / 8 (0.00%) 0 0 / 8 (0.00%) 0 0 / 8 (0.00%) 0 0 / 8 (0.00%) 0 0 / 8 (0.00%) 0 0 / 8 (0.00%) 0		
Immune system disorders SERUM SICKNESS subjects affected / exposed occurrences (all)	 0 / 8 (0.00%) 0		
Reproductive system and breast disorders			

EPIDIDYMAL CYST			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
ERECTILE DYSFUNCTION			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			
COUGH			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
EPISTAXIS			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
NASAL CONGESTION			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
OROPHARYNGEAL PAIN			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
SINUS CONGESTION			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
SLEEP APNOEA SYNDROME			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
UPPER RESPIRATORY TRACT CONGESTION			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Psychiatric disorders			
ANXIETY			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		

DEPRESSION			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
INSOMNIA			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Investigations			
ALANINE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
ASPARTATE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
BLOOD AMYLASE INCREASED			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
BLOOD CREATINE PHOSPHOKINASE ABNORMAL			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
BLOOD CREATINE PHOSPHOKINASE INCREASED			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
BLOOD CREATININE INCREASED			
subjects affected / exposed	2 / 8 (25.00%)		
occurrences (all)	2		
BLOOD GLUCOSE INCREASED			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
BLOOD PRESSURE INCREASED			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
BLOOD UREA INCREASED			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		

CREATININE RENAL CLEARANCE DECREASED			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
ELECTROCARDIOGRAM QT PROLONGED			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
ELECTROCARDIOGRAM ST SEGMENT DEPRESSION			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
GAMMA-GLUTAMYLTRANSFERASE INCREASED			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
LIPASE INCREASED			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Injury, poisoning and procedural complications			
CONTUSION			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
EXPOSURE TO TOXIC AGENT			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
JOINT SPRAIN			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
MOUTH INJURY			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
MUSCLE INJURY			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
MUSCLE RUPTURE			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		

MUSCLE STRAIN			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
POST-TRAUMATIC PAIN			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
PROCEDURAL PAIN			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
SKIN LACERATION			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
SOFT TISSUE INJURY			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Cardiac disorders			
ATRIAL FIBRILLATION			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
CORONARY ARTERY DISEASE			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
CARPAL TUNNEL SYNDROME			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
DIZZINESS			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
HEADACHE			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
HYPOREFLEXIA			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
PARAESTHESIA			

subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
PRESYNCOPE			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
RESTLESS LEGS SYNDROME			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
EOSINOPHILIA			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
LEUKOPENIA			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
NEUTROPENIA			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Eye disorders			
CATARACT			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
SCLERAL PIGMENTATION			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
ABDOMINAL DISCOMFORT			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
ABDOMINAL PAIN			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
ABDOMINAL PAIN UPPER			

subjects affected / exposed	0 / 8 (0.00%)			
occurrences (all)	0			
CONSTIPATION				
subjects affected / exposed	0 / 8 (0.00%)			
occurrences (all)	0			
DIARRHOEA				
subjects affected / exposed	0 / 8 (0.00%)			
occurrences (all)	0			
DRY MOUTH				
subjects affected / exposed	0 / 8 (0.00%)			
occurrences (all)	0			
DUODENITIS				
subjects affected / exposed	0 / 8 (0.00%)			
occurrences (all)	0			
DYSPEPSIA				
subjects affected / exposed	0 / 8 (0.00%)			
occurrences (all)	0			
FLATULENCE				
subjects affected / exposed	0 / 8 (0.00%)			
occurrences (all)	0			
GASTRITIS				
subjects affected / exposed	0 / 8 (0.00%)			
occurrences (all)	0			
GASTROENTERITIS VIRAL				
subjects affected / exposed	0 / 8 (0.00%)			
occurrences (all)	0			
GASTROOESOPHAGEAL REFLUX DISEASE				
subjects affected / exposed	0 / 8 (0.00%)			
occurrences (all)	0			
HERNIA				
subjects affected / exposed	0 / 8 (0.00%)			
occurrences (all)	0			
HIATUS HERNIA				
subjects affected / exposed	1 / 8 (12.50%)			
occurrences (all)	1			

NAUSEA			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
PYREXIA			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
VOMITING			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Hepatobiliary disorders			
HEPATIC STEATOSIS			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
HYPERBILIRUBINAEMIA			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
LIVER DISORDER			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Skin and subcutaneous tissue disorders			
DERMATITIS			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
DERMATITIS CONTACT			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
ECZEMA			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
ERYTHEMA			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
TINEA CRURIS			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
URTICARIA			

subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
VITILIGO			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Renal and urinary disorders			
CALCULUS URINARY			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
HAEMATURIA			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
NEPHROLITHIASIS			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
PROTEINURIA			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
PYURIA			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
RENAL FAILURE CHRONIC			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Endocrine disorders			
HYPERPARATHYROIDISM			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
HYPOTHYROIDISM			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Musculoskeletal and connective tissue disorders			
ARTHRALGIA			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
BACK PAIN			

subjects affected / exposed	0 / 8 (0.00%)			
occurrences (all)	0			
FLANK PAIN				
subjects affected / exposed	0 / 8 (0.00%)			
occurrences (all)	0			
JOINT SWELLING				
subjects affected / exposed	0 / 8 (0.00%)			
occurrences (all)	0			
MUSCULOSKELETAL PAIN				
subjects affected / exposed	0 / 8 (0.00%)			
occurrences (all)	0			
MUSCULOSKELETAL STIFFNESS				
subjects affected / exposed	0 / 8 (0.00%)			
occurrences (all)	0			
MYALGIA				
subjects affected / exposed	0 / 8 (0.00%)			
occurrences (all)	0			
NECK PAIN				
subjects affected / exposed	0 / 8 (0.00%)			
occurrences (all)	0			
NODULE ON EXTREMITY				
subjects affected / exposed	1 / 8 (12.50%)			
occurrences (all)	1			
OSTEOARTHRITIS				
subjects affected / exposed	0 / 8 (0.00%)			
occurrences (all)	0			
PAIN IN EXTREMITY				
subjects affected / exposed	0 / 8 (0.00%)			
occurrences (all)	0			
SYNOVIAL CYST				
subjects affected / exposed	0 / 8 (0.00%)			
occurrences (all)	0			
TENDON DISORDER				
subjects affected / exposed	1 / 8 (12.50%)			
occurrences (all)	1			
TENDONITIS				

subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Infections and infestations			
BRONCHITIS			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
EAR INFECTION			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
INFLUENZA			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
NASOPHARYNGITIS			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
ORAL HERPES			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
PHARYNGITIS			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
POST PROCEDURAL INFECTION			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
RESPIRATORY TRACT INFECTION			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
SINUSITIS			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
TONSILLITIS			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
TOOTH INFECTION			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		

TRACHEITIS			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
URINARY TRACT INFECTION			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
VIRAL INFECTION			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
VIRAL UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Metabolism and nutrition disorders			
DEHYDRATION			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
DIABETES MELLITUS			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
GOUT			
subjects affected / exposed	2 / 8 (25.00%)		
occurrences (all)	3		
HYPERCHOLESTEROLAEMIA			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
HYPERGLYCAEMIA			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
HYPERLIPIDAEMIA			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
HYPERTRIGLYCERIDAEMIA			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
TYPE 2 DIABETES MELLITUS			

subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
20 January 2010	To remove the 300 mg dose level of RDEA594 from the study based on data that has recently become available from Cohort 2 of the completed RDEA594-201 pilot pharmacodynamic study.
12 February 2010	To allow for extended dosing of subjects by adding an optional double-blind Extension Period for subjects who successfully complete the 4-week Double-Blind Treatment Period and attend the follow-up visit.
29 March 2010	To broaden the age range for study participants from a maximum of 75 years to a maximum of 80 years of age and to allow a shorter minimum duration for prior allopurinol use for entry into the study.
01 April 2010	To add a 600 mg dose level of RDEA594 to the study based on a preliminary analysis of the recently concluded 28-day, randomized, double-blind, placebo-controlled, monotherapy, dose-response study, study RDEA594-202.
29 April 2010	To modify the primary study endpoint and to increase the sample size of Cohorts 2 and 3 of the study based on this new primary endpoint.
27 May 2010	The study entry criteria amended to better reflect the gout population under treatment by allowing patients to enter receiving a daily dose of allopurinol between 200 mg and 600 mg instead of only 300 mg per day, rheumatoid arthritis or other autoimmune disease are only excluded if they require treatment, a history of malignancy is only excluded if within 5 years, and a Body Mass Index up to 48 kg/m2 is permitted.
12 August 2010	To extend the duration of treatment with RDEA594 in the Extension Period from 5 months to 11 months.
17 January 2011	To allow for an open label extension to further extend the duration of treatment with RDEA594 in combination with allopurinol as long as the investigator judges that the patient continues to benefit from treatment.
22 November 2011	To amend the target serum urate (sUA) value for dose escalation to 6.0 mg/dL in the Open-Label Extension Period.
25 July 2013	To expand guidance on subject hydration and to expand the management algorithm if a subject experiences an elevated serum creatinine or kidney stone.
10 January 2014	To modify the lesinurad and allopurinol combination Study RDEA594-203 in all countries where the study is ongoing to ensure patient safety.
07 October 2015	To require all active subjects who are receiving lesinurad 400 mg or 600 mg in combination with allopurinol to have their dose of lesinurad reduced to 200 mg.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported