# Clinical trial results:
# Randomized, Double-Blind, Multicenter, Placebo-Controlled, Safety and Efficacy Study of RDEA594 Versus Placebo in the Treatment of Hyperuricemia in Patients with Gout

## Summary

| | |
|---|---|
| EudraCT number | 2009-013055-30 |
| Trial protocol | ES DE GB CZ BG |
| Global end of trial date | 06 September 2011 |

### Results information

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 05 February 2017 |
| First version publication date | 05 February 2017 |

## Trial information

### Trial identification

| | |
|---|---|
| Sponsor protocol code | RDEA594-202 |

### Additional study identifiers

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

Notes:

### Sponsors

| | |
|---|---|
| Sponsor organisation name | Ardea Biosciences, Inc. |
| Sponsor organisation address | 9390 Towne Centre Drive, San Diego, United States, 92121 |
| Public contact | Maple Fung, MD, Ardea Biosciences, Inc., 1 8586526500 x, |
| Scientific contact | Maple Fung, MD, Ardea Biosciences, Inc., 1 8586526500 x, mfung@ardeabio.com |

Notes:

### Paediatric regulatory details

| | |
|---|---|
| Is trial part of an agreed paediatric investigation plan (PIP) | No |
| Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial? | No |
| Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial? | No |

Notes:

## Results analysis stage

| | |
|---|---|
| Analysis stage | Final |
| Date of interim/final analysis | 26 March 2010 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 26 March 2010 |
| Global end of trial reached? | Yes |
| Global end of trial date | 06 September 2011 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

To compare the proportion of subjects whose serum urate (sUA) level is < 6.0 mg/dL after 28 days of dosing by treatment group.

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 | 21 August 2009 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

## Population of trial subjects

### Subjects enrolled per country

| | |
|---|---|
| Country: Number of subjects enrolled | Bulgaria: 39 |
| Country: Number of subjects enrolled | Canada: 37 |
| Country: Number of subjects enrolled | Czech Republic: 10 |
| Country: Number of subjects enrolled | Germany: 6 |
| Country: Number of subjects enrolled | Poland: 27 |
| Country: Number of subjects enrolled | Georgia: 15 |
| Country: Number of subjects enrolled | United States: 9 |
| Worldwide total number of subjects | 143 |
| EEA total number of subjects | 82 |

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 | 0 |

| | |
|---|---|
| months) | |
| Children (2-11 years) | 0 |
| Adolescents (12-17 years) | 0 |
| Adults (18-64 years) | 124 |
| From 65 to 84 years | 19 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

Subjects were to be screened within 28 days prior to the first dose of study drug (Day 0) and up to 14 days before initiation of colchicine treatment.

### Period 1

| | |
|---|---|
| Period 1 title | Main |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator, Monitor, Data analyst |

### Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | lesinurad 200 mg |

Arm description: -

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | lesinurad 200 mg |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

200 mg

| | |
|---|---|
| **Arm title** | lesinurad 400 mg |

Arm description: -

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | lesinurad 400 mg |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

400 mg

| | |
|---|---|
| **Arm title** | lesinurad 600 mg |

Arm description: -

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | lesinurad 600 mg |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

600 mg

| | |
|---|---|
| **Arm title** | Placebo |

| Arm description: - | |
|---|---|
| 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[1]** | lesinurad 200 mg | lesinurad 400 mg | lesinurad 600 mg |
|---|---|---|---|
| Started | 31 | 33 | 32 |
| Completed | 28 | 27 | 30 |
| Not completed | 3 | 6 | 2 |
| Consent withdrawn by subject | 3 | 2 | - |
| N/A | - | 1 | - |
| Adverse event, non-fatal | - | 2 | - |
| Lost to follow-up | - | 1 | 1 |
| Protocol deviation | - | - | 1 |

| **Number of subjects in period 1[1]** | Placebo |
|---|---|
| Started | 27 |
| Completed | 23 |
| Not completed | 4 |
| Consent withdrawn by subject | 1 |
| N/A | - |
| Adverse event, non-fatal | - |
| Lost to follow-up | 2 |
| Protocol deviation | 1 |

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: Subjects were withdrawn prior to dosing of study medication.

## Period 2

| Period 2 title | Open Label Extension |
|---|---|
| Is this the baseline period? | No |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator, Monitor, Data analyst |

## Arms

| **Arm title** | Pooled |
|---|---|
| Arm description: - | |
| Arm type | Experimental |
| Investigational medicinal product name | lesinurad 200 mg, 400 mg, 600 mg, Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

200 mg, 400 mg, 600 mg

| **Number of subjects in period 2[2]** | Pooled |
|---|---|
| Started | 50 |
| Completed | 8 |
| Not completed | 42 |
| Discharged after study closure | 4 |
| Consent withdrawn by subject | 9 |
| N/A | 3 |
| Adverse event, non-fatal | 6 |
| Investigator Judgment | 1 |
| Site Closures | 14 |
| Lost to follow-up | 1 |
| Protocol deviation | 4 |

Notes:

[2] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: Subjects were withdrawn prior to dosing of study medication.

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | lesinurad 200 mg |
| Reporting group description: - | |
| Reporting group title | lesinurad 400 mg |
| Reporting group description: - | |
| Reporting group title | lesinurad 600 mg |
| Reporting group description: - | |
| Reporting group title | Placebo |
| Reporting group description: - | |

| Reporting group values | lesinurad 200 mg | lesinurad 400 mg | lesinurad 600 mg |
|---|---|---|---|
| Number of subjects | 31 | 33 | 32 |
| Age categorical<br>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) | 28 | 29 | 27 |
| From 65-84 years | 3 | 4 | 5 |
| 85 years and over | 0 | 0 | 0 |
| Age Continuous \|<br>Units: years | | | |
| arithmetic mean | 51 | 52.8 | 53.4 |
| standard deviation | ± 11.3 | ± 9.2 | ± 12.6 |
| Gender, Male/Female<br>Units: Participants | | | |
| Male | 31 | 32 | 31 |
| Female | 0 | 1 | 1 |
| Region of Enrollment<br>Units: Subjects | | | |
| Bulgaria | 8 | 10 | 7 |
| Canada | 6 | 10 | 12 |
| Czech Republic | 1 | 1 | 3 |
| Germany | 2 | 2 | 1 |
| Poland | 7 | 5 | 3 |
| Republic of Georgia | 3 | 4 | 4 |
| USA | 4 | 1 | 2 |
| Age, Customized<br>Units: Subjects | | | |
| <65 | 28 | 29 | 27 |
| >=65 | 3 | 4 | 5 |

| **Reporting group values** | Placebo | Total | |
|---|---|---|---|
| Number of subjects | 27 | 123 | |
| Age categorical<br>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) | 23 | 107 | |
| From 65-84 years | 4 | 16 | |
| 85 years and over | 0 | 0 | |
| Age Continuous \|<br>Units: years | | | |
| arithmetic mean | 49.9 | | |
| standard deviation | ± 11.2 | - | |
| Gender, Male/Female<br>Units: Participants | | | |
| Male | 27 | 121 | |
| Female | 0 | 2 | |
| Region of Enrollment<br>Units: Subjects | | | |
| Bulgaria | 8 | 33 | |
| Canada | 8 | 36 | |
| Czech Republic | 2 | 7 | |
| Germany | 0 | 5 | |
| Poland | 6 | 21 | |
| Republic of Georgia | 3 | 14 | |
| USA | 0 | 7 | |
| Age, Customized<br>Units: Subjects | | | |
| <65 | 23 | 107 | |
| >=65 | 4 | 16 | |

## End points

### End points reporting groups

| | |
|---|---|
| Reporting group title | lesinurad 200 mg |
| Reporting group description: - | |
| Reporting group title | lesinurad 400 mg |
| Reporting group description: - | |
| Reporting group title | lesinurad 600 mg |
| Reporting group description: - | |
| Reporting group title | Placebo |
| Reporting group description: - | |
| Reporting group title | Pooled |
| Reporting group description: - | |

### Primary: To compare the proportion of subjects whose serum urate (sUA) level is < 6.0 mg/dL after 28 days of dosing by treatment group.

| | |
|---|---|
| End point title | To compare the proportion of subjects whose serum urate (sUA) level is < 6.0 mg/dL after 28 days of dosing by treatment group. |
| End point description: | |
| End point type | Primary |
| End point timeframe: 28 Days | |

| End point values | lesinurad 200 mg | lesinurad 400 mg | lesinurad 600 mg | Placebo |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 26 | 26 | 26 | 21 |
| Units: Number of events | | | | |
| number (not applicable) | 7.7 | 30.8 | 38.5 | 0 |

### Statistical analyses

| Statistical analysis title | Number of Subjects with sUA < 6.0 mg/dL |
|---|---|
| Comparison groups | lesinurad 200 mg v Placebo |
| Number of subjects included in analysis | 47 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.4949 |
| Method | Fisher exact |

| Statistical analysis title | Number of Subjects with sUA < 6.0 mg/dL |
|---|---|
| Comparison groups | lesinurad 600 mg v Placebo |
| Number of subjects included in analysis | 47 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.0033 |
| Method | Fisher exact |

| Statistical analysis title | Number of Subjects with sUA < 6.0 mg/dL |
|---|---|
| Comparison groups | lesinurad 400 mg v Placebo |
| Number of subjects included in analysis | 47 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.0112 |
| Method | Fisher exact |

**Secondary: To evaluate the proportion of subjects whose sUA levels are <6.0 mg/dL, <5.0 mg/dL and <4.0 mg/dL at each weekly study visit during the Double-Blind Period.**

| End point title | To evaluate the proportion of subjects whose sUA levels are <6.0 mg/dL, <5.0 mg/dL and <4.0 mg/dL at each weekly study visit during the Double-Blind Period. |
|---|---|

End point description:

| End point type | Secondary |
|---|---|

End point timeframe:

28 Days

| End point values | lesinurad 200 mg | lesinurad 400 mg | lesinurad 600 mg | Placebo |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 31 | 33 | 32 | 27 |
| Units: Number | | | | |
| number (not applicable) | | | | |
| <6.0 mg/dL at Day 7 | 9.7 | 12.1 | 13.8 | 0 |
| <6.0 mg/dL at Day 14 | 3.4 | 33.3 | 33.3 | 4.5 |
| <6.0 mg/dL at Day 21 | 3.8 | 25.9 | 46.2 | 0 |
| <6.0 mg/dL at Day 28 | 7.7 | 30.8 | 38.5 | 0 |
| <5.0 mg/dL at Day 7 | 0 | 3 | 3.4 | 0 |
| <5.0 mg/dL at Day 14 | 0 | 13.3 | 7.4 | 0 |
| <5.0 mg/dL at Day 21 | 0 | 3.7 | 23.1 | 0 |
| <5.0 mg/dL at Day 28 | 3.8 | 7.7 | 15.4 | 0 |
| <4.0 mg/dL at Day 7 | 0 | 3 | 0 | 0 |
| <4.0 mg/dL at Day 14 | 0 | 0 | 0 | 0 |

| | | | | |
|---|---|---|---|---|
| <4.0 mg/dL at Day 21 | 0 | 0 | 7.7 | 0 |
| <4.0 mg/dL at Day 28 | 0 | 0 | 0 | 0 |

**Statistical analyses**

| **Statistical analysis title** | sUA levels <6.0 mg/dL, <5.0 mg/dL and <4.0 mg/dL |
|---|---|
| Comparison groups | lesinurad 200 mg v Placebo |
| Number of subjects included in analysis | 58 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 1 |
| Method | Fisher exact |

| **Statistical analysis title** | sUA levels <6.0 mg/dL, <5.0 mg/dL and <4.0 mg/dL |
|---|---|
| Comparison groups | lesinurad 600 mg v Placebo |
| Number of subjects included in analysis | 59 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 1 |
| Method | Fisher exact |

| **Statistical analysis title** | sUA levels <6.0 mg/dL, <5.0 mg/dL and <4.0 mg/dL |
|---|---|
| Comparison groups | lesinurad 400 mg v Placebo |
| Number of subjects included in analysis | 60 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 1 |
| Method | Fisher exact |

**Secondary: To evaluate the absolute and percent reduction from baseline in sUA levels at each weekly study visit. (Main Period)**

| End point title | To evaluate the absolute and percent reduction from baseline in sUA levels at each weekly study visit. (Main Period) |
|---|---|
| End point description: | |
| Value provided by randomized treatment | |
| End point type | Secondary |
| End point timeframe: | |
| Up to day 28 | |

| End point values | lesinurad 200 mg | lesinurad 400 mg | lesinurad 600 mg | Placebo |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 31 | 33 | 32 | 27 |
| Units: Number | | | | |
| number (not applicable) | | | | |
| Day 7 Absolute reduction from baseline | -2.15 | -2.33 | -2.46 | -0.17 |
| Day 7 Percent reduction from baseline | -21.88 | -22.32 | -24.33 | -0.96 |
| Day 14 Absolute reduction from baseline | -1.67 | -2.61 | -3.11 | -0.15 |
| Day 14 Percent reduction from baseline | -16.87 | -25.09 | -31.18 | -0.37 |
| Day 21 Absolute reduction from baseline | -1.58 | -2.34 | -3.65 | -0.06 |
| Day 21 Percent reduction from baseline | -15.67 | -21.96 | -36.68 | 0.52 |
| Day 28 Absolute reduction from baseline | -1.73 | -2.92 | -2.94 | -0.02 |
| Day 28 Percent reduction from baseline | -17.7 | -28.92 | -29.11 | 0.75 |

**Statistical analyses**

| Statistical analysis title | Absolute and percent reduction from baseline |
|---|---|
| Comparison groups | lesinurad 200 mg v Placebo |
| Number of subjects included in analysis | 58 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | < 0.01 |
| Method | ANCOVA |

| Statistical analysis title | Absolute and percent reduction from baseline |
|---|---|
| Comparison groups | lesinurad 600 mg v Placebo |
| Number of subjects included in analysis | 59 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | < 0.01 |
| Method | ANCOVA |

| Statistical analysis title | Absolute and percent reduction from baseline |
|---|---|
| Comparison groups | lesinurad 400 mg v Placebo |

| | |
|---|---|
| Number of subjects included in analysis | 60 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | < 0.01 |
| Method | ANCOVA |

## Secondary: To evaluate the percentage change in 24-hour urine urate level (excretion) from baseline to Day 28.

| | |
|---|---|
| End point title | To evaluate the percentage change in 24-hour urine urate level (excretion) from baseline to Day 28. |

End point description:

| | |
|---|---|
| End point type | Secondary |

End point timeframe:

28 Days

| End point values | lesinurad 200 mg | lesinurad 400 mg | lesinurad 600 mg | Placebo |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 31 | 33 | 32 | 27 |
| Units: Number | | | | |
| number (not applicable) | 7.58 | 1.79 | 3.21 | -10.45 |

### Statistical analyses

| Statistical analysis title | Percentage change in 24-hour urine urate level |
|---|---|
| Comparison groups | lesinurad 200 mg v Placebo |
| Number of subjects included in analysis | 58 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.4267 |
| Method | ANCOVA |

| Statistical analysis title | Percentage change in 24-hour urine urate level |
|---|---|
| Comparison groups | lesinurad 400 mg v Placebo |
| Number of subjects included in analysis | 60 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.873 |
| Method | ANCOVA |

| Statistical analysis title | Percentage change in 24-hour urine urate level |
|---|---|
| Comparison groups | lesinurad 600 mg v Placebo |
| Number of subjects included in analysis | 59 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.7872 |
| Method | ANCOVA |

## Secondary: To evaluate the incidence of gout flares. (Main Period)

| End point title | To evaluate the incidence of gout flares. (Main Period) |
|---|---|

End point description:

| End point type | Secondary |
|---|---|

End point timeframe:

28 Days

| End point values | lesinurad 200 mg | lesinurad 400 mg | lesinurad 600 mg | Placebo |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 31 | 33 | 32 | 27 |
| Units: Percent | | | | |
| number (not applicable) | 9.7 | 12.1 | 12.5 | 3.7 |

### Statistical analyses

No statistical analyses for this end point

## Secondary: To evaluate the safety and tolerability of RDEA594 in subjects with gout. (Main period)

| End point title | To evaluate the safety and tolerability of RDEA594 in subjects with gout. (Main period) |
|---|---|

End point description:

| End point type | Secondary |
|---|---|

End point timeframe:

28 Days and through extension

| End point values | lesinurad 200 mg | lesinurad 400 mg | lesinurad 600 mg | Placebo |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 31 | 33 | 32 | 27 |
| Units: Percent (Subjects with TEAEs) | | | | |
| number (not applicable) | 25.8 | 45.5 | 34.4 | 22.2 |

## Statistical analyses

No statistical analyses for this end point

## Secondary: To evaluate the proportion of subjects whose sUA level decreases to or is maintained at <6.0 mg/dL in the Open-Label Extension Period.

| End point title | To evaluate the proportion of subjects whose sUA level decreases to or is maintained at <6.0 mg/dL in the Open-Label Extension Period. |
|---|---|

End point description:

| End point type | Secondary |
|---|---|

End point timeframe:

18 Months

| End point values | Pooled | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 48 | | | |
| Units: n/N | | | | |
| number (not applicable) | | | | |
| Week 2 - Extension | 19.6 | | | |
| Week 4 - Extension | 10.6 | | | |
| Week 6 - Extension | 12.5 | | | |
| Week 8 - Extension | 26.2 | | | |
| Week 10 - Extension | 50 | | | |
| Week 12 - Extension | 37.5 | | | |
| Week 14 - Extension | 31.6 | | | |
| Week 16 - Extension | 34.3 | | | |
| Week 18 - Extension | 37.5 | | | |
| Week 20 - Extension | 37.1 | | | |
| Week 22 - Extension | 50 | | | |
| Week 28 - Extension | 77.8 | | | |
| Week 36 - Extension | 50 | | | |
| Week 44 - Extension | 87.5 | | | |
| Week 52 - Extension | 85.7 | | | |
| Week 60 - Extension | 80 | | | |
| Week 68 - Extension | 100 | | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: To evaluate the absolute and percent reduction from baseline in sUA levels at each weekly study visit. (Open-Label Extension)

| End point title | To evaluate the absolute and percent reduction from baseline in sUA levels at each weekly study visit. (Open-Label Extension) |
|---|---|
| End point description:<br>Value provided by maximum dose level. | |
| End point type | Secondary |
| End point timeframe:<br>28 Days and through extension | |

| **End point values** | Pooled | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 48 | | | |
| Units: Number | | | | |
| number (not applicable) | | | | |
| Week 2 Absolute reduction from baseline | -1.07 | | | |
| Week 2 Percent reduction from baseline | -11.3 | | | |
| Week 4 Absolute reduction from baseline | -0.87 | | | |
| Week 4 Percent reduction from baseline | -8.47 | | | |
| Week 6 Absolute reduction from baseline | -1.31 | | | |
| Week 6 Percent reduction from baseline | -13.27 | | | |
| Week 8 Absolute reduction from baseline | -1.2 | | | |
| Week 8 Percent reduction from baseline | -12.29 | | | |
| Week 10 Absolute reduction from baseline | -1.71 | | | |
| Week10 Percent reduction from baseline | -20.75 | | | |
| Week 12 Absolute reduction from baseline | -1.39 | | | |
| Week 12 Percent reduction from baseline | -15.18 | | | |
| Week 14 Absolute reduction from baseline | -1.36 | | | |
| Week 14 Percent reduction from baseline | -15.43 | | | |
| Week 16 Absolute reduction from baseline | -1.46 | | | |

| | | | | |
|---|---|---|---|---|
| Week 16 Percent reduction from baseline | -16.89 | | | |
| Week 18 Absolute reduction from baseline | -2.18 | | | |
| Week 18 Percent reduction from baseline | -22.33 | | | |
| Week 20 Absolute reduction from baseline | -1.67 | | | |
| Week 20 Percent reduction from baseline | -18.41 | | | |
| Week 22 Absolute reduction from baseline | -2.7 | | | |
| Week 22 Percent reduction from baseline | -31.94 | | | |
| Week 28 Absolute reduction from baseline | -2.8 | | | |
| Week 28 Percent reduction from baseline | -32.22 | | | |
| Week 36 Absolute reduction from baseline | -2.47 | | | |
| Week 36 Percent reduction from baseline | -27.96 | | | |
| Week 44 Absolute reduction from baseline | -2.49 | | | |
| Week 44 Percent reduction from baseline | -28.11 | | | |
| Week 52 Absolute reduction from baseline | -2.33 | | | |
| Wee 52 Percent reduction from baseline | -27.55 | | | |
| Week 60 Absolute reduction from baseline | -2.7 | | | |
| Week 60 Percent reduction from baseline | -32.3 | | | |
| Week 68 Absolute reduction from baseline | -2.8 | | | |
| Week 68 Percent reduction from baseline | -36.84 | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: To evaluate the incidence of gout flares. (Open-label Extension)

| End point title | To evaluate the incidence of gout flares. (Open-label Extension) |
|---|---|

End point description:

| End point type | Secondary |
|---|---|

End point timeframe:

28 Days and through extension

| End point values | Pooled | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 50 | | | |
| Units: Gout Flare Rate (per 28 days) | | | | |
| number (not applicable) | | | | |
| Month 1 | 0.0406 | | | |
| Month 2 | 0.1804 | | | |
| Month 3 | 0.0962 | | | |
| Month 4 | 0.0522 | | | |
| Month 5 | 0 | | | |
| Month 6 | 0.056 | | | |
| Month 7 | 0 | | | |
| Month 8 | 0.0996 | | | |
| Month 9 | 0 | | | |
| Month 10 | 0.1167 | | | |
| Month 11 | 0 | | | |
| Month 12 | 0.1267 | | | |
| Month 13 | 0.2857 | | | |
| Month 14 | 0 | | | |
| Month 15 | 0 | | | |
| Month 16 | 0 | | | |
| Month 17 | 0 | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: To evaluate the safety and tolerability of RDEA594 in subjects with gout. (Open-label extension)

| End point title | To evaluate the safety and tolerability of RDEA594 in subjects with gout. (Open-label extension) |
|---|---|

End point description:

| End point type | Secondary |
|---|---|

End point timeframe:

28 Days and through extension

| End point values | Pooled | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 50 | | | |
| Units: Percent (Subjects with AE) | | | | |
| number (not applicable) | 64 | | | |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

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

| | |
|---|---|
| Assessment type | Systematic |

### Dictionary used

| | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 12.0 |

### Reporting groups

| | |
|---|---|
| Reporting group title | main period 200 mg |
| Reporting group description: - | |
| Reporting group title | main period 600 mg |
| Reporting group description: - | |
| Reporting group title | main period 400 mg |
| Reporting group description: - | |
| Reporting group title | main period placebo |
| Reporting group description: - | |
| Reporting group title | open-label extension period maximum dose 200 mg |
| Reporting group description: - | |
| Reporting group title | open-label extension period maximum dose 400 mg |
| Reporting group description: - | |
| Reporting group title | open-label extension period maximum dose 600 mg |
| Reporting group description: - | |

| Serious adverse events | main period 200 mg | main period 600 mg | main period 400 mg |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 32 (0.00%) | 0 / 33 (0.00%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Gastrointestinal disorders | | | |
| Gastrooesophageal reflux disease | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 32 (0.00%) | 0 / 33 (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 |
| Renal and urinary disorders | | | |
| Renal failure acute | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 32 (0.00%) | 0 / 33 (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 placebo | open-label extension period maximum dose 200 mg | open-label extension period maximum dose 400 mg |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | 0 / 4 (0.00%) | 0 / 15 (0.00%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Gastrointestinal disorders | | | |
| Gastrooesophageal reflux disease | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | 0 / 4 (0.00%) | 0 / 15 (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 |
| Renal and urinary disorders | | | |
| Renal failure acute | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | 0 / 4 (0.00%) | 0 / 15 (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 maximum dose 600 mg | | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | 0 | | |
| Gastrointestinal disorders | | | |
| Gastrooesophageal reflux disease | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | | |
| occurrences causally related to treatment / all | 0 / 3 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Renal and urinary disorders | | | |
| Renal failure acute | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | | |
| occurrences causally related to treatment / all | 0 / 3 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

Frequency threshold for reporting non-serious adverse events: 0 %

| **Non-serious adverse events** | main period 200 mg | main period 600 mg | main period 400 mg |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 8 / 31 (25.81%) | 11 / 32 (34.38%) | 15 / 33 (45.45%) |
| Vascular disorders | | | |
| Epistaxis | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 32 (0.00%) | 0 / 33 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Flushing | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 32 (0.00%) | 1 / 33 (3.03%) |
| occurrences (all) | 0 | 0 | 1 |
| Hypertension | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | 0 / 32 (0.00%) | 1 / 33 (3.03%) |
| occurrences (all) | 1 | 0 | 1 |
| General disorders and administration site conditions | | | |
| Adverse drug reaction | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 32 (0.00%) | 0 / 33 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Chills | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 1 / 32 (3.13%) | 0 / 33 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Fatigue | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 1 / 32 (3.13%) | 0 / 33 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Oedema peripheral | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 32 (0.00%) | 1 / 33 (3.03%) |
| occurrences (all) | 0 | 0 | 1 |
| Pyrexia | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 32 (0.00%) | 0 / 33 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Sensation of pressure | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 1 / 32 (3.13%) | 0 / 33 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 32 (0.00%) | 0 / 33 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|---|---|---|---|
| Oropharyngeal pain | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 32 (0.00%) | 1 / 33 (3.03%) |
| occurrences (all) | 0 | 0 | 1 |
| Investigations | | | |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 32 (0.00%) | 0 / 33 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood creatine phosphokinase increased | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 32 (0.00%) | 0 / 33 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood creatinine increased | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 32 (0.00%) | 1 / 33 (3.03%) |
| occurrences (all) | 0 | 0 | 1 |
| Blood triglycerides increased | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 32 (0.00%) | 0 / 33 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Creatinine renal clearance decreased | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 32 (0.00%) | 0 / 33 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lipase increased | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 32 (0.00%) | 0 / 33 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Liver function test abnormal | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 32 (0.00%) | 0 / 33 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Renal function test abnormal | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 32 (0.00%) | 0 / 33 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Injury, poisoning and procedural complications | | | |
| Contusion | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 32 (0.00%) | 0 / 33 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Excoriation | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 32 (0.00%) | 0 / 33 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|---|---|---|---|
| Muscle strain | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 32 (0.00%) | 0 / 33 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Periorbital haematoma | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 32 (0.00%) | 0 / 33 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin laceration | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 32 (0.00%) | 0 / 33 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tendon injury | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 32 (0.00%) | 0 / 33 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cardiac disorders | | | |
| Arrhythmia | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 32 (0.00%) | 0 / 33 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Atrial fibrillation | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 32 (0.00%) | 0 / 33 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 1 / 32 (3.13%) | 1 / 33 (3.03%) |
| occurrences (all) | 0 | 1 | 1 |
| Sciatica | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 32 (0.00%) | 0 / 33 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Sensory disturbance | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 1 / 32 (3.13%) | 0 / 33 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Ear and labyrinth disorders | | | |
| Otitis media | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 32 (0.00%) | 0 / 33 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vertigo | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 32 (0.00%) | 1 / 33 (3.03%) |
| occurrences (all) | 0 | 0 | 2 |
| Eye disorders | | | |

| | | | |
|---|---|---|---|
| Conjunctivitis | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 32 (0.00%) | 0 / 33 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastrointestinal disorders | | | |
| Abdominal discomfort | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 32 (0.00%) | 0 / 33 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 1 / 32 (3.13%) | 0 / 33 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Abdominal pain upper | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 32 (0.00%) | 1 / 33 (3.03%) |
| occurrences (all) | 0 | 0 | 1 |
| Abdominal tenderness | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 32 (0.00%) | 1 / 33 (3.03%) |
| occurrences (all) | 0 | 0 | 1 |
| Constipation | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 32 (0.00%) | 0 / 33 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Diarrhoea | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | 1 / 32 (3.13%) | 0 / 33 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Dry mouth | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 32 (0.00%) | 0 / 33 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dysgeusia | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 32 (0.00%) | 1 / 33 (3.03%) |
| occurrences (all) | 0 | 0 | 1 |
| Dyspepsia | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 32 (0.00%) | 2 / 33 (6.06%) |
| occurrences (all) | 0 | 0 | 2 |
| Melaena | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 32 (0.00%) | 0 / 33 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nausea | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 32 (0.00%) | 0 / 33 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Toothache | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 32 (0.00%) | 0 / 33 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vomiting | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 32 (0.00%) | 1 / 33 (3.03%) |
| occurrences (all) | 0 | 0 | 2 |
| Skin and subcutaneous tissue disorders | | | |
| Pruritus | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 32 (0.00%) | 1 / 33 (3.03%) |
| occurrences (all) | 0 | 0 | 1 |
| Rash | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 32 (0.00%) | 1 / 33 (3.03%) |
| occurrences (all) | 0 | 0 | 1 |
| Renal and urinary disorders | | | |
| Dysuria | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 1 / 32 (3.13%) | 0 / 33 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Pollakiuria | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 32 (0.00%) | 0 / 33 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Urge incontinence | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 32 (0.00%) | 0 / 33 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 1 / 32 (3.13%) | 0 / 33 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Back pain | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 2 / 32 (6.25%) | 0 / 33 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Bursitis | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 32 (0.00%) | 1 / 33 (3.03%) |
| occurrences (all) | 0 | 0 | 1 |
| Muscle spasms | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 31 (3.23%) | 0 / 32 (0.00%) | 0 / 33 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Myalgia | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 32 (0.00%) | 0 / 33 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pain in extremity | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | 1 / 32 (3.13%) | 0 / 33 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Infections and infestations | | | |
| Bronchitis | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 32 (0.00%) | 0 / 33 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastroenteritis | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 32 (0.00%) | 0 / 33 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nasopharyngitis | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | 1 / 32 (3.13%) | 3 / 33 (9.09%) |
| occurrences (all) | 1 | 1 | 3 |
| Sinusitis | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 32 (0.00%) | 0 / 33 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tooth abscess | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 32 (0.00%) | 1 / 33 (3.03%) |
| occurrences (all) | 0 | 0 | 1 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 1 / 32 (3.13%) | 1 / 33 (3.03%) |
| occurrences (all) | 0 | 1 | 1 |
| Viral infection | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | 0 / 32 (0.00%) | 0 / 33 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Metabolism and nutrition disorders | | | |
| Gout | | | |
| subjects affected / exposed | 3 / 31 (9.68%) | 8 / 32 (25.00%) | 4 / 33 (12.12%) |
| occurrences (all) | 3 | 10 | 6 |
| Hypercholesterolaemia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 32 (0.00%) | 0 / 33 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| **Non-serious adverse events** | main period placebo | open-label extension period maximum dose 200 mg | open-label extension period maximum dose 400 mg |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 6 / 27 (22.22%) | 1 / 4 (25.00%) | 12 / 15 (80.00%) |
| Vascular disorders | | | |
| Epistaxis | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | 0 / 4 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Flushing | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | 0 / 4 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypertension | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | 0 / 4 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 0 | 3 |
| General disorders and administration site conditions | | | |
| Adverse drug reaction | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | 0 / 4 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Chills | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | 0 / 4 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Fatigue | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | 0 / 4 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 0 | 3 |
| Oedema peripheral | | | |
| subjects affected / exposed | 1 / 27 (3.70%) | 0 / 4 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Pyrexia | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | 0 / 4 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Sensation of pressure | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | 0 / 4 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Respiratory, thoracic and mediastinal | | | |

| | | | |
|---|---|---|---|
| disorders | | | |
| Cough | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | 0 / 4 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Oropharyngeal pain | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | 0 / 4 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Investigations | | | |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 1 / 27 (3.70%) | 0 / 4 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Blood creatine phosphokinase increased | | | |
| subjects affected / exposed | 1 / 27 (3.70%) | 0 / 4 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 1 | 0 | 3 |
| Blood creatinine increased | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | 0 / 4 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood triglycerides increased | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | 0 / 4 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 0 | 3 |
| Creatinine renal clearance decreased | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | 0 / 4 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lipase increased | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | 0 / 4 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Liver function test abnormal | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | 1 / 4 (25.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Renal function test abnormal | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | 0 / 4 (0.00%) | 2 / 15 (13.33%) |
| occurrences (all) | 0 | 0 | 6 |
| Injury, poisoning and procedural complications | | | |
| Contusion | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 27 (0.00%) | 0 / 4 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Excoriation | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | 0 / 4 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Muscle strain | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | 0 / 4 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Periorbital haematoma | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | 0 / 4 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin laceration | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | 0 / 4 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tendon injury | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | 0 / 4 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cardiac disorders | | | |
| Arrhythmia | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | 0 / 4 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Atrial fibrillation | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | 1 / 4 (25.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 2 / 27 (7.41%) | 0 / 4 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Sciatica | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | 0 / 4 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Sensory disturbance | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | 0 / 4 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Ear and labyrinth disorders | | | |

| | | | |
|---|---|---|---|
| Otitis media | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | 0 / 4 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vertigo | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | 0 / 4 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Eye disorders | | | |
| Conjunctivitis | | | |
| subjects affected / exposed | 1 / 27 (3.70%) | 0 / 4 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Gastrointestinal disorders | | | |
| Abdominal discomfort | | | |
| subjects affected / exposed | 1 / 27 (3.70%) | 0 / 4 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | 0 / 4 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Abdominal pain upper | | | |
| subjects affected / exposed | 1 / 27 (3.70%) | 0 / 4 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 1 | 0 | 3 |
| Abdominal tenderness | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | 0 / 4 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Constipation | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | 0 / 4 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Diarrhoea | | | |
| subjects affected / exposed | 1 / 27 (3.70%) | 0 / 4 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Dry mouth | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | 0 / 4 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dysgeusia | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | 0 / 4 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dyspepsia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 27 (0.00%) | 0 / 4 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Melaena | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | 0 / 4 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nausea | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | 0 / 4 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Toothache | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | 0 / 4 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vomiting | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | 0 / 4 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin and subcutaneous tissue disorders | | | |
| Pruritus | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | 0 / 4 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rash | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | 0 / 4 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Renal and urinary disorders | | | |
| Dysuria | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | 0 / 4 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 0 | 3 |
| Pollakiuria | | | |
| subjects affected / exposed | 1 / 27 (3.70%) | 0 / 4 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Urge incontinence | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | 0 / 4 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | 0 / 4 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Back pain | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 27 (0.00%) | 0 / 4 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 0 | 6 |
| Bursitis | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | 0 / 4 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Muscle spasms | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | 0 / 4 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Myalgia | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | 0 / 4 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pain in extremity | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | 0 / 4 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Infections and infestations | | | |
| Bronchitis | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | 0 / 4 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastroenteritis | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | 0 / 4 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nasopharyngitis | | | |
| subjects affected / exposed | 1 / 27 (3.70%) | 0 / 4 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Sinusitis | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | 0 / 4 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tooth abscess | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | 0 / 4 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | 0 / 4 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Viral infection | | | |
| subjects affected / exposed | 1 / 27 (3.70%) | 0 / 4 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |

| | | | |
|---|---|---|---|
| Metabolism and nutrition disorders | | | |
| Gout | | | |
| subjects affected / exposed | 1 / 27 (3.70%) | 0 / 4 (0.00%) | 7 / 15 (46.67%) |
| occurrences (all) | 2 | 0 | 22 |
| Hypercholesterolaemia | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | 0 / 4 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| **Non-serious adverse events** | open-label extension period maximum dose 600 mg | | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 21 / 31 (67.74%) | | |
| Vascular disorders | | | |
| Epistaxis | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | | |
| occurrences (all) | 3 | | |
| Flushing | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Hypertension | | | |
| subjects affected / exposed | 2 / 31 (6.45%) | | |
| occurrences (all) | 6 | | |
| General disorders and administration site conditions | | | |
| Adverse drug reaction | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | | |
| occurrences (all) | 3 | | |
| Chills | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Fatigue | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Oedema peripheral | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Pyrexia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 31 (3.23%) | | |
| occurrences (all) | 3 | | |
| Sensation of pressure | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | | |
| occurrences (all) | 3 | | |
| Oropharyngeal pain | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Investigations | | | |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Blood creatine phosphokinase increased | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | | |
| occurrences (all) | 3 | | |
| Blood creatinine increased | | | |
| subjects affected / exposed | 2 / 31 (6.45%) | | |
| occurrences (all) | 6 | | |
| Blood triglycerides increased | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Creatinine renal clearance decreased | | | |
| subjects affected / exposed | 2 / 31 (6.45%) | | |
| occurrences (all) | 6 | | |
| Lipase increased | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | | |
| occurrences (all) | 3 | | |
| Liver function test abnormal | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Renal function test abnormal | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 31 (3.23%) | | |
| occurrences (all) | 3 | | |
| Injury, poisoning and procedural complications | | | |
| Contusion | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | | |
| occurrences (all) | 3 | | |
| Excoriation | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | | |
| occurrences (all) | 6 | | |
| Muscle strain | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | | |
| occurrences (all) | 3 | | |
| Periorbital haematoma | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | | |
| occurrences (all) | 3 | | |
| Skin laceration | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | | |
| occurrences (all) | 3 | | |
| Tendon injury | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | | |
| occurrences (all) | 3 | | |
| Cardiac disorders | | | |
| Arrhythmia | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | | |
| occurrences (all) | 2 | | |
| Atrial fibrillation | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | | |
| occurrences (all) | 3 | | |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | | |
| occurrences (all) | 3 | | |
| Sciatica | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | | |
| occurrences (all) | 3 | | |
| Sensory disturbance | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Ear and labyrinth disorders | | | |
| Otitis media | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | | |
| occurrences (all) | 3 | | |
| Vertigo | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Eye disorders | | | |
| Conjunctivitis | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Gastrointestinal disorders | | | |
| Abdominal discomfort | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Abdominal pain | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | | |
| occurrences (all) | 4 | | |
| Abdominal pain upper | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | | |
| occurrences (all) | 3 | | |
| Abdominal tenderness | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Constipation | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | | |
| occurrences (all) | 3 | | |
| Diarrhoea | | | |
| subjects affected / exposed | 2 / 31 (6.45%) | | |
| occurrences (all) | 6 | | |
| Dry mouth | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | | |
| occurrences (all) | 3 | | |
| Dysgeusia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed<br>occurrences (all) | 0 / 31 (0.00%)<br>0 | | |
| Dyspepsia<br>subjects affected / exposed<br>occurrences (all) | 0 / 31 (0.00%)<br>0 | | |
| Melaena<br>subjects affected / exposed<br>occurrences (all) | 1 / 31 (3.23%)<br>3 | | |
| Nausea<br>subjects affected / exposed<br>occurrences (all) | 3 / 31 (9.68%)<br>9 | | |
| Toothache<br>subjects affected / exposed<br>occurrences (all) | 1 / 31 (3.23%)<br>3 | | |
| Vomiting<br>subjects affected / exposed<br>occurrences (all) | 2 / 31 (6.45%)<br>6 | | |
| Skin and subcutaneous tissue disorders | | | |
| Pruritus<br>subjects affected / exposed<br>occurrences (all) | 0 / 31 (0.00%)<br>0 | | |
| Rash<br>subjects affected / exposed<br>occurrences (all) | 0 / 31 (0.00%)<br>0 | | |
| Renal and urinary disorders | | | |
| Dysuria<br>subjects affected / exposed<br>occurrences (all) | 0 / 31 (0.00%)<br>0 | | |
| Pollakiuria<br>subjects affected / exposed<br>occurrences (all) | 0 / 31 (0.00%)<br>0 | | |
| Urge incontinence<br>subjects affected / exposed<br>occurrences (all) | 1 / 31 (3.23%)<br>3 | | |
| Musculoskeletal and connective tissue disorders | | | |

| | | | |
|---|---|---|---|
| Arthralgia | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | | |
| occurrences (all) | 3 | | |
| Back pain | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | | |
| occurrences (all) | 4 | | |
| Bursitis | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Muscle spasms | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Myalgia | | | |
| subjects affected / exposed | 2 / 31 (6.45%) | | |
| occurrences (all) | 6 | | |
| Pain in extremity | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Infections and infestations | | | |
| Bronchitis | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | | |
| occurrences (all) | 3 | | |
| Gastroenteritis | | | |
| subjects affected / exposed | 2 / 31 (6.45%) | | |
| occurrences (all) | 6 | | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | | |
| occurrences (all) | 4 | | |
| Sinusitis | | | |
| subjects affected / exposed | 2 / 31 (6.45%) | | |
| occurrences (all) | 6 | | |
| Tooth abscess | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | | |
| occurrences (all) | 3 | | |
| Upper respiratory tract infection | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 31 (3.23%) | | |
| occurrences (all) | 4 | | |
| Viral infection | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Metabolism and nutrition disorders | | | |
| Gout | | | |
| subjects affected / exposed | 9 / 31 (29.03%) | | |
| occurrences (all) | 40 | | |
| Hypercholesterolaemia | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | | |
| occurrences (all) | 3 | | |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---|---|
| 31 August 2009 | Changes were made to the protocol to address new safety information from the US FDA about colchicine and the related concerns raised by German Bundesinstitut fur Arzneimittel und Medizinprodukte (BfArM). |
| 15 December 2009 | The protocol was primarily amended to allow for extended dosing of subjucts by adding an optional Open-Label Extension Period for subjects who successfully complete the 4-week Double-Blind Treatment Period and attend the follow-up visit. |

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported