



## Clinical trial results:

### A Multi-Center, Randomized, Double-Blind, Placebo Controlled Trial of the Safety of Rilonacept for the Prophylaxis of Gout Flares in Patients on Urate-Lowering Therapy.

#### Summary

|                          |                 |
|--------------------------|-----------------|
| EudraCT number           | 2008-007784-16  |
| Trial protocol           | DE              |
| Global end of trial date | 14 January 2011 |

#### Results information

|                                |               |
|--------------------------------|---------------|
| Result version number          | v1            |
| This version publication date  | 31 March 2017 |
| First version publication date | 31 March 2017 |

#### Trial information

##### Trial identification

|                       |              |
|-----------------------|--------------|
| Sponsor protocol code | IL1T-GA-0815 |
|-----------------------|--------------|

##### Additional study identifiers

|                                    |                      |
|------------------------------------|----------------------|
| ISRCTN number                      | -                    |
| ClinicalTrials.gov id (NCT number) | NCT00856206          |
| WHO universal trial number (UTN)   | -                    |
| Other trial identifiers            | Study Name: RE-SURGE |

Notes:

#### Sponsors

|                              |   |
|------------------------------|---|
| Sponsor organisation name    | Regeneron Pharmaceuticals, Inc.   |
| Sponsor organisation address | 777 Old Saw Mill River Rd., Tarrytown, United States, 10591                                   |
| Public contact               | Clinical Trials information, Regeneron Pharmaceuticals, Inc.,<br>clinicaltrials@regeneron.com |
| Scientific contact           | Clinical Trials information, Regeneron Pharmaceuticals, Inc.,<br>clinicaltrials@regeneron.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                       | 16 February 2011 |
| Is this the analysis of the primary completion data? | No               |

|                                  |                 |
|----------------------------------|-----------------|
| Global end of trial reached?     | Yes             |
| Global end of trial date         | 14 January 2011 |
| Was the trial ended prematurely? | No              |

Notes:

## General information about the trial

Main objective of the trial:

The primary objective of this study is to assess the safety and tolerability of 160 mg of subcutaneous (SC) therapy with Rilonacept in the prophylaxis of gout flares in subjects on uric acid-lowering therapy.

Protection of trial subjects:

This study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with the International Conference on Harmonisation (ICH) guidelines for Good Clinical Practice (GCP) and applicable regulatory requirements.

Background therapy: -

Evidence for comparator: -

|   |               |
|---|---------------|
| Actual start date of recruitment                          | 23 March 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 | Germany: 14        |
| Country: Number of subjects enrolled | India: 22          |
| Country: Number of subjects enrolled | Indonesia: 14      |
| Country: Number of subjects enrolled | South Africa: 570  |
| Country: Number of subjects enrolled | Taiwan: 11         |
| Country: Number of subjects enrolled | United States: 684 |
| Worldwide total number of subjects   | 1315               |
| EEA total number of subjects         | 14                 |

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) | 1110 |
| From 65 to 84 years  | 205  |
| 85 years and over    | 0    |

## Subject disposition

### Recruitment

Recruitment details:

The study was conducted at 71 study sites in United States and rest of world (ROW) between 23 March 2009 to 14 January 2011. A total of 2311 subjects were screened in the study.

### Pre-assignment

Screening details:

Out of 2311 subjects, 1315 were randomized and treated in the study. Subjects were randomized in 3:1 ratio to receive Rilonacept 160 mg or placebo.

### Period 1

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

### Arms

|                              |         |
|------------------------------|---------|
| Are arms mutually exclusive? | Yes     |
| <b>Arm title</b>             | Placebo |

Arm description:

Two subcutaneous injections of Placebo (for Rilonacept) as a loading dose on Day 1 followed by a single injection once a week (qw) from Week 1 to Week 15.

|  |                      |
|--|----------------------|
| Arm type                               | Placebo              |
| Investigational medicinal product name | Placebo              |
| Investigational medicinal product code |                      |
| Other name                             |                      |
| Pharmaceutical forms                   | Powder for injection |
| Routes of administration               | Subcutaneous use     |

Dosage and administration details:

Subcutaneous injection in left and right upper arm, the left and right abdomen, and the left and right thigh.

|                  |                   |
|------------------|-------------------|
| <b>Arm title</b> | Rilonacept 160 mg |
|------------------|-------------------|

Arm description:

Two subcutaneous injections of Rilonacept 160 mg (for a total of 320 mg) as a loading dose on Day 1, followed by a single 160 mg injection of Rilonacept qw from Week 1 to Week 15.

|  |                      |
|--|----------------------|
| Arm type                               | Experimental         |
| Investigational medicinal product name | Rilonacept           |
| Investigational medicinal product code |                      |
| Other name                             |                      |
| Pharmaceutical forms                   | Powder for injection |
| Routes of administration               | Subcutaneous use     |

Dosage and administration details:

Subcutaneous injection in left and right upper arm, the left and right abdomen, and the left and right thigh.

| <b>Number of subjects in period 1</b> | Placebo | Rilonacept 160 mg |
|---------------------------------------|---------|-------------------|
| Started                               | 330     | 985               |
| Completed                             | 276     | 824               |
| Not completed                         | 54      | 161               |
| Other than specified above            | 3       | 10                |
| Consent withdrawn by subject          | 15      | 36                |
| Death                                 | 2       | 2                 |
| Adverse event                         | 10      | 46                |
| Decision by the Sponsor               | 4       | 8                 |
| Lost to follow-up                     | 13      | 39                |
| Lack of efficacy                      | 1       | 2                 |
| Protocol deviation                    | 6       | 18                |

## Baseline characteristics

### Reporting groups

|   |                   |
|---|-------------------|
| Reporting group title   | Placebo           |
| Reporting group description:  |                   |
| Two subcutaneous injections of Placebo (for Rilonacept) as a loading dose on Day 1 followed by a single injection once a week (qw) from Week 1 to Week 15.                          |                   |
| Reporting group title   | Rilonacept 160 mg |
| Reporting group description:  |                   |
| Two subcutaneous injections of Rilonacept 160 mg (for a total of 320 mg) as a loading dose on Day 1, followed by a single 160 mg injection of Rilonacept qw from Week 1 to Week 15. |                   |

| Reporting group values                    | Placebo | Rilonacept 160 mg | Total |
|---|---------|-------------------|-------|
| Number of subjects                        | 330     | 985               | 1315  |
| Age categorical<br>Units: Subjects        |         |                   |       |
| Age continuous<br>Units: years            |         |                   |       |
| arithmetic mean                           | 52.4    | 52.8              |       |
| standard deviation                        | ± 10.55 | ± 11.48           | -     |
| Gender categorical<br>Units: Subjects     |         |                   |       |
| Female                                    | 33      | 128               | 161   |
| Male                                      | 297     | 857               | 1154  |
| Ethnicity<br>Units: Subjects              |         |                   |       |
| Hispanic or Latino                        | 11      | 38                | 49    |
| Not Hispanic or Latino                    | 319     | 947               | 1266  |
| Unknown or Not Reported                   | 0       | 0                 | 0     |
| Race<br>Units: Subjects                   |         |                   |       |
| American Indian or Alaska Native          | 2       | 7                 | 9     |
| Asian                                     | 47      | 115               | 162   |
| Native Hawaiian or Other Pacific Islander | 1       | 3                 | 4     |
| Black or African American                 | 70      | 202               | 272   |
| White                                     | 210     | 658               | 868   |
| More than one race                        | 0       | 0                 | 0     |
| Unknown or Not Reported                   | 0       | 0                 | 0     |

## End points

### End points reporting groups

|   |                   |
|---|-------------------|
| Reporting group title   | Placebo           |
| Reporting group description:<br>Two subcutaneous injections of Placebo (for Rilonacept) as a loading dose on Day 1 followed by a single injection once a week (qw) from Week 1 to Week 15.                          |                   |
| Reporting group title   | Rilonacept 160 mg |
| Reporting group description:<br>Two subcutaneous injections of Rilonacept 160 mg (for a total of 320 mg) as a loading dose on Day 1, followed by a single 160 mg injection of Rilonacept qw from Week 1 to Week 15. |                   |

### Primary: Percentage of Subjects With Treatment-Emergent Adverse Events (TEAEs)

|   |  |
|---|--|
| End point title   | Percentage of Subjects With Treatment-Emergent Adverse Events (TEAEs) <sup>[1]</sup> |
| End point description:<br>Any untoward medical occurrence in a subject who received investigational medicinal product (IMP) was considered an AE without regard to possibility of causal relationship with this treatment. Treatment-emergent adverse events (TEAEs) were defined as AEs that developed or worsened or became serious during on-treatment period (time from the administration of first dose of study drug up to 35 days after the last dose of study drug). A serious adverse event (SAE) was defined as any untoward medical occurrence that resulted in any of the following outcomes: death, life-threatening, required initial or prolonged in-patient hospitalization, persistent or significant disability/incapacity, congenital anomaly/birth defect, or considered as medically important event. Any TEAE included subjects with both serious and non-serious AEs. Safety analysis set that included all subjects who received any study drug and safety analyses were based on the treatment received. |  |
| End point type  | Primary  |
| End point timeframe:<br>Baseline up to Week 20  |  |
| Notes:<br>[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.<br>Justification: As the endpoint is descriptive in nature, no statistical analysis is provided.  |  |

| End point values                                   | Placebo         | Rilonacept 160 mg |  |  |
|--|-----------------|-------------------|--|--|
| Subject group type                                 | Reporting group | Reporting group   |  |  |
| Number of subjects analysed                        | 330             | 935               |  |  |
| Units: percentage of participants                  |                 |                   |  |  |
| number (not applicable)                            |                 |                   |  |  |
| With at least 1 TEAE                               | 59.1            | 66.6              |  |  |
| With TEAEs related to study drug                   | 13              | 27.5              |  |  |
| With serious TEAEs                                 | 3.9             | 3.1               |  |  |
| With TEAEs resulting in drug Withdrawal            | 3.3             | 5                 |  |  |
| With serious TEAEs resulting in drug withdrawal    | 1.8             | 1.1               |  |  |
| With TEAEs leading to study discontinuation        | 3               | 4.7               |  |  |
| With serious TEAE leading to study discontinuation | 1.5             | 1                 |  |  |
| Treatment emergent deaths                          | 0.3             | 0.2               |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Gout Flares Per Subject Assessed From Day 1 to Day 112 (Week 16)

|   |  |
|---|--|
| End point title   | Number of Gout Flares Per Subject Assessed From Day 1 to Day 112 (Week 16) |
| End point description:<br>A gout flare was defined as subject reported acute articular pain typical of a gout attack that required treatment with an anti-inflammatory therapeutic: had at least 3 of the following 4 signs or symptoms: joint swelling, tenderness, redness, and pain and with at least 1 of the following: rapid onset of pain, decreased range of motion, joint warmth or other symptoms similar to a prior gout flare. Number of gout flares per subject was reported for this outcome measure. For drop-outs, only flares occurred before Day 112 were counted, regardless whether the flares occurred during the treatment period or not. Full analysis set (FAS) that included all randomized subjects who received any study medication, and was based on the treatment allocated by the Interactive voice response system (IVRS) at randomization (as randomized). Here, number of subjects analyzed=subjects with available data for this endpoint. |  |
| End point type  | Secondary  |
| End point timeframe:<br>Day 1 to Day 112 (Week 16)  |  |

| End point values                     | Placebo         | Rilonacept 160 mg |  |  |
|--------------------------------------|-----------------|-------------------|--|--|
| Subject group type                   | Reporting group | Reporting group   |  |  |
| Number of subjects analysed          | 323             | 952               |  |  |
| Units: Gout flares                   |                 |                   |  |  |
| arithmetic mean (standard deviation) | 1.73 (± 2.69)   | 0.51 (± 1.17)     |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of Subjects With at Least One Flare From Day 1 to Day 112 (Week 16)

|  |  |
|--|--|
| End point title  | Percentage of Subjects With at Least One Flare From Day 1 to Day 112 (Week 16) |
| End point description:<br>A gout flare was defined as subject reported acute articular pain typical of a gout attack that required treatment with an anti-inflammatory therapeutic: had at least 3 of the following 4 signs or symptoms: joint swelling, tenderness, redness, and pain and with at least 1 of the following: rapid onset of pain, decreased range of motion, joint warmth or other symptoms similar to a prior gout flare. Percentage of subjects with at least one gout flare was reported for this outcome measure. For drop-outs, only flares occurred before Day 112 were counted, regardless whether the flares occurred during the treatment |  |



period or not. FAS that included all randomized subjects who received any study medication, and was based on the treatment allocated by the IVRS at randomization (as randomized).

|                            |           |
|----------------------------|-----------|
| End point type             | Secondary |
| End point timeframe:       |           |
| Day 1 to Day 112 (Week 16) |           |

| End point values              | Placebo         | Rilonacept 160 mg |  |  |
|-------------------------------|-----------------|-------------------|--|--|
| Subject group type            | Reporting group | Reporting group   |  |  |
| Number of subjects analysed   | 330             | 985               |  |  |
| Units: percentage of subjects |                 |                   |  |  |
| number (not applicable)       | 51.1            | 25.7              |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of Subjects With at Least Two Flares From Day 1 to Day 112 (Week 16)

|                 |   |
|-----------------|---|
| End point title | Percentage of Subjects With at Least Two Flares From Day 1 to Day 112 (Week 16) |
|-----------------|---|

End point description:

A gout flare was defined as subject reported acute articular pain typical of a gout attack that required treatment with an anti-inflammatory therapeutic: had at least 3 of the following 4 signs or symptoms: joint swelling, tenderness, redness, and pain and with at least 1 of the following: rapid onset of pain, decreased range of motion, joint warmth or other symptoms similar to a prior gout flare. Percentage of subjects with at least two gout flare was reported for this outcome measure. For drop-outs, only flares occurred before Day 112 were counted regardless whether the flares occurred during the treatment period or not. FAS that included all randomized subjects who received any study medication, and was based on the treatment allocated by the IVRS at randomization (as randomized).

|                            |           |
|----------------------------|-----------|
| End point type             | Secondary |
| End point timeframe:       |           |
| Day 1 to Day 112 (Week 16) |           |

| End point values              | Placebo         | Rilonacept 160 mg |  |  |
|-------------------------------|-----------------|-------------------|--|--|
| Subject group type            | Reporting group | Reporting group   |  |  |
| Number of subjects analysed   | 330             | 985               |  |  |
| Units: percentage of subjects |                 |                   |  |  |
| number (not applicable)       | 51.1            | 25.7              |  |  |

### Statistical analyses

No statistical analyses for this end point

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**Secondary: Number of Gout Flare Days Per Subject From Day 1 to Day 112 (Week 16)**

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|                 |   |
|-----------------|---|
| End point title | Number of Gout Flare Days Per Subject From Day 1 to Day 112 (Week 16) |
|-----------------|---|

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**End point description:**

A gout flare was defined as subjects reported acute articular pain typical of a gout attack that required treatment with an anti-inflammatory therapeutic: had at least 3 of the following 4 signs or symptoms: joint swelling, tenderness, redness, and pain and with at least 1 of the following: rapid onset of pain, decreased range of motion, joint warmth or other symptoms similar to a prior gout flare. Number of gout flares per subject was reported for this outcome measure. Flare days were counted up to Week 16, regardless of whether or not the flares occurred during the treatment period. FAS that included all randomized participants who received any study medication, and was based on the treatment allocated by the IVRS at randomization (as randomized). Here, number of subjects analyzed=subjects with available data for this endpoint.

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

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**End point timeframe:**

Day 1 to Day 112 (Week 16)

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|                                      |                 |                   |  |  |
|--------------------------------------|-----------------|-------------------|--|--|
| <b>End point values</b>              | Placebo         | Rilonacept 160 mg |  |  |
| Subject group type                   | Reporting group | Reporting group   |  |  |
| Number of subjects analysed          | 323             | 952               |  |  |
| Units: Gout flare Days               |                 |                   |  |  |
| arithmetic mean (standard deviation) | 7.66 (± 11.79)  | 2.66 (± 7.69)     |  |  |

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**Statistical analyses**

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No statistical analyses for this end point

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## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Adverse Events (AEs) were collected from signature of the informed consent form up to the final visit (Week 20) regardless of seriousness or relationship to investigational product.

Adverse event reporting additional description:

Reported adverse events are treatment-emergent adverse events that is AEs that developed/worsened during the 'on treatment period' (time from the administration of first dose of study drug up to 35 days after the last dose of study drug).

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

### Dictionary used

|                 |        |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

|                    |      |
|--------------------|------|
| Dictionary version | 12.0 |
|--------------------|------|

### Reporting groups

|                       |         |
|-----------------------|---------|
| Reporting group title | Placebo |
|-----------------------|---------|

Reporting group description:

Two subcutaneous injections of Placebo (for Rilonacept) as a loading dose on Day 1 followed by a single injection qw from Week 1 to Week 15.

|                       |                   |
|-----------------------|-------------------|
| Reporting group title | Rilonacept 160 mg |
|-----------------------|-------------------|

Reporting group description:

Two subcutaneous injections of Rilonacept 160 mg (for a total of 320 mg) as a loading dose on Day 1, followed by a single 160 mg injection of Rilonacept qw from Week 1 to Week 15.

| Serious adverse events  | Placebo          | Rilonacept 160 mg |  |
|---|------------------|-------------------|--|
| Total subjects affected by serious adverse events                   |                  |                   |  |
| subjects affected / exposed   | 13 / 330 (3.94%) | 31 / 985 (3.15%)  |  |
| number of deaths (all causes)                                       | 1                | 2                 |  |
| number of deaths resulting from adverse events                      |                  |                   |  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                  |                   |  |
| Breast cancer   |                  |                   |  |
| subjects affected / exposed   | 0 / 330 (0.00%)  | 1 / 985 (0.10%)   |  |
| occurrences causally related to treatment / all                     | 0 / 0            | 0 / 1             |  |
| deaths causally related to treatment / all                          | 0 / 0            | 0 / 0             |  |
| Oropharyngeal cancer stage unspecified                              |                  |                   |  |
| subjects affected / exposed   | 0 / 330 (0.00%)  | 1 / 985 (0.10%)   |  |
| occurrences causally related to treatment / all                     | 0 / 0            | 0 / 1             |  |
| deaths causally related to treatment / all                          | 0 / 0            | 0 / 0             |  |
| Prostate cancer   |                  |                   |  |

|  |                 |                 |  |
|--|-----------------|-----------------|--|
| subjects affected / exposed                          | 0 / 330 (0.00%) | 2 / 985 (0.20%) |  |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 2           |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           |  |
| Vascular disorders                                   |                 |                 |  |
| Aneurysm   |                 |                 |  |
| subjects affected / exposed                          | 0 / 330 (0.00%) | 1 / 985 (0.10%) |  |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           |  |
| Bleeding varicose vein                               |                 |                 |  |
| subjects affected / exposed                          | 0 / 330 (0.00%) | 1 / 985 (0.10%) |  |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           |  |
| Hypertension   |                 |                 |  |
| subjects affected / exposed                          | 1 / 330 (0.30%) | 1 / 985 (0.10%) |  |
| occurrences causally related to treatment / all      | 0 / 1           | 0 / 1           |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           |  |
| General disorders and administration site conditions |                 |                 |  |
| Cyst   |                 |                 |  |
| subjects affected / exposed                          | 1 / 330 (0.30%) | 0 / 985 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           |  |
| Death  |                 |                 |  |
| subjects affected / exposed                          | 1 / 330 (0.30%) | 0 / 985 (0.00%) |  |
| occurrences causally related to treatment / all      | 1 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all           | 1 / 1           | 0 / 0           |  |
| Pyrexia  |                 |                 |  |
| subjects affected / exposed                          | 0 / 330 (0.00%) | 1 / 985 (0.10%) |  |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           |  |
| Psychiatric disorders                                |                 |                 |  |
| Bipolar disorder                                     |                 |                 |  |
| subjects affected / exposed                          | 1 / 330 (0.30%) | 1 / 985 (0.10%) |  |
| occurrences causally related to treatment / all      | 0 / 1           | 0 / 1           |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| Injury, poisoning and procedural complications  |                 |                 |  |
| Animal bite                                     |                 |                 |  |
| subjects affected / exposed                     | 0 / 330 (0.00%) | 1 / 985 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Cardiac disorders                               |                 |                 |  |
| Acute coronary syndrome                         |                 |                 |  |
| subjects affected / exposed                     | 1 / 330 (0.30%) | 1 / 985 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Atrial fibrillation                             |                 |                 |  |
| subjects affected / exposed                     | 0 / 330 (0.00%) | 2 / 985 (0.20%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 2           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Myocardial infarction                           |                 |                 |  |
| subjects affected / exposed                     | 0 / 330 (0.00%) | 2 / 985 (0.20%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 2           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 2           |  |
| Nervous system disorders                        |                 |                 |  |
| Cerebrovascular accident                        |                 |                 |  |
| subjects affected / exposed                     | 1 / 330 (0.30%) | 2 / 985 (0.20%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 2           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Nerve compression                               |                 |                 |  |
| subjects affected / exposed                     | 0 / 330 (0.00%) | 1 / 985 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Transient ischaemic attack                      |                 |                 |  |
| subjects affected / exposed                     | 0 / 330 (0.00%) | 1 / 985 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Blood and lymphatic system disorders            |                 |                 |  |
| Anaemia   |                 |                 |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| subjects affected / exposed                     | 0 / 330 (0.00%) | 2 / 985 (0.20%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 2           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| <b>Gastrointestinal disorders</b>               |                 |                 |  |
| Gastric ulcer haemorrhage                       |                 |                 |  |
| subjects affected / exposed                     | 0 / 330 (0.00%) | 1 / 985 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Gastroduodenitis                                |                 |                 |  |
| subjects affected / exposed                     | 0 / 330 (0.00%) | 1 / 985 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Intestinal perforation                          |                 |                 |  |
| subjects affected / exposed                     | 0 / 330 (0.00%) | 1 / 985 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Large intestine perforation                     |                 |                 |  |
| subjects affected / exposed                     | 1 / 330 (0.30%) | 0 / 985 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Pancreatitis                                    |                 |                 |  |
| subjects affected / exposed                     | 0 / 330 (0.00%) | 1 / 985 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Pancreatitis acute                              |                 |                 |  |
| subjects affected / exposed                     | 1 / 330 (0.30%) | 0 / 985 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Peptic ulcer perforation                        |                 |                 |  |
| subjects affected / exposed                     | 0 / 330 (0.00%) | 1 / 985 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Upper gastrointestinal haemorrhage              |                 |                 |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| subjects affected / exposed                     | 0 / 330 (0.00%) | 1 / 985 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Hepatobiliary disorders                         |                 |                 |  |
| Bile duct stone                                 |                 |                 |  |
| subjects affected / exposed                     | 0 / 330 (0.00%) | 1 / 985 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Cholangitis                                     |                 |                 |  |
| subjects affected / exposed                     | 0 / 330 (0.00%) | 1 / 985 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Cholelithiasis                                  |                 |                 |  |
| subjects affected / exposed                     | 0 / 330 (0.00%) | 1 / 985 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Skin and subcutaneous tissue disorders          |                 |                 |  |
| Drug eruption                                   |                 |                 |  |
| subjects affected / exposed                     | 1 / 330 (0.30%) | 1 / 985 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 1 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Renal and urinary disorders                     |                 |                 |  |
| Renal impairment                                |                 |                 |  |
| subjects affected / exposed                     | 0 / 330 (0.00%) | 1 / 985 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Musculoskeletal and connective tissue disorders |                 |                 |  |
| Back pain                                       |                 |                 |  |
| subjects affected / exposed                     | 0 / 330 (0.00%) | 1 / 985 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Gouty tophus                                    |                 |                 |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| subjects affected / exposed                     | 0 / 330 (0.00%) | 1 / 985 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Osteoarthritis                                  |                 |                 |  |
| subjects affected / exposed                     | 0 / 330 (0.00%) | 1 / 985 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Infections and infestations                     |                 |                 |  |
| Arthritis bacterial                             |                 |                 |  |
| subjects affected / exposed                     | 0 / 330 (0.00%) | 1 / 985 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Bronchitis                                      |                 |                 |  |
| subjects affected / exposed                     | 0 / 330 (0.00%) | 1 / 985 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Cellulitis                                      |                 |                 |  |
| subjects affected / exposed                     | 2 / 330 (0.61%) | 1 / 985 (0.10%) |  |
| occurrences causally related to treatment / all | 1 / 2           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Diverticulitis                                  |                 |                 |  |
| subjects affected / exposed                     | 0 / 330 (0.00%) | 1 / 985 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Meningitis viral                                |                 |                 |  |
| subjects affected / exposed                     | 1 / 330 (0.30%) | 0 / 985 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Sepsis  |                 |                 |  |
| subjects affected / exposed                     | 0 / 330 (0.00%) | 1 / 985 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Urinary tract infection                         |                 |                 |  |



|   |                 |                 |  |
|---|-----------------|-----------------|--|
| subjects affected / exposed                     | 0 / 330 (0.00%) | 1 / 985 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Metabolism and nutrition disorders              |                 |                 |  |
| Diabetes mellitus                               |                 |                 |  |
| subjects affected / exposed                     | 1 / 330 (0.30%) | 0 / 985 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Gout  |                 |                 |  |
| subjects affected / exposed                     | 1 / 330 (0.30%) | 2 / 985 (0.20%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 2           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |

Frequency threshold for reporting non-serious adverse events: 5 %

| <b>Non-serious adverse events</b>                     | Placebo           | Rilonacept 160 mg  |  |
|---|-------------------|--------------------|--|
| Total subjects affected by non-serious adverse events |                   |                    |  |
| subjects affected / exposed                           | 74 / 330 (22.42%) | 266 / 985 (27.01%) |  |
| Injury, poisoning and procedural complications        |                   |                    |  |
| Accidental overdose                                   |                   |                    |  |
| subjects affected / exposed                           | 20 / 330 (6.06%)  | 54 / 985 (5.48%)   |  |
| occurrences (all)                                     | 21                | 61                 |  |
| Nervous system disorders                              |                   |                    |  |
| Headache  |                   |                    |  |
| subjects affected / exposed                           | 26 / 330 (7.88%)  | 90 / 985 (9.14%)   |  |
| occurrences (all)                                     | 45                | 169                |  |
| General disorders and administration site conditions  |                   |                    |  |
| Injection site erythema                               |                   |                    |  |
| subjects affected / exposed                           | 1 / 330 (0.30%)   | 61 / 985 (6.19%)   |  |
| occurrences (all)                                     | 1                 | 195                |  |
| Musculoskeletal and connective tissue disorders       |                   |                    |  |
| Arthralgia  |                   |                    |  |
| subjects affected / exposed                           | 20 / 330 (6.06%)  | 65 / 985 (6.60%)   |  |
| occurrences (all)                                     | 41                | 85                 |  |
| Pain in extremity                                     |                   |                    |  |

|                             |                  |                  |  |
|-----------------------------|------------------|------------------|--|
| subjects affected / exposed | 15 / 330 (4.55%) | 52 / 985 (5.28%) |  |
| occurrences (all)           | 21               | 74               |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date             | Amendment  |
|------------------|--|
| 30 November 2009 | It included the following changes: -Specified that subjects with a history of inadequate urate-lowering response to allopurinol, or a history of allergic reaction, contraindication, or intolerance to allopurinol, were ineligible for the study (for those subjects treated with allopurinol); -Specified that who had an absolute or relative contraindication to naproxen, oral glucocorticoids (e.g, prednisolone, prednisone), and colchicine were ineligible for the study; and also specified stopping rules for discontinuation of study drug; -Clarified that mandatory immediate termination from the study was required if a subject becomes pregnant during the study. |

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported