



Clinical trial results:

A Multicenter, Randomized, Double-blind, Placebo-controlled, Parallel Group Study of CNTO 136 (sirukumab), a Human Anti-IL-6 Monoclonal Antibody, Administered Subcutaneously, in Subjects with Active Rheumatoid Arthritis Despite DMARD Therapy

Summary

| | |
|--------------------------|------------------|
| EudraCT number | 2010-022242-24 |
| Trial protocol | LT BG |
| Global end of trial date | 06 December 2016 |

Results information

| | |
|--------------------------------|------------------|
| Result version number | v1 (current) |
| This version publication date | 22 December 2017 |
| First version publication date | 22 December 2017 |

Trial information

Trial identification

| | |
|-----------------------|----------|
| Sponsor protocol code | CR100866 |
|-----------------------|----------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01604343 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Janssen-Cilag International N.V. |
| Sponsor organisation address | Archimedesweg 29, Leiden, Netherlands, 2333 |
| Public contact | Clinical Registry Group, Janssen-Cilag International N.V, ClinicalTrialsEU@its.jnj.com |
| Scientific contact | Clinical Registry Group, Janssen-Cilag International N.V, ClinicalTrialsEU@its.jnj.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 | 06 December 2016 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 06 December 2016 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The main objective of this study was to assess the efficacy of sirukumab as measured by the reduction of the signs and symptoms of rheumatoid arthritis (RA) and inhibition of radiographic progression in subjects with moderately to severely active RA who were refractory to disease-modifying antirheumatic drugs (DMARDs).

Protection of trial subjects:

Safety assessment was evaluated throughout the study based on reported adverse events (AEs), clinical laboratory tests, vital sign measurements, physical examinations, and concomitant medication review.

Background therapy: -

Evidence for comparator: -

| | |
|---|--------------|
| Actual start date of recruitment | 24 July 2012 |
| Long term follow-up planned | Yes |
| Long term follow-up rationale | Safety |
| Long term follow-up duration | 4 Months |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|-------------------------|
| Country: Number of subjects enrolled | Bulgaria: 18 |
| Country: Number of subjects enrolled | Canada: 11 |
| Country: Number of subjects enrolled | Chile: 68 |
| Country: Number of subjects enrolled | Colombia: 41 |
| Country: Number of subjects enrolled | Croatia: 10 |
| Country: Number of subjects enrolled | Japan: 168 |
| Country: Number of subjects enrolled | Korea, Republic of: 68 |
| Country: Number of subjects enrolled | Lithuania: 98 |
| Country: Number of subjects enrolled | Mexico: 115 |
| Country: Number of subjects enrolled | Malaysia: 7 |
| Country: Number of subjects enrolled | Poland: 169 |
| Country: Number of subjects enrolled | Romania: 15 |
| Country: Number of subjects enrolled | Russian Federation: 201 |
| Country: Number of subjects enrolled | Serbia: 144 |
| Country: Number of subjects enrolled | Taiwan: 24 |
| Country: Number of subjects enrolled | Ukraine: 152 |
| Country: Number of subjects enrolled | United States: 261 |

| | |
|--------------------------------------|-------------------|
| Country: Number of subjects enrolled | South Africa: 100 |
| Worldwide total number of subjects | 1670 |
| EEA total number of subjects | 310 |

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) | 1422 |
| From 65 to 84 years | 248 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 2746 subjects were screened of which 1670 subjects were randomized and received at least one administration of study treatment.

Period 1

| | |
|------------------------------|--|
| Period 1 title | Prior to W52 administration(through W52) |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator |

Arms

| | |
|------------------------------|---------|
| Are arms mutually exclusive? | Yes |
| Arm title | Placebo |

Arm description:

Subjects received placebo subcutaneously (SC) every 2 weeks (q2w) from Week 0 up to Week 50. Subjects who met early escape (EE) criteria at Week 18, or late escape (LE) at Week 40, or crossover (CO) at Week 52 were re-randomized to receive sirukumab 50 or 100 mg through Week 104. Subjects who completed study agent administration up to Week 104 and did not elect for long term extension (LTE) were followed up for safety from Week 104 up to Week 120.

| | |
|--|--|
| Arm type | Placebo |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection in pre-filled syringe |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Subject received placebo subcutaneously (SC) every 2 weeks (q2w) from Week 0 up to Week 50.

| | |
|------------------|---------------------|
| Arm title | Sirukumab 50 mg q4w |
|------------------|---------------------|

Arm description:

All subjects received 50 mg of sirukumab subcutaneously every 4 weeks (q4w) for 104 Weeks and in between placebo SC injections was received at Weeks 2, 6, and q4w through Week 104.

| | |
|--|--|
| Arm type | Experimental |
| Investigational medicinal product name | Sirukumab |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection in pre-filled syringe |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Subjects received 50 mg of sirukumab subcutaneously every 4 weeks (q4w) for 104 weeks.

| | |
|------------------|----------------------|
| Arm title | Sirukumab 100 mg q2w |
|------------------|----------------------|

Arm description:

All subjects received 100 mg of sirukumab SC injections at Weeks 0, 2, and q2w through Week 104. Subjects who completed study agent administration up to Week 104 and did not elect for long term extension (LTE) were followed up for safety from Week 104 up to Week 120.

| | |
|----------|--------------|
| Arm type | Experimental |
|----------|--------------|

| | |
|--|--|
| Investigational medicinal product name | Sirukumab |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection in pre-filled syringe |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Subjects received 100 mg of sirukumab SC injections at Weeks 0, 2, and q2w through Week 104.

| Number of subjects in period 1 | Placebo | Sirukumab 50 mg q4w | Sirukumab 100 mg q2w |
|--------------------------------|---------|---------------------|----------------------|
| Started | 556 | 557 | 557 |
| Completed | 247 | 481 | 470 |
| Not completed | 309 | 76 | 87 |
| Adverse event, serious fatal | 5 | 3 | 5 |
| Consent withdrawn by subject | 19 | 12 | 16 |
| Physician decision | 4 | 1 | 2 |
| Re-randomized at Week 18/40 | 211 | - | - |
| Adverse event, non-fatal | 25 | 40 | 41 |
| Other | 15 | 10 | 6 |
| Pregnancy | 1 | 1 | - |
| Lost to follow-up | 5 | 4 | 3 |
| Lack of efficacy | 24 | 5 | 14 |

Period 2

| | |
|------------------------------|-------------------------|
| Period 2 title | Week 52 to Week 104 |
| Is this the baseline period? | No |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator |

Arms

| | |
|------------------------------|--------------------------------------|
| Are arms mutually exclusive? | No |
| Arm title | Placebo to 50 mg q4w due to EE/LE/CO |

Arm description:

All subjects who were assigned to placebo group and who met EE at Week 18 or LE at Week 40 or CO at Week 52 were re- randomized to receive subcutaneous (SC) sirukumab 50 mg dose regimen q4w up to Week 104.

| | |
|----------|--------------|
| Arm type | Experimental |
|----------|--------------|

| | |
|--|--|
| Investigational medicinal product name | Sirukumab |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection in pre-filled syringe |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Subjects who were assigned to placebo group and who met early escape (EE) at Week 18 or LE at Week 40 or CO at Week 52 were re-randomized to receive subcutaneous (SC) sirukumab 50 mg dose regimen q4w up to Week 104.

| | |
|------------------|---------------------|
| Arm title | Sirukumab 50 mg q4w |
|------------------|---------------------|

Arm description:

All subjects received 50 mg of sirukumab subcutaneously every 4 weeks (q4w) for 104 weeks and in between placebo SC injections was received at Weeks 2, 6, and q4w through week 104.

| | |
|--|--|
| Arm type | Experimental |
| Investigational medicinal product name | Sirukumab |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection in pre-filled syringe |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Subjects received 50 mg of sirukumab subcutaneously every 4 weeks (q4w) for 104 weeks.

| | |
|------------------|---------------------------------------|
| Arm title | Placebo to 100 mg q2w due to EE/LE/CO |
|------------------|---------------------------------------|

Arm description:

All subjects who were assigned to placebo group and who met EE at Week 18 or LE at Week 40 or CO at Week 52 were re-randomized to receive subcutaneous (SC) sirukumab 100 mg dose regimen q2w up to Week 104.

| | |
|--|--|
| Arm type | Experimental |
| Investigational medicinal product name | Sirukumab |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection in pre-filled syringe |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Subjects who were assigned to placebo group and who met EE at Week 18 or LE at Week 40 or CO at Week 52 were re-randomized to receive subcutaneous (SC) sirukumab 100 mg dose regimen q2w up to Week 104.

| | |
|------------------|----------------------|
| Arm title | Sirukumab 100 mg q2w |
|------------------|----------------------|

Arm description:

All subjects received 100 mg of sirukumab SC injections at Weeks 0, 2, and q2w through Week 104.

| | |
|--|--|
| Arm type | Experimental |
| Investigational medicinal product name | Sirukumab |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection in pre-filled syringe |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Subjects received 100 mg of sirukumab SC injections at Weeks 0, 2, and q2w through Week 104.

| Number of subjects in period 2 | Placebo to 50 mg q4w due to EE/LE/CO | Sirukumab 50 mg q4w | Placebo to 100 mg q2w due to EE/LE/CO |
|--------------------------------|--|------------------------|---|
| | | | |
| Started | 243 | 481 | 241 |
| Treated | 242 | 481 | 241 |
| Completed | 200 | 414 | 195 |
| Not completed | 43 | 67 | 46 |
| Adverse event, serious fatal | 4 | 2 | 5 |
| Consent withdrawn by subject | 7 | 12 | 8 |
| Physician decision | 1 | - | - |
| Adverse event, non-fatal | 12 | 26 | 21 |
| Other | 11 | 11 | 6 |
| Pregnancy | - | 1 | 2 |
| Lost to follow-up | 2 | 4 | 2 |
| Lack of efficacy | 6 | 11 | 2 |

| Number of subjects in period 2 | Sirukumab 100 mg q2w |
|--------------------------------|-------------------------|
| Started | 470 |
| Treated | 470 |
| Completed | 429 |
| Not completed | 41 |
| Adverse event, serious fatal | - |
| Consent withdrawn by subject | 4 |
| Physician decision | 2 |
| Adverse event, non-fatal | 27 |
| Other | 3 |
| Pregnancy | 1 |
| Lost to follow-up | 1 |
| Lack of efficacy | 3 |

Period 3

| | |
|------------------------------|---------------------------------|
| Period 3 title | Post Treatment Safety Follow Up |
| Is this the baseline period? | No |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator |

Arms

| | |
|------------------------------|-----|
| Are arms mutually exclusive? | Yes |
|------------------------------|-----|

| | |
|---|---|
| Arm title | Placebo |
| Arm description: Subjects who completed study agent administration up to Week 104 and did not elect for long term extension (LTE) were followed up for safety from Week 104 up to Week 120. | |
| Arm type | Placebo |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection in pre-filled syringe |
| Routes of administration | Subcutaneous use |
| Dosage and administration details: Subject received placebo subcutaneously (SC) every 2 weeks (q2w) from Week 0 up to Week 50. | |
| Arm title | Placebo to 50 mg q4w due to EE/LE/CO |
| Arm description: Subjects who completed study agent administration up to Week 104 and did not elect for long term extension (LTE) were followed up for safety from Week 104 up to Week 120. | |
| Arm type | Experimental |
| Investigational medicinal product name | Placebo, Sirukumab |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection in pre-filled syringe |
| Routes of administration | Subcutaneous use |
| Dosage and administration details: Subjects who were assigned to placebo group and who met early escape (EE) at Week 18 or LE at Week 40 or CO at Week 52 were re-randomized to receive subcutaneous (SC) sirukumab 50 mg dose regimen q4w up to Week 104. | |
| Arm title | Sirukumab 50 mg q4w |
| Arm description: Subjects who completed study agent administration up to Week 104 and did not elect for long term extension (LTE) were followed up for safety from Week 104 up to Week 120. | |
| Arm type | Experimental |
| Investigational medicinal product name | Sirukumab |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection in pre-filled syringe |
| Routes of administration | Subcutaneous use |
| Dosage and administration details: Subjects received 50 mg of sirukumab subcutaneously every 4 weeks (q4w) for 104 weeks. | |
| Arm title | Placebo to Sirukumab 100 mg q2w due to EE/LE/CO |
| Arm description: Subjects who completed study agent administration up to Week 104 and did not elect for long term extension (LTE) were followed up for safety from Week 104 up to Week 120. | |
| Arm type | Experimental |
| Investigational medicinal product name | Placebo, Sirukumab |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection in pre-filled syringe |
| Routes of administration | Subcutaneous use |
| Dosage and administration details: Subjects who were assigned to placebo group and who met EE at Week 18 or LE at Week 40 or CO at Week 52 were re-randomized to receive subcutaneous (SC) sirukumab 100 mg dose regimen q2w up to Week 104. | |
| Arm title | Sirukumab 100 mg q2w |

Arm description:

Subjects who completed study agent administration up to Week 104 and did not elect for long term extension (LTE) were followed up for safety from Week 104 up to Week 120.

| | |
|--|--|
| Arm type | Experimental |
| Investigational medicinal product name | Sirukumab |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection in pre-filled syringe |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Subjects received 100 mg of sirukumab SC injections at Weeks 0, 2, and q2w through Week 104.

| Number of subjects in period 3 | Placebo | Placebo to 50 mg q4w due to EE/LE/CO | Sirukumab 50 mg q4w |
|--------------------------------|---------|--|------------------------|
| | | | |
| Started | 109 | 27 | 105 |
| Safety Population | 109 | 26 | 105 |
| Completed | 79 | 20 | 72 |
| Not completed | 30 | 7 | 33 |
| Consent withdrawn by subject | 12 | 4 | 11 |
| Other | 15 | 2 | 20 |
| Lost to follow-up | 3 | 1 | 2 |

| Number of subjects in period 3 | Placebo to Sirukumab 100 mg q2w due to EE/LE/CO | Sirukumab 100 mg q2w |
|--------------------------------|--|-------------------------|
| | | |
| Started | 36 | 114 |
| Safety Population | 36 | 114 |
| Completed | 26 | 85 |
| Not completed | 10 | 29 |
| Consent withdrawn by subject | 3 | 14 |
| Other | 6 | 14 |
| Lost to follow-up | 1 | 1 |

Baseline characteristics

Reporting groups

| | |
|---|----------------------|
| Reporting group title | Placebo |
| Reporting group description: | |
| Subjects received placebo subcutaneously (SC) every 2 weeks (q2w) from Week 0 up to Week 50. Subjects who met early escape (EE) criteria at Week 18, or late escape (LE) at Week 40, or crossover (CO) at Week 52 were re-randomized to receive sirukumab 50 or 100 mg through Week 104. Subjects who completed study agent administration up to Week 104 and did not elect for long term extension (LTE) were followed up for safety from Week 104 up to Week 120. | |
| Reporting group title | Sirukumab 50 mg q4w |
| Reporting group description: | |
| All subjects received 50 mg of sirukumab subcutaneously every 4 weeks (q4w) for 104 Weeks and in between placebo SC injections was received at Weeks 2, 6, and q4w through Week 104. | |
| Reporting group title | Sirukumab 100 mg q2w |
| Reporting group description: | |
| All subjects received 100 mg of sirukumab SC injections at Weeks 0, 2, and q2w through Week 104. Subjects who completed study agent administration up to Week 104 and did not elect for long term extension (LTE) were followed up for safety from Week 104 up to Week 120. | |

| Reporting group values | Placebo | Sirukumab 50 mg q4w | Sirukumab 100 mg q2w |
|---|---------|---------------------|----------------------|
| Number of subjects | 556 | 557 | 557 |
| Title for AgeCategorical Units: subjects | | | |
| Children (2-11 years) | 0 | 0 | 0 |
| Adolescents (12-17 years) | 0 | 0 | 0 |
| Adults (18-64 years) | 466 | 478 | 478 |
| From 65 to 84 years | 90 | 79 | 79 |
| 85 years and over | 0 | 0 | 0 |
| Title for AgeContinuous Units: years | | | |
| arithmetic mean | 52.9 | 52.9 | 53 |
| standard deviation | ± 11.85 | ± 11.8 | ± 11.31 |
| Title for Gender Units: subjects | | | |
| Female | 436 | 447 | 452 |
| Male | 120 | 110 | 105 |

| Reporting group values | Total | | |
|---|-------|--|--|
| Number of subjects | 1670 | | |
| Title for AgeCategorical Units: subjects | | | |
| Children (2-11 years) | 0 | | |
| Adolescents (12-17 years) | 0 | | |
| Adults (18-64 years) | 1422 | | |
| From 65 to 84 years | 248 | | |
| 85 years and over | 0 | | |
| Title for AgeContinuous Units: years | | | |
| arithmetic mean | | | |

| | | | |
|--------------------|---|--|--|
| standard deviation | - | | |
|--------------------|---|--|--|

| | | | |
|------------------|------|--|--|
| Title for Gender | | | |
| Units: subjects | | | |
| Female | 1335 | | |
| Male | 335 | | |

End points

End points reporting groups

| | |
|---|---|
| Reporting group title | Placebo |
| Reporting group description: Subjects received placebo subcutaneously (SC) every 2 weeks (q2w) from Week 0 up to Week 50. Subjects who met early escape (EE) criteria at Week 18, or late escape (LE) at Week 40, or crossover (CO) at Week 52 were re-randomized to receive sirukumab 50 or 100 mg through Week 104. Subjects who completed study agent administration up to Week 104 and did not elect for long term extension (LTE) were followed up for safety from Week 104 up to Week 120. | |
| Reporting group title | Sirukumab 50 mg q4w |
| Reporting group description: All subjects received 50 mg of sirukumab subcutaneously every 4 weeks (q4w) for 104 Weeks and in between placebo SC injections was received at Weeks 2, 6, and q4w through Week 104. | |
| Reporting group title | Sirukumab 100 mg q2w |
| Reporting group description: All subjects received 100 mg of sirukumab SC injections at Weeks 0, 2, and q2w through Week 104. Subjects who completed study agent administration up to Week 104 and did not elect for long term extension (LTE) were followed up for safety from Week 104 up to Week 120. | |
| Reporting group title | Placebo to 50 mg q4w due to EE/LE/CO |
| Reporting group description: All subjects who were assigned to placebo group and who met EE at Week 18 or LE at Week 40 or CO at Week 52 were re- randomized to receive subcutaneous (SC) sirukumab 50 mg dose regimen q4w up to Week 104. | |
| Reporting group title | Sirukumab 50 mg q4w |
| Reporting group description: All subjects received 50 mg of sirukumab subcutaneously every 4 weeks (q4w) for 104 weeks and in between placebo SC injections was received at Weeks 2, 6, and q4w through week 104. | |
| Reporting group title | Placebo to 100 mg q2w due to EE/LE/CO |
| Reporting group description: All subjects who were assigned to placebo group and who met EE at Week 18 or LE at Week 40 or CO at Week 52 were re-randomized to receive subcutaneous (SC) sirukumab 100 mg dose regimen q2w up to Week 104. | |
| Reporting group title | Sirukumab 100 mg q2w |
| Reporting group description: All subjects received 100 mg of sirukumab SC injections at Weeks 0, 2, and q2w through Week 104. | |
| Reporting group title | Placebo |
| Reporting group description: Subjects who completed study agent administration up to Week 104 and did not elect for long term extension (LTE) were followed up for safety from Week 104 up to Week 120. | |
| Reporting group title | Placebo to 50 mg q4w due to EE/LE/CO |
| Reporting group description: Subjects who completed study agent administration up to Week 104 and did not elect for long term extension (LTE) were followed up for safety from Week 104 up to Week 120. | |
| Reporting group title | Sirukumab 50 mg q4w |
| Reporting group description: Subjects who completed study agent administration up to Week 104 and did not elect for long term extension (LTE) were followed up for safety from Week 104 up to Week 120. | |
| Reporting group title | Placebo to Sirukumab 100 mg q2w due to EE/LE/CO |
| Reporting group description: Subjects who completed study agent administration up to Week 104 and did not elect for long term extension (LTE) were followed up for safety from Week 104 up to Week 120. | |
| Reporting group title | Sirukumab 100 mg q2w |
| Reporting group description: Subjects who completed study agent administration up to Week 104 and did not elect for long term extension (LTE) were followed up for safety from Week 104 up to Week 120. | |

Primary: Percentage of Subjects With an American College of Rheumatology (ACR) 20 Response at Week 16

| | |
|---|--|
| End point title | Percentage of Subjects With an American College of Rheumatology (ACR) 20 Response at Week 16 |
| End point description: ACR 20 response is defined as greater than or equal to (\geq) 20 percent (%) improvement in both tender joint count (TJC, 68 joints) and swollen joint count (SJC, 66 joints) and \geq 20% improvement in 3 of following 5 assessments: Subject's assessment of pain using visual analog scale (VAS) (0-10 scale, 0=no pain and 10=worst possible pain), Subject's global assessment of disease activity by using VAS (scale ranges from 0 to 10, [0=very well to 10=very poor]), Physician's global assessment of disease activity using VAS (scale ranges from 0 to 10, [0=no arthritis activity to 10=extremely active arthritis]), Subject's assessment of physical function as measured by Health Assessment Questionnaire-Disability Index (HAQ-DI) (scale ranges from 0-no difficulty, to 3-inability to perform a task in that area), and Serum C-reactive protein (CRP). Full analysis set included all randomized subjects. Subjects were set to non-responders if meeting TF criteria prior to week 16 or having data missing. | |
| End point type | Primary |
| End point timeframe: Week 16 | |

| End point values | Placebo | Sirukumab 50 mg q4w | Sirukumab 100 mg q2w | |
|-------------------------------|-----------------|---------------------|----------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 556 | 557 | 557 | |
| Units: Percentage of Subjects | | | | |
| number (not applicable) | 26.4 | 54.8 | 53.5 | |

Statistical analyses

| | |
|---|-------------------------------|
| Statistical analysis title | Statistical Analysis-1 |
| Comparison groups | Placebo v Sirukumab 50 mg q4w |
| Number of subjects included in analysis | 1113 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | < 0.001 |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Percentage Difference |
| Point estimate | 28.4 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 22.8 |
| upper limit | 33.8 |

| | |
|-----------------------------------|------------------------|
| Statistical analysis title | Statistical Analysis-2 |
|-----------------------------------|------------------------|

| | |
|---|--------------------------------|
| Comparison groups | Placebo v Sirukumab 100 mg q2w |
| Number of subjects included in analysis | 1113 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | < 0.001 |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Percentage Difference |
| Point estimate | 27.1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 21.6 |
| upper limit | 32.6 |

Primary: Change from Baseline in van der Heijde-modified Sharp (vdH-S) Score at Week 52

| | |
|------------------------|---|
| End point title | Change from Baseline in van der Heijde-modified Sharp (vdH-S) Score at Week 52 |
| End point description: | vdH-S score is sum of joint erosion score and joint space narrowing (JSN) score. Joint erosion assessment is scored according to the surface area involved, from 0 to 5, with 0 indicating no erosion and 5 indicating complete collapse of bone whereas the JSN assessment including subluxation, is scored from 0 (normal) to 4 (bony ankylosis or complete luxation). Total score ranges from 0 (best) to 448 (worst) with higher scores indicating more joint damage. Efficacy FAS for radiographic assessment includes all randomized subjects who received at least 1 (partial or complete) dose of study agent and who had non-missing baseline vdH-S score. Subjects were analyzed according to randomized treatments they were assigned to, regardless of the treatment groups they actually received. This score was based on imputed value by EE Rules (set scores after EE to missing for placebo arm) and then missing data rules in all treatment groups (imputed using linear extrapolation method). |
| End point type | Primary |
| End point timeframe: | |
| Baseline, Week 52 | |

| End point values | Placebo | Sirukumab 50 mg q4w | Sirukumab 100 mg q2w | |
|--------------------------------------|-----------------|---------------------|----------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 550 | 553 | 551 | |
| Units: Units on a Scale | | | | |
| arithmetic mean (standard deviation) | 3.69 (± 9.245) | 0.50 (± 2.961) | 0.46 (± 3.258) | |

Statistical analyses

| | |
|----------------------------|--------------------------------|
| Statistical analysis title | Statistical Analysis-2 |
| Comparison groups | Placebo v Sirukumab 100 mg q2w |

| | |
|---|-----------------------|
| Number of subjects included in analysis | 1101 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | < 0.001 |
| Method | van der waerden ANOVA |

| | |
|---|-------------------------------|
| Statistical analysis title | Statistical Analysis-1 |
| Comparison groups | Placebo v Sirukumab 50 mg q4w |
| Number of subjects included in analysis | 1103 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | < 0.001 |
| Method | van der waerden ANOVA |

Secondary: Change from Baseline in Health Assessment Questionnaire-Disability Index (HAQ-DI) Score at Week 24

| | |
|-----------------|--|
| End point title | Change from Baseline in Health Assessment Questionnaire-Disability Index (HAQ-DI) Score at Week 24 |
|-----------------|--|

End point description:

The HAQ-DI score is an evaluation of the functional status for a subject. The 20- question instrument assesses the degree of difficulty a person has in accomplishing tasks in 8 functional areas (dressing, arising, eating, walking, hygiene, reaching, gripping, and activities of daily living). Responses in each functional area are scored from 0, indicating no difficulty, to 3, indicating inability to perform a task in that area. Overall score was computed as the sum of domain scores and divided by the number of domains answered. Total possible score range: 0-3 where 0 = least difficulty and 3 = extreme difficulty. Full analysis set included all randomized subjects. Subjects were analyzed according to randomized treatment groups they were assigned to, regardless of the treatments they actually received. Last Observation Carried Forward (LOCF) method was used to impute missing values. Last Observation at or prior EE was used to replace the data after EE for subjects who met EE criteria.

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

End point timeframe:

Baseline, Week 24

| End point values | Placebo | Sirukumab 50 mg q4w | Sirukumab 100 mg q2w | |
|--------------------------------------|---------------------|---------------------|----------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 556 | 557 | 557 | |
| Units: Units on Scale | | | | |
| arithmetic mean (standard deviation) | -0.2179 (± 0.53081) | -0.4262 (± 0.57631) | -0.4610 (± 0.56784) | |

Statistical analyses

| | |
|-----------------------------------|-------------------------------|
| Statistical analysis title | Statistical Analysis-1 |
| Comparison groups | Placebo v Sirukumab 50 mg q4w |

| | |
|---|-----------------------------------|
| Number of subjects included in analysis | 1113 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | < 0.001 |
| Method | ANCOVA |
| Parameter estimate | Least Square (LS) mean difference |
| Point estimate | -0.226 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.29 |
| upper limit | -0.17 |

| | |
|---|--------------------------------|
| Statistical analysis title | Statistical Analysis-2 |
| Comparison groups | Placebo v Sirukumab 100 mg q2w |
| Number of subjects included in analysis | 1113 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | < 0.001 |
| Method | ANCOVA |
| Parameter estimate | LS mean difference |
| Point estimate | -0.256 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.32 |
| upper limit | -0.2 |

Secondary: Percentage of Subjects With an American College of Rheumatology (ACR) 50 Response at Week 24

| | |
|-----------------|--|
| End point title | Percentage of Subjects With an American College of Rheumatology (ACR) 50 Response at Week 24 |
|-----------------|--|

End point description:

ACR 50 response is defined as $\geq 50\%$ improvement in both TJC (68 joints) and SJC (66 joints) and $\geq 50\%$ improvement in 3 of the following 5 assessments: Subject's assessment of pain using VAS (0-10 scale, 0=no pain and 10=worst possible pain), Subject's global assessment of disease activity by using VAS (the scale ranges from 0 to 10, [0 =very well to 10 =very poor]), Physician's global assessment of disease activity using VAS (the scale ranges from 0 to 10, [0=no arthritis activity to 10=extremely active arthritis]), Subject's assessment of physical function as measured by HAQ-DI (the scale ranges from 0, indicating no difficulty, to 3, indicating inability to perform a task in that area), and Serum CRP. FAS included all randomized subjects. Subjects were analyzed according to randomized treatment groups they were assigned to, regardless of the treatments they actually received. Subjects were set to non-responders if meeting EE or TF criteria prior to week 24 or having data missing.

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

End point timeframe:

Week 24

| End point values | Placebo | Sirukumab 50 mg q4w | Sirukumab 100 mg q2w | |
|-------------------------------|-----------------|---------------------|----------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 556 | 557 | 557 | |
| Units: Percentage of Subjects | | | | |
| number (not applicable) | 12.4 | 30.2 | 33.2 | |

Statistical analyses

| Statistical analysis title | Statistical Analysis-1 |
|---|-------------------------------|
| Comparison groups | Placebo v Sirukumab 50 mg q4w |
| Number of subjects included in analysis | 1113 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | < 0.001 |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Percentage Difference |
| Point estimate | 17.8 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 13.1 |
| upper limit | 22.4 |

| Statistical analysis title | Statistical Analysis-2 |
|---|--------------------------------|
| Comparison groups | Placebo v Sirukumab 100 mg q2w |
| Number of subjects included in analysis | 1113 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | < 0.001 |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Percentage Difference |
| Point estimate | 20.8 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 16.1 |
| upper limit | 25.6 |

Secondary: Percentage of Subjects With Disease Activity Index Score 28 (DAS28) (C-reactive protein [CRP]) Remission at Week 24

| | |
|---|---|
| End point title | Percentage of Subjects With Disease Activity Index Score 28 (DAS28) (C-reactive protein [CRP]) Remission at Week 24 |
| End point description: | |
| <p>The DAS28 based on C-Reactive Protein (CRP) is a statistically derived index combining tender joints (28 joints), swollen joints (28 joints), CRP and patient's global assessment of disease activity. The set of 28 joint count is based on evaluation of the shoulder, elbow, wrist, metacarpophalangeal (MCP) MCP1 to MCP5, proximal interphalangeal (PIP) PIP1 to PIP5 joints of both the upper right extremity and the upper left extremity as well as the knee joints of lower right and lower left extremities. The values are 0=best to 10=worst. The Disease Activity Index Score 28 (DAS28) C-reactive protein (CRP) remission is defined as a DAS28 (CRP) value of less than 2.6 at a visit. Full analysis set included all randomized subjects. Subjects were analyzed according to randomized treatment groups they were assigned to, regardless of the treatments they actually received. Subjects were set to not achieving DAS28 remission if meeting EE or TF criteria prior to week 24 or having data missing.</p> | |
| End point type | Secondary |
| End point timeframe: | |
| Week 24 | |

| End point values | Placebo | Sirukumab 50 mg q4w | Sirukumab 100 mg q2w | |
|-------------------------------|-----------------|---------------------|----------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 556 | 557 | 557 | |
| Units: Percentage of Subjects | | | | |
| number (not applicable) | 5.6 | 26.0 | 25.5 | |

Statistical analyses

| | |
|---|-------------------------------|
| Statistical analysis title | Statistical Analysis-1 |
| Comparison groups | Placebo v Sirukumab 50 mg q4w |
| Number of subjects included in analysis | 1113 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | < 0.001 |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Percentage Difference |
| Point estimate | 20.5 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 16.4 |
| upper limit | 24.6 |

| | |
|-----------------------------------|--------------------------------|
| Statistical analysis title | Statistical Analysis-2 |
| Comparison groups | Placebo v Sirukumab 100 mg q2w |

| | |
|---|-------------------------|
| Number of subjects included in analysis | 1113 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | < 0.001 |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Percentage Difference |
| Point estimate | 19.9 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 15.8 |
| upper limit | 24 |

Secondary: Percentage of Subjects With Major Clinical Response (MCR) at Week 52

| | |
|-----------------|--|
| End point title | Percentage of Subjects With Major Clinical Response (MCR) at Week 52 |
|-----------------|--|

End point description:

MCR was defined as subject achieving ACR 70 response for 6 continuous months (24 weeks) in study period (i.e., through Week 52). An ACR 70 response is defined as $\geq 70\%$ improvement in both TJC (68 joints) and SJC (66 joints) and $\geq 70\%$ improvement in 3 of following 5 assessments Subject's assessment of pain using VAS, Subject's global assessment of disease activity by using VAS, Physician's global assessment of disease activity using VAS, Subject's assessment of physical function as measured by HAQ-DI and Serum CRP. FAS was defined as all randomized subjects. Subjects were analyzed according to randomized treatment groups they were assigned to, regardless of the treatments they actually received. Subjects were set to non-responders if meeting EE, LE or TF criteria prior to week 52 or having data missing.

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

End point timeframe:

Week 52

| End point values | Placebo | Sirukumab 50 mg q4w | Sirukumab 100 mg q2w | |
|-------------------------------|-----------------|---------------------|----------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 556 | 557 | 557 | |
| Units: Percentage of Subjects | | | | |
| number (not applicable) | 1.8 | 5.4 | 9.0 | |

Statistical analyses

| | |
|----------------------------|-------------------------------|
| Statistical analysis title | Statistical Analysis-1 |
| Comparison groups | Placebo v Sirukumab 50 mg q4w |

| | |
|---|-------------------------|
| Number of subjects included in analysis | 1113 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | < 0.001 |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Percentage Difference |
| Point estimate | 3.6 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.4 |
| upper limit | 508 |

| | |
|---|--------------------------------|
| Statistical analysis title | Statistical Analysis-2 |
| Comparison groups | Placebo v Sirukumab 100 mg q2w |
| Number of subjects included in analysis | 1113 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | < 0.001 |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Percentage Difference |
| Point estimate | 7.2 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 4.6 |
| upper limit | 9.8 |

Secondary: Percentage of Subjects With an American College of Rheumatology (ACR) 20 Response Through Week 52

| | |
|-----------------|---|
| End point title | Percentage of Subjects With an American College of Rheumatology (ACR) 20 Response Through Week 52 |
|-----------------|---|

End point description:

ACR 20 response is defined as $\geq 20\%$ improvement in both TJC(68 joints) and SJC(66 joints) and $\geq 20\%$ improvement in 3 of the following 5 assessments: Subject's assessment of pain using VAS 0-10 scale, 0=no pain and 10=worst possible pain), Subject's global assessment of disease activity by using VAS(scale ranges from 0 to 10, [0=very well to 10=very poor]), Physician's global assessment of disease activity using VAS (scale ranges from 0 to 10, [0=no arthritis activity to 10=extremely active arthritis]), Subject's assessment of physical function as measured by HAQ-DI (scale ranges from 0, indicating no difficulty, to 3, indicating inability to perform a task in that area), and Serum CRP. FAS included all randomized subjects. Subjects were analyzed according to randomized treatment groups they were assigned to, regardless of the treatments they actually received. Subjects were set to non-responders after meeting EE, LE or TF criteria (whichever is earliest) or if having data missing.

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

End point timeframe:

Week 2, 4, 6, 8, 12, 18, 20, 24, 28, 32, 36, 40, 44, 48, and 52

| End point values | Placebo | Sirukumab 50 mg q4w | Sirukumab 100 mg q2w | |
|-------------------------------|-----------------|---------------------|----------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 556 | 557 | 557 | |
| Units: Percentage of Subjects | | | | |
| number (not applicable) | | | | |
| Week 2 | 7.4 | 18.3 | 15.4 | |
| Week 4 | 14.2 | 36.3 | 33.8 | |
| Week 6 | 20.3 | 45.8 | 46.9 | |
| Week 8 | 25.9 | 47.2 | 51.3 | |
| Week 12 | 27.3 | 53.1 | 53.3 | |
| Week 18 | 29.3 | 54.4 | 56.9 | |
| Week 20 | 29.5 | 53.7 | 52.8 | |
| Week 24 | 27.0 | 53.7 | 56.0 | |
| Week 28 | 31.5 | 53.1 | 57.3 | |
| Week 32 | 29.5 | 53.3 | 56.7 | |
| Week 36 | 28.4 | 54.0 | 58.2 | |
| Week 40 | 28.8 | 53.3 | 53.3 | |
| Week 44 | 27.7 | 49.2 | 54.0 | |
| Week 48 | 26.8 | 50.1 | 54.8 | |
| Week 52 | 26.6 | 49.9 | 54.8 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With an American College of Rheumatology (ACR) 50 Response

| | |
|-----------------|---|
| End point title | Percentage of Subjects With an American College of Rheumatology (ACR) 50 Response |
|-----------------|---|

End point description:

ACR 50 response is defined as $\geq 50\%$ improvement in both TJC(68 joints) and SJC(66 joints) and $\geq 50\%$ improvement in 3 of the following 5 assessments: Subject's assessment of pain using VAS(0-10 scale, 0=no pain and 10=worst possible pain), Subject's global assessment of disease activity by using VAS(scale ranges from 0 to 10,[0=very well to 10=very poor]), Physician's global assessment of disease activity using VAS (scale ranges from 0 to 10, [0=no arthritis activity to 10=extremely active arthritis]), Subject's assessment of physical function as measured by HAQ-DI(scale ranges from 0, indicating no difficulty, to 3, indicating inability to perform a task in that area) and Serum CRP. FAS was defined as all randomized subjects. Subjects were analyzed according to randomized treatment groups they were assigned to, regardless of the treatments they actually received. Subjects were set to non-responders after meeting EE, LE or TF criteria (whichever is earliest) or if having data missing.

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

End point timeframe:

Week 2, 4, 6, 8, 12, 16, 18, 20, 28, 32, 36, 40, 44, 48 and 52

| End point values | Placebo | Sirukumab 50 mg q4w | Sirukumab 100 mg q2w | |
|-------------------------------|-----------------|---------------------|----------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 556 | 557 | 557 | |
| Units: Percentage of Subjects | | | | |
| number (not applicable) | | | | |
| Week 2 | 1.1 | 3.2 | 2.0 | |
| Week 4 | 2.5 | 9.2 | 9.9 | |
| Week 6 | 4.1 | 15.6 | 14.0 | |
| Week 8 | 7.7 | 20.3 | 18.9 | |
| Week 12 | 10.1 | 24.6 | 28.0 | |
| Week 16 | 10.8 | 30.0 | 26.2 | |
| Week 18 | 11.7 | 31.2 | 31.2 | |
| Week 20 | 13.5 | 32.7 | 33.4 | |
| Week 28 | 15.1 | 31.6 | 33.0 | |
| Week 32 | 14.0 | 33.6 | 35.0 | |
| Week 36 | 12.2 | 33.4 | 34.5 | |
| Week 40 | 13.3 | 31.1 | 33.4 | |
| Week 44 | 14.2 | 31.4 | 33.9 | |
| Week 48 | 14.4 | 32.9 | 34.8 | |
| Week 52 | 13.8 | 30.3 | 35.5 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With an American College of Rheumatology (ACR) 70 Response Through Week 52

| | |
|-----------------|---|
| End point title | Percentage of Subjects With an American College of Rheumatology (ACR) 70 Response Through Week 52 |
|-----------------|---|

End point description:

ACR 70 response is defined as $\geq 70\%$ improvement in both TJC(68 joints) and SJC(66 joints) and $\geq 70\%$ improvement in 3 of the following 5 assessments: Subject's assessment of pain using VAS(0-10 scale, 0=no pain and 10=worst possible pain), Subject's global assessment of disease activity by using VAS (scale ranges from 0 to 10,[0=very well to 10=very poor]), Physician's global assessment of disease activity using VAS (scale ranges from 0 to 10,[0=no arthritis activity to 10=extremely active arthritis]), Subject's assessment of physical function as measured by HAQ-DI(scale ranges from 0, indicating no difficulty, to 3, indicating inability to perform a task in that area) and Serum CRP. FAS was defined as all randomized subjects. Subjects were analyzed according to randomized treatment groups they were assigned to, regardless of the treatments they actually received. Subjects were set to non-responders after meeting EE, LE or TF criteria (whichever is earliest) or if having data missing.

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

End point timeframe:

Week 2, 4, 6, 8, 12, 16, 18, 20, 24, 28, 32, 36, 40, 44, 48 and 52

| End point values | Placebo | Sirukumab 50 mg q4w | Sirukumab 100 mg q2w | |
|-------------------------------|-----------------|---------------------|----------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 556 | 557 | 557 | |
| Units: Percentage of Subjects | | | | |
| number (not applicable) | | | | |
| Week 2 | 0.4 | 0.7 | 0.4 | |
| Week 4 | 0.5 | 2.0 | 3.1 | |
| Week 6 | 1.6 | 4.7 | 4.5 | |
| Week 8 | 1.6 | 7.2 | 7.2 | |
| Week 12 | 3.1 | 10.4 | 10.6 | |
| Week 16 | 4.0 | 13.5 | 13.5 | |
| Week 18 | 4.3 | 12.6 | 14.7 | |
| Week 20 | 4.0 | 13.1 | 16.0 | |
| Week 24 | 3.4 | 14.9 | 16.3 | |
| Week 28 | 5.2 | 16.0 | 16.5 | |
| Week 32 | 4.7 | 17.4 | 17.2 | |
| Week 36 | 4.7 | 15.8 | 16.2 | |
| Week 40 | 5.0 | 16.9 | 17.6 | |
| Week 44 | 5.2 | 16.3 | 17.1 | |
| Week 48 | 6.8 | 18.5 | 17.8 | |
| Week 52 | 5.4 | 16.5 | 18.5 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With an American College of Rheumatology (ACR) 90 Response Through Week 52

| | |
|-----------------|---|
| End point title | Percentage of Subjects With an American College of Rheumatology (ACR) 90 Response Through Week 52 |
|-----------------|---|

End point description:

ACR 90 response is defined as $\geq 90\%$ improvement in both TJC(68 joints) and SJC(66 joints) and $\geq 90\%$ improvement in 3 of the following 5 assessments: Subject's assessment of pain using VAS(0-10 scale, 0=no pain and 10=worst possible pain), Subject's global assessment of disease activity by using VAS(scale ranges from 0 to 10, [0=very well to 10=very poor]), Physician's global assessment of disease activity using VAS(scale ranges from 0 to 10,[0=no arthritis activity to 10=extremely active arthritis]), Subject's assessment of physical function as measured by HAQ-DI (scale ranges from 0, indicating no difficulty, to 3, indicating inability to perform a task in that area) and Serum CRP. FAS was defined as all randomized subjects. Subjects were analyzed according to randomized treatment groups they were assigned to, regardless of the treatments they actually received. Subjects were set to non-responders after meeting EE, LE or TF criteria (whichever is earliest) or if having data missing.

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

End point timeframe:

Week 2, 4, 6, 8, 12, 16, 18, 20, 24, 28, 32, 36, 40, 44, 48 and 52

| End point values | Placebo | Sirukumab 50 mg q4w | Sirukumab 100 mg q2w | |
|-------------------------------|-----------------|---------------------|----------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 556 | 557 | 557 | |
| Units: Percentage of Subjects | | | | |
| number (not applicable) | | | | |
| Week 2 | 0 | 0 | 0 | |
| Week 4 | 0 | 0.2 | 0.2 | |
| Week 6 | 0.2 | 0.2 | 0.2 | |
| Week 8 | 0.2 | 1.1 | 0.5 | |
| Week 12 | 0.5 | 2.2 | 1.8 | |
| Week 16 | 0.9 | 2.5 | 2.9 | |
| Week 18 | 1.1 | 2.5 | 2.5 | |
| Week 20 | 0.5 | 3.6 | 4.1 | |
| Week 24 | 0.5 | 3.4 | 5.2 | |
| Week 28 | 0.4 | 4.5 | 4.7 | |
| Week 32 | 1.1 | 4.1 | 5.7 | |
| Week 36 | 0.9 | 4.8 | 5.4 | |
| Week 40 | 0.7 | 5.4 | 6.1 | |
| Week 44 | 0.5 | 5.0 | 6.6 | |
| Week 48 | 0.7 | 4.7 | 6.3 | |
| Week 52 | 1.3 | 4.5 | 5.6 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Disease Activity Index Score 28 (DAS28) C-reactive Protein (CRP) Response Through Week 52

| | |
|-----------------|---|
| End point title | Percentage of Subjects With Disease Activity Index Score 28 (DAS28) C-reactive Protein (CRP) Response Through Week 52 |
|-----------------|---|

End point description:

DAS28 based on CRP is a statistically derived index combining tender joints (28 joints), swollen joints (28 joints), CRP and patient's global assessment of disease activity. The values are 0=best to 10=worst. Good responders: improvement from baseline greater than (>) 1.2 with DAS28 less than or equal to (<=) 3.2; moderate responders: improvement from baseline >1.2 with DAS28 >3.2 to <=5.1 or improvement from baseline >0.6 to <=1.2 with DAS28 <=5.1; non-responders: improvement from baseline <=0.6 or improvement from baseline >0.6 and <=1.2 with DAS28 >5.1. FAS included all randomized subjects. Subjects were analyzed according to randomized treatment groups they were assigned to, regardless of the treatments they actually received. Subjects were set to non-responders after meeting EE, LE or TF criteria (whichever is earliest) or if having data missing.

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

End point timeframe:

Week 2, 4, 6, 8, 12, 16, 18, 20, 24, 28, 32, 36, 40, 44, 48 and 52

| End point values | Placebo | Sirukumab 50 mg q4w | Sirukumab 100 mg q2w | |
|-------------------------------|-----------------|---------------------|----------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 556 | 557 | 557 | |
| Units: Percentage of Subjects | | | | |
| number (not applicable) | | | | |
| Week 2 | 18.5 | 72.0 | 72.4 | |
| Week 4 | 28.1 | 80.1 | 78.3 | |
| Week 6 | 36.7 | 82.4 | 80.3 | |
| Week 8 | 38.5 | 81.7 | 81.3 | |
| Week 12 | 43.7 | 83.3 | 81.3 | |
| Week 16 | 42.6 | 80.4 | 79.5 | |
| Week 18 | 41.5 | 79.7 | 79.4 | |
| Week 20 | 41.5 | 73.8 | 72.5 | |
| Week 24 | 37.9 | 71.5 | 72.2 | |
| Week 28 | 41.2 | 69.7 | 72.2 | |
| Week 32 | 41.4 | 68.2 | 70.6 | |
| Week 36 | 39.7 | 67.7 | 69.8 | |
| Week 40 | 39.2 | 66.8 | 67.9 | |
| Week 44 | 37.6 | 63.2 | 64.6 | |
| Week 48 | 36.7 | 61.9 | 64.6 | |
| Week 52 | 35.6 | 62.5 | 64.3 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Disease Activity Index Score 28 (DAS28) C-reactive Protein (CRP) Through Week 52

| | |
|-----------------|--|
| End point title | Change From Baseline in Disease Activity Index Score 28 (DAS28) C-reactive Protein (CRP) Through Week 52 |
|-----------------|--|

End point description:

DAS28 based on C-Reactive Protein (CRP) is a statistically derived index combining tender joints (28 joints), swollen joints (28 joints), CRP and patient's global assessment of disease activity. The values are 0=best to 10=worst. A negative change from baseline in DAS28 (CRP) (that is, a decrease from baseline) indicates improvement from baseline. FAS included all randomized subjects. Subjects were analyzed according to randomized treatment groups they were assigned to, regardless of the treatments they actually received. Last Observation Carried Forward (LOCF) method was used to impute missing values. Last Observation at or prior EE/LE was used to replace the data after EE/LE for subjects who met EE/LE criteria.

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

End point timeframe:

Baseline, Week 2, 4, 6, 8, 12, 16, 18, 20, 24, 28, 32, 36, 40, 44, 48 and 52

| End point values | Placebo | Sirukumab 50 mg q4w | Sirukumab 100 mg q2w | |
|--------------------------------------|-------------------|---------------------|----------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 556 | 557 | 557 | |
| Units: Units on a Scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Change at Week 2 | -0.319 (± 0.7677) | -1.316 (± 0.7776) | -1.284 (± 0.7605) | |
| Change at Week 4 | -0.515 (± 0.9287) | -1.638 (± 0.9759) | -1.627 (± 0.9529) | |
| Change at Week 6 | -0.707 (± 1.0599) | -1.886 (± 1.0622) | -1.888 (± 1.0340) | |
| Change at Week 8 | -0.754 (± 1.1013) | -2.016 (± 1.1183) | -2.031 (± 1.1138) | |
| Change at Week 12 | -0.881 (± 1.1727) | -2.187 (± 1.1995) | -2.185 (± 1.1950) | |
| Change at Week 16 | -0.908 (± 1.2834) | -2.264 (± 1.2443) | -2.282 (± 1.2283) | |
| Change at Week 18 | -0.895 (± 1.2986) | -2.286 (± 1.2690) | -2.335 (± 1.2314) | |
| Change at Week 20 | -0.920 (± 1.2973) | -2.367 (± 1.3368) | -2.380 (± 1.3158) | |
| Change at Week 24 | -0.912 (± 1.3180) | -2.356 (± 1.3599) | -2.402 (± 1.3048) | |
| Change at Week 28 | -0.979 (± 1.3752) | -2.417 (± 1.4068) | -2.440 (± 1.3245) | |
| Change at Week 32 | -1.010 (± 1.3904) | -2.451 (± 1.4141) | -2.479 (± 1.3304) | |
| Change at Week 36 | -1.019 (± 1.4020) | -2.461 (± 1.3951) | -2.497 (± 1.3231) | |
| Change at Week 40 | -0.985 (± 1.4054) | -2.462 (± 1.4180) | -2.459 (± 1.3901) | |
| Change at Week 44 | -0.994 (± 1.4117) | -2.442 (± 1.4364) | -2.477 (± 1.4381) | |
| Change at Week 48 | -1.026 (± 1.4755) | -2.482 (± 1.4630) | -2.488 (± 1.3783) | |
| Change at Week 52 | -0.992 (± 1.4431) | -2.491 (± 1.4305) | -2.476 (± 1.4109) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Disease Activity Index Score 28 (DAS28) (C-reactive protein [CRP]) Remission Through Week 52

| | |
|-----------------|--|
| End point title | Percentage of Subjects with Disease Activity Index Score 28 (DAS28) (C-reactive protein [CRP]) Remission Through Week 52 |
|-----------------|--|

End point description:

DAS28 based on C-Reactive Protein (CRP) is a statistically derived index combining tender joints (28 joints), swollen joints (28 joints), CRP and patient's global assessment of disease activity. The set of 28 joint count is based on evaluation of the shoulder, elbow, wrist, metacarpophalangeal (MCP) MCP1 to MCP5, proximal interphalangeal (PIP) PIP1 to PIP5 joints of both the upper right extremity and the upper left extremity as well as the knee joints of lower right and lower left extremities. The values are 0=best to 10=worst. DAS28 (CRP) remission is defined as a DAS28 (CRP) value of less than 2.6 at a visit. Full analysis set included all randomized subjects. Subjects were analyzed according to randomized treatment groups they were assigned to, regardless of the treatments they actually received. Subjects were set to not achieving DAS28 remission after meeting EE, LE or TF criteria (whichever is earliest) or

if having data missing.

| | |
|--|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Week 2, 4, 6, 8, 12, 16, 18, 20, 28, 32, 36, 40, 44, 48 and 52 | |

| End point values | Placebo | Sirukumab 50 mg q4w | Sirukumab 100 mg q2w | |
|-------------------------------|-----------------|---------------------|----------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 556 | 557 | 557 | |
| Units: Percentage of Subjects | | | | |
| number (not applicable) | | | | |
| Week 2 | 0.5 | 2.5 | 2.7 | |
| Week 4 | 1.6 | 7.9 | 9.3 | |
| Week 6 | 3.1 | 10.2 | 12.6 | |
| Week 8 | 3.2 | 13.6 | 17.8 | |
| Week 12 | 4.3 | 18.3 | 19.6 | |
| Week 16 | 5.8 | 21.2 | 21.9 | |
| Week 18 | 6.1 | 22.8 | 23.7 | |
| Week 20 | 5.8 | 26.4 | 25.5 | |
| Week 24 | 5.6 | 26.0 | 25.5 | |
| Week 28 | 7.7 | 27.5 | 27.1 | |
| Week 32 | 7.7 | 29.6 | 28.4 | |
| Week 36 | 8.5 | 29.1 | 28.0 | |
| Week 40 | 7.2 | 27.8 | 27.3 | |
| Week 44 | 8.5 | 28.2 | 27.5 | |
| Week 48 | 9.0 | 29.6 | 30.2 | |
| Week 52 | 8.8 | 30.0 | 29.1 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Simplified Disease Activity Index (SDAI) Score Through Week 52

| | |
|-----------------|--|
| End point title | Change From Baseline in Simplified Disease Activity Index (SDAI) Score Through Week 52 |
|-----------------|--|

End point description:

SDAI score is a derived score combining tender joints (28 joints), swollen joints (28 joints), patient's global assessment of disease activity, physician's global assessments of disease activity, and CRP. The total score range is from 0 to 86 with a lower score indicating less disease activity. A negative change from baseline indicates an improvement and a positive change from baseline indicates a worsening. FAS included all randomized subjects. Subjects were analyzed according to randomized treatment groups they were assigned to, regardless of the treatments they actually received. Last Observation Carried Forward (LOCF) method was used to impute missing values. Last Observation at or prior EE/LE was used to replace the data after EE/LE for subjects who met EE/LE criteria. Last Observation at or prior EE/LE was used to replace the data after EE/LE for subjects who met EE/LE criteria.

| | |
|--|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Baseline, Week 2, 4, 6, 8, 12, 16, 18, 20, 24, 28, 32, 36, 40, 44, 48 and 52 | |

| End point values | Placebo | Sirukumab 50 mg q4w | Sirukumab 100 mg q2w | |
|--------------------------------------|-----------------------|-----------------------|-----------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 556 | 557 | 557 | |
| Units: Units on a Scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Change at Week 2 | -4.5129 (± 9.68032) | -9.1095 (± 9.64598) | -7.9649 (± 9.58765) | |
| Change at Week 4 | -7.3134 (± 11.87959) | -13.3976 (± 12.00410) | -12.2156 (± 11.65262) | |
| Change at Week 6 | -9.5833 (± 13.15531) | -16.1013 (± 12.80166) | -15.4404 (± 12.18642) | |
| Change at Week 8 | -10.0752 (± 13.54599) | -17.6624 (± 12.98109) | -17.1302 (± 12.92830) | |
| Change at Week 12 | -11.5975 (± 14.53181) | -19.6639 (± 13.67016) | -19.0635 (± 13.63444) | |
| Change at Week 16 | -11.3507 (± 15.72864) | -20.3221 (± 14.14177) | -20.0652 (± 13.85171) | |
| Change at Week 18 | -10.6805 (± 16.31549) | -20.1215 (± 14.75683) | -20.4858 (± 13.72370) | |
| Change at Week 20 | -11.0425 (± 16.42770) | -20.8300 (± 15.31245) | -20.8508 (± 14.44400) | |
| Change at Week 24 | -11.1443 (± 16.37909) | -20.7459 (± 15.48312) | -21.0858 (± 14.57962) | |
| Change at Week 28 | -11.7828 (± 17.04652) | -21.3535 (± 15.98762) | -21.5524 (± 14.69362) | |
| Change at Week 32 | -12.0835 (± 17.11297) | -21.8176 (± 16.15549) | -21.8530 (± 14.58393) | |
| Change at Week 36 | -12.2107 (± 17.24703) | -21.9077 (± 15.95251) | -22.1040 (± 14.54871) | |
| Change at Week 40 | -11.9185 (± 17.32206) | -21.7862 (± 16.12260) | -21.6692 (± 15.33635) | |
| Change at Week 44 | -11.8730 (± 17.41934) | -21.4843 (± 16.33985) | -21.5514 (± 15.78476) | |
| Change at Week 48 | -11.9055 (± 17.91398) | -21.7238 (± 16.45520) | -21.7991 (± 15.34514) | |
| Change at Week 52 | -11.7647 (± 17.61074) | -21.9130 (± 16.32611) | -21.7344 (± 15.64620) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Clinical Disease Activity Index (CDAI) Score Through Week 52

| | |
|-----------------|--|
| End point title | Change From Baseline in Clinical Disease Activity Index (CDAI) Score Through Week 52 |
|-----------------|--|

End point description:

CDAI score is a derived score of 4 components: tender joints (28 joints), swollen joints (28 joints), patient's global assessment of disease activity, and physician's global assessments of disease activity. Total score ranges from 0 to 76 with a lower score indicating less disease activity. A negative change in CDAI score indicates an improvement in disease activity and a positive change in score indicates a worsening of disease activity. FAS included all randomized subjects. Subjects were analyzed according

to randomized treatment groups they were assigned to, regardless of the treatments they actually received. Last Observation Carried Forward (LOCF) method was used to impute missing values. Last Observation at or prior EE/LE was used to replace the data after EE/LE for subjects who met EE/LE criteria.

| | |
|--|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Baseline, Week 2, 4, 6, 8, 12, 16, 18, 20, 24, 28, 32, 36, 40, 44, 48 and 52 | |

| End point values | Placebo | Sirukumab 50 mg q4w | Sirukumab 100 mg q2w | |
|--------------------------------------|-------------------|---------------------|----------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 556 | 557 | 557 | |
| Units: Units on a Scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Change at Week 2 | -4.38 (± 9.210) | -6.82 (± 9.350) | -5.65 (± 9.014) | |
| Change at Week 4 | -7.09 (± 11.241) | -11.13 (± 11.699) | -9.88 (± 11.166) | |
| Change at Week 6 | -9.24 (± 12.407) | -13.79 (± 12.416) | -13.10 (± 11.599) | |
| Change at Week 8 | -9.72 (± 12.714) | -15.37 (± 12.593) | -14.79 (± 12.438) | |
| Change at Week 12 | -11.19 (± 13.625) | -17.36 (± 13.223) | -16.74 (± 13.098) | |
| Change at Week 16 | -10.86 (± 14.716) | -18.04 (± 13.651) | -17.75 (± 13.261) | |
| Change at Week 18 | -10.24 (± 15.245) | -17.82 (± 14.291) | -18.17 (± 13.204) | |
| Change at Week 20 | -10.57 (± 15.338) | -18.53 (± 14.809) | -18.57 (± 13.910) | |
| Change at Week 24 | -10.68 (± 15.302) | -18.45 (± 14.936) | -18.80 (± 14.075) | |
| Change at Week 28 | -11.27 (± 15.926) | -19.06 (± 15.395) | -19.27 (± 14.168) | |
| Change at Week 32 | -11.55 (± 15.950) | -19.57 (± 15.549) | -19.56 (± 14.095) | |
| Change at Week 36 | -11.70 (± 16.099) | -19.66 (± 15.455) | -19.80 (± 14.084) | |
| Change at Week 40 | -11.46 (± 16.236) | -19.54 (± 15.640) | -19.3 (± 14.833) | |
| Change at Week 44 | -11.41 (± 16.126) | -19.24 (± 15.888) | -19.26 (± 15.264) | |
| Change at Week 48 | -11.47 (± 16.594) | -19.47 (± 15.951) | -19.50 (± 14.871) | |
| Change at Week 52 | -11.38 (± 16.348) | -19.67 (± 15.834) | -19.44 (± 15.115) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Simplified Disease Activity Index based (SDAI-based) American College of Rheumatology (ACR)/ European League Against

Rheumatism (EULAR) Remission Through Week 52

| | |
|-----------------|---|
| End point title | Percentage of Subjects With Simplified Disease Activity Index based (SDAI-based) American College of Rheumatology (ACR)/ European League Against Rheumatism (EULAR) Remission Through Week 52 |
|-----------------|---|

End point description:

SDAI-based ACR/EULAR remission in subject at visit if SDAI score of ≤ 3.3 . SDAI score is derived by combining 5 disease assessments: tender joint (28 joints), swollen joint (28 joints) counts, PGA of disease activity by using VAS (scale ranges from 0 to 10 [0 = very well to 10 = very poor]), PhGA of disease activity using VAS (scale ranges from 0 to 10 [0=no arthritis to 10=extremely active arthritis]) and CRP. Change from baseline measures change in disease activity, negative change shows improvement and positive change shows worsening. FAS included all randomized subjects. Subjects were analyzed according to randomized treatment groups they were assigned to, regardless of the treatments they actually received. Subjects were set to not achieving SDAI-based remission after meeting EE, LE or TF criteria (whichever is earliest) or if having data missing.

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

End point timeframe:

Week 2, 4, 6, 8, 12, 16, 18, 20, 24, 28, 32, 36, 40, 44, 48 and 52

| End point values | Placebo | Sirukumab 50 mg q4w | Sirukumab 100 mg q2w | |
|-------------------------------|-----------------|---------------------|----------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 556 | 557 | 557 | |
| Units: Percentage of Subjects | | | | |
| number (not applicable) | | | | |
| Week 2 | 0.2 | 0 | 0 | |
| Week 4 | 0.4 | 0.2 | 1.3 | |
| Week 6 | 0.4 | 1.6 | 2.3 | |
| Week 8 | 0.7 | 2.9 | 2.9 | |
| Week 12 | 1.6 | 4.8 | 5.2 | |
| Week 16 | 2.2 | 5.4 | 6.6 | |
| Week 18 | 1.6 | 6.3 | 6.8 | |
| Week 20 | 1.6 | 7.5 | 7.7 | |
| Week 24 | 2.3 | 8.1 | 9.5 | |
| Week 28 | 2.3 | 9.0 | 8.4 | |
| Week 32 | 2.9 | 9.7 | 10.2 | |
| Week 36 | 1.8 | 10.1 | 10.6 | |
| Week 40 | 2.5 | 11.5 | 11.5 | |
| Week 44 | 2.5 | 9.7 | 11.7 | |
| Week 48 | 3.8 | 11.3 | 10.4 | |
| Week 52 | 3.2 | 11.5 | 10.6 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Boolean-based American College of Rheumatology (ACR)/ European League Against Rheumatism (EULAR) Remission Through Week 52

| | |
|-----------------|--|
| End point title | Percentage of Subjects With Boolean-based American College |
|-----------------|--|

End point description:

A subject was considered as having achieved the Boolean-based American College of Rheumatology (ACR)/ European League Against Rheumatism (EULAR) remission at a visit if all of the following 4 criteria were met at that visit: Tender joint count (68 joints) less than or equal to (\leq) 1; Swollen joint count (66 joints) \leq 1; CRP \leq 1 milligram per deciliter (mg/dL); Patient's Global Assessment of Disease Activity \leq 1 on a 0 (very well) to 10 (very poor) VAS. FAS included all randomized subjects. Subjects were analyzed according to randomized treatment groups they were assigned to, regardless of the treatments they actually received. Subjects were set to not achieving Boolean-based remission after meeting EE, LE or TF criteria (whichever is earliest) or if having data missing.

End point type Secondary

End point timeframe:

Week 2, 4, 6, 8, 12, 16, 18, 20, 24, 28, 32, 36, 40, 44, 48 and 52

| End point values | Placebo | Sirukumab 50 mg q4w | Sirukumab 100 mg q2w | |
|-------------------------------|-----------------|---------------------|----------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 556 | 557 | 557 | |
| Units: Percentage of Subjects | | | | |
| number (not applicable) | | | | |
| Week 2 | 0.2 | 0.4 | 0 | |
| Week 4 | 0.2 | 0.4 | 0.7 | |
| Week 6 | 0 | 0.9 | 0.9 | |
| Week 8 | 0.2 | 1.3 | 1.8 | |
| Week 12 | 1.3 | 2.9 | 3.1 | |
| Week 16 | 1.6 | 3.2 | 4.7 | |
| Week 18 | 0.7 | 3.6 | 4.7 | |
| Week 20 | 1.3 | 4.3 | 5.6 | |
| Week 24 | 0.9 | 4.3 | 7.0 | |
| Week 28 | 1.1 | 5.2 | 6.1 | |
| Week 32 | 2.3 | 5.0 | 6.5 | |
| Week 36 | 1.3 | 7.0 | 7.9 | |
| Week 40 | 0.9 | 5.9 | 7.9 | |
| Week 44 | 1.4 | 5.7 | 7.9 | |
| Week 48 | 1.8 | 7.0 | 7.0 | |
| Week 52 | 2.2 | 7.0 | 5.7 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Health Assessment Questionnaire-Disability Index (HAQ-DI) Score Through Week 52

End point title Change from Baseline in Health Assessment Questionnaire-Disability Index (HAQ-DI) Score Through Week 52

End point description:

The HAQ-DI score is an evaluation of the functional status for a subject. The 20- question instrument assesses the degree of difficulty a person has in accomplishing tasks in 8 functional areas (dressing, arising, eating, walking, hygiene, reaching, gripping, and activities of daily living). Responses in each

functional area are scored from 0, indicating no difficulty, to 3, indicating inability to perform a task in that area. Overall score was computed as the sum of domain scores and divided by the number of domains answered. Total possible score range: 0-3 where 0 = least difficulty and 3 = extreme difficulty. Full analysis set included all randomized subjects. Subjects were analyzed according to randomized treatment groups they were assigned to, regardless of the treatments they actually received. LOCF method was used to impute missing values. Last Observation at or prior EE/LE was used to replace the data after EE/LE for subjects who met EE/LE criteria.

| | |
|--|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Baseline, Week 2, 4, 6, 8, 12, 16, 18, 20, 28, 32, 36, 40, 44, 48 and 52 | |

| End point values | Placebo | Sirukumab 50 mg q4w | Sirukumab 100 mg q2w | |
|--------------------------------------|-------------------|---------------------|----------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 556 | 557 | 557 | |
| Units: Units on a Scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Change at Week 2 | -0.075 (± 0.3809) | -0.139 (± 0.3744) | -0.128 (± 0.3939) | |
| Change at Week 4 | -0.130 (± 0.4444) | -0.244 (± 0.4498) | -0.254 (± 0.4184) | |
| Change at Week 6 | -0.170 (± 0.4657) | -0.318 (± 0.4989) | -0.360 (± 0.4910) | |
| Change at Week 8 | -0.172 (± 0.4824) | -0.362 (± 0.5163) | -0.388 (± 0.5163) | |
| Change at Week 12 | -0.191 (± 0.5055) | -0.387 (± 0.5512) | -0.399 (± 0.5364) | |
| Change at Week 16 | -0.201 (± 0.5439) | -0.409 (± 0.5736) | -0.433 (± 0.5489) | |
| Change at Week 18 | -0.217 (± 0.5266) | -0.431 (± 0.5744) | -0.464 (± 0.5496) | |
| Change at Week 20 | -0.209 (± 0.5275) | -0.429 (± 0.6074) | -0.474 (± 0.5797) | |
| Change at Week 28 | -0.232 (± 0.5515) | -0.438 (± 0.5837) | -0.471 (± 0.5763) | |
| Change at Week 32 | -0.225 (± 0.5462) | -0.441 (± 0.6017) | -0.483 (± 0.5886) | |
| Change at Week 36 | -0.226 (± 0.5585) | -0.444 (± 0.5961) | -0.461 (± 0.5810) | |
| Change at Week 40 | -0.230 (± 0.5586) | -0.447 (± 0.5900) | -0.431 (± 0.5921) | |
| Change at Week 44 | -0.228 (± 0.5601) | -0.442 (± 0.6182) | -0.456 (± 0.5956) | |
| Change at Week 48 | -0.227 (± 0.5727) | -0.447 (± 0.6207) | -0.481 (± 0.6043) | |
| Change at Week 52 | -0.225 (± 0.5693) | -0.453 (± 0.6127) | -0.470 (± 0.5959) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Curve (AUC) of Change from Baseline in HAQ-DI Score

From Week 0 Through Week 24 and From Week 0 Through Week 52

| | |
|-----------------|--|
| End point title | Area Under the Curve (AUC) of Change from Baseline in HAQ-DI Score From Week 0 Through Week 24 and From Week 0 Through Week 52 |
|-----------------|--|

End point description:

AUC of change from baseline in HAQ-DI score is AUC of change from baseline in HAQ-DI score versus the time. AUC was calculated based on measurement at scheduled visits using trapezoidal rule. Functional status was determined as cumulative measure of HAQ-DI over 1 year by using AUC of change from baseline in HAQ-DI score through week 52. Decreases in AUC of change from baseline in HAQ-DI indicate a greater average improvement in physical function over time. FAS included all randomized subjects. Subjects were analyzed according to randomized treatment groups they were assigned to, regardless of the treatments they actually received. LOCF method was used to impute missing values. Last Observation at or prior EE/LE was used to replace the data after EE/LE for subjects who met EE/LE criteria.

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

End point timeframe:

Week 0 Through Week 24 and 52

| End point values | Placebo | Sirukumab 50 mg q4w | Sirukumab 100 mg q2w | |
|--------------------------------------|-------------------------|--------------------------|--------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 556 | 557 | 557 | |
| Units: Units on a Scale*Day | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 0 Through Week 24 | -28.85 (\pm 69.783) | -57.99 (\pm 76.384) | -61.71 (\pm 75.189) | |
| Week 0 Through Week 52 | -73.55 (\pm 170.636) | -145.30 (\pm 184.630) | -153.03 (\pm 180.633) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Health Assessment Questionnaire-Disability Index (HAQ-DI) Response Through Week 52

| | |
|-----------------|--|
| End point title | Percentage of Subjects With Health Assessment Questionnaire-Disability Index (HAQ-DI) Response Through Week 52 |
|-----------------|--|

End point description:

HAQ-DI response was defined as change of less than -0.22 from baseline in HAQ-DI score. HAQ-DI score is a 20-question instrument assesses the degree of difficulty a person has in accomplishing tasks in 8 functional areas (dressing, arising, eating, walking, hygiene, reaching, gripping, and activities of daily living). Responses in each functional area are scored from 0, indicating no difficulty, to 3, indicating inability to perform a task in that area. Overall score was computed as the sum of domain scores and divided by the number of domains answered. Total possible score range 0-3 where 0 = least difficulty and 3 = extreme difficulty. FAS included all randomized subjects. Subjects were analyzed according to randomized treatment groups they were assigned to, regardless of the treatments they actually received. LOCF method was used to impute missing values. Last Observation at or prior EE/LE was used to replace the data after EE/LE for subjects who met EE/LE criteria.

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

End point timeframe:

Week 2, 4, 6, 8, 12, 16, 18, 20, 24, 28, 32, 36, 40, 44, 48 and 52

| End point values | Placebo | Sirukumab 50 mg q4w | Sirukumab 100 mg q2w | |
|-------------------------------|-----------------|---------------------|----------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 556 | 557 | 557 | |
| Units: Percentage of Subjects | | | | |
| number (not applicable) | | | | |
| Week 2 | 34.4 | 40.6 | 37.0 | |
| Week 4 | 38.1 | 49.2 | 52.2 | |
| Week 6 | 42.4 | 56.2 | 58.0 | |
| Week 8 | 44.1 | 56.2 | 61.0 | |
| Week 12 | 44.6 | 60.1 | 60.9 | |
| Week 16 | 45.5 | 60.9 | 61.9 | |
| Week 18 | 45.9 | 62.7 | 65.4 | |
| Week 20 | 46.2 | 61.4 | 65.4 | |
| Week 24 | 46.9 | 63.0 | 65.4 | |
| Week 28 | 47.8 | 64.8 | 63.4 | |
| Week 32 | 46.9 | 62.8 | 63.7 | |
| Week 36 | 47.3 | 63.9 | 63.7 | |
| Week 40 | 47.3 | 63.7 | 61.8 | |
| Week 44 | 47.3 | 62.1 | 63.2 | |
| Week 48 | 47.3 | 61.8 | 64.6 | |
| Week 52 | 47.1 | 63.4 | 64.5 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Health Assessment Questionnaire-Disability Index (HAQ-DI) Score of Less Than or Equal to 0.5

| | |
|-----------------|--|
| End point title | Percentage of Subjects With Health Assessment Questionnaire-Disability Index (HAQ-DI) Score of Less Than or Equal to 0.5 |
|-----------------|--|

End point description:

HAQ-DI score is an evaluation of the functional status for a subject. The 20- question instrument assesses the degree of difficulty a person has in accomplishing tasks in 8 functional areas (dressing, arising, eating, walking, hygiene, reaching, gripping, and activities of daily living). Responses in each functional area are scored from 0, indicating no difficulty, to 3, indicating inability to perform a task in that area. Overall score was computed as the sum of domain scores and divided by the number of domains answered. Total possible score range 0-3 where 0 = least difficulty and 3 = extreme difficulty. FAS included all randomized subjects. Subjects were analyzed according to randomized treatment groups they were assigned to, regardless of the treatments they actually received. LOCF method was used to impute missing values. Last Observation at or prior EE/LE was used to replace the data after EE/LE for subjects who met EE/LE criteria.

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

End point timeframe:

Week 2, 4, 6, 8, 12, 16, 18, 20, 24, 28, 32, 36, 40, 44, 48 and 52

| End point values | Placebo | Sirukumab 50 mg q4w | Sirukumab 100 mg q2w | |
|-------------------------------|-----------------|---------------------|----------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 556 | 557 | 557 | |
| Units: Percentage of Subjects | | | | |
| number (not applicable) | | | | |
| Week 2 | 7.9 | 12.2 | 11.5 | |
| Week 4 | 9.9 | 15.6 | 16.3 | |
| Week 6 | 9.5 | 18.3 | 21.2 | |
| Week 8 | 10.6 | 21.7 | 21.0 | |
| Week 12 | 12.2 | 22.8 | 23.3 | |
| Week 16 | 13.3 | 24.6 | 26.8 | |
| Week 18 | 13.7 | 24.6 | 25.9 | |
| Week 20 | 13.1 | 26.0 | 27.5 | |
| Week 24 | 13.1 | 25.9 | 27.5 | |
| Week 28 | 13.8 | 26.2 | 28.7 | |
| Week 32 | 13.7 | 26.0 | 28.7 | |
| Week 36 | 13.7 | 27.5 | 27.5 | |
| Week 40 | 13.7 | 27.3 | 26.2 | |
| Week 44 | 13.1 | 27.8 | 27.6 | |
| Week 48 | 13.8 | 28.2 | 30.0 | |
| Week 52 | 12.4 | 27.5 | 29.3 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in van der Heijde-modified Sharp (vdH-S) Score at Week 24

| | |
|-----------------|--|
| End point title | Change from Baseline in van der Heijde-modified Sharp (vdH-S) Score at Week 24 |
|-----------------|--|

End point description:

vdH-S score is sum of joint erosion score and joint space narrowing (JSN) score. Joint erosion assessment is scored according to the surface area involved, from 0 to 5, with 0 indicating no erosion and 5 indicating complete collapse of bone whereas the JSN assessment including subluxation, is scored from 0 (normal) to 4 (bony ankylosis or complete luxation). Total score ranges from 0 (best) to 448 (worst) with higher scores indicating more joint damage. Efficacy FAS for radiographic assessment includes all randomized subjects who received at least 1 (partial or complete) dose of study agent and who had non-missing baseline vdH-S score. Subjects were analyzed according to randomized treatments they were assigned to, regardless of the treatment groups they actually received. This score was based on imputed value by EE Rules (set scores after EE to missing for placebo arm) and then missing data rules (imputed using linear extrapolation method).

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

End point timeframe:

Baseline, Week 24

| End point values | Placebo | Sirukumab 50 mg q4w | Sirukumab 100 mg q2w | |
|--------------------------------------|-----------------|---------------------|----------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 550 | 553 | 551 | |
| Units: Units on a Scale | | | | |
| arithmetic mean (standard deviation) | 1.96 (± 5.390) | 0.35 (± 2.149) | 0.30 (± 2.165) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in van der Heijde-modified Sharp (vdH-S) Sub-score by Type of Damage (erosion or JSN) at Week 24 and 52

| | |
|-----------------|--|
| End point title | Change From Baseline in van der Heijde-modified Sharp (vdH-S) Sub-score by Type of Damage (erosion or JSN) at Week 24 and 52 |
|-----------------|--|

End point description:

vdH-S score measures structural damage progression as sum of JE and JSN scores(S).JE is summary of erosion severity in 32 of hands(H) and 12 of feet(F) joints,scored as per surface area-from 0 (no erosion) to 5 (complete(CM) collapse of bone). Maximum (MAX) JES for H-160 (32*5) and MAX JES for F-120 (12*10 [5*2 sides of foot]). MAX JES is 280 whereas JSN is summary of severity of 30 of H and 12 of F joints, scored to subluxation from 0(normal) to 4(bony ankylosis or CM luxation). MAX JSNS for H-120(30*4), and MAX JSS for F-48(12*4). MAX JSNS is 168.Thus MAX JES-280 combined with MAX JSNS-168 gives worst possible vdH-SS of 448.Efficacy FAS population for radiographic assessments included here. Subjects analyzed according to randomized treatment they were assigned to, regardless of treatments they actually received. Imputed value based on EE Rules (set scores after EE to missing for placebo arm) and then missing data rules in all treatment groups (using linear extrapolation method).

| | |
|--------------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Baseline, Week 24 and 52 | |

| End point values | Placebo | Sirukumab 50 mg q4w | Sirukumab 100 mg q2w | |
|--------------------------------------|-----------------|---------------------|----------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 550 | 553 | 551 | |
| Units: Units on a Scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Erosion Score: Change at Week 24 | 1.21 (± 3.348) | 0.10 (± 1.306) | 0.08 (± 1.321) | |
| JSN Score: Change at Week 24 | 0.76 (± 2.540) | 0.24 (± 1.404) | 0.21 (± 1.537) | |
| Erosion Score: Change at Week 52 | 2.23 (± 5.903) | 0.12 (± 1.809) | 0.08 (± 2.005) | |
| JSN Score: Change at Week 52 | 1.46 (± 4.311) | 0.38 (± 1.839) | 0.38 (± 2.184) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in van der Heijde-modified Sharp (vdH-S) Sub-

score by Region Hand or Feet and Type Erosion or JSN at Week 24 and 52

| | |
|-----------------|--|
| End point title | Change from Baseline in van der Heijde-modified Sharp (vdH-S) Sub-score by Region Hand or Feet and Type Erosion or JSN at Week 24 and 52 |
|-----------------|--|

End point description:

vdH-S score measures structural damage progression as sum of JE and JSN scores(S).JE is summary of erosion severity in 32 of hands(H) and 12 of feet(F) joints,scored as per surface area-from 0 (no erosion) to 5 (complete(CM) collapse of bone). Maximum (MAX) JES for H-160 (32*5) and MAX JES for F-120 (12*10 [5*2 sides of foot]). MAX JES is 280 whereas JSN is summary of severity of 30 of H and 12 of F joints, scored to subluxation from 0(normal) to 4(bony ankylosis or CM luxation). MAX JSNS for H-120(30*4), and MAX JSS for F-48(12*4). MAX JSNS is 168.Thus MAX JES-280 combined with MAX JSNS-168 gives worst possible vdH-SS of 448.Efficacy FAS population for radiographic assessments included here. Subjects analyzed according to randomized treatment they were assigned to, regardless of treatments they actually received. Imputed value based on EE Rules (set scores after EE to missing for placebo arm) and then missing data rules in all treatment groups (using linear extrapolation method).

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

End point timeframe:

Baseline, Week 24 and 52

| End point values | Placebo | Sirukumab 50 mg q4w | Sirukumab 100 mg q2w | |
|---|-----------------|---------------------|----------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 550 | 553 | 551 | |
| Units: Units on a Scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Change in Hand Erosion Score at Week 24 | 0.74 (± 2.406) | 0.07 (± 0.920) | 0.03 (± 0.966) | |
| Change in Hand JSN Score at Week 24 | 0.51 (± 1.818) | 0.16 (± 1.025) | 0.16 (± 1.021) | |
| Change in Foot Erosion Score at Week 24 | 0.46 (± 1.459) | 0.03 (± 0.682) | 0.05 (± 0.754) | |
| Change in Foot JSN Score at Week 24 | 0.25 (± 1.207) | 0.09 (± 0.722) | 0.06 (± 1.152) | |
| Change in Hand Erosion Score at Week 52 | 1.43 (± 4.378) | 0.09 (± 1.296) | 0.03 (± 1.312) | |
| Change in Hand JSN Score at Week 52 | 0.98 (± 3.196) | 0.25 (± 1.378) | 0.28 (± 1.808) | |
| Change in Foot Erosion Score at Week 52 | 0.80 (± 2.460) | 0.03 (± 0.955) | 0.06 (± 1.302) | |
| Change in Foot JSN Score at Week 52 | 0.48 (± 2.013) | 0.13 (± 0.929) | 0.10 (± 1.171) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Change From Baseline in van der Heijde Modified Sharp Score (vdH-S Score) Greater Than Smallest Detectable Change (SDC) at Weeks 24 and 52

| | |
|-----------------|--|
| End point title | Percentage of Subjects With Change From Baseline in van der Heijde Modified Sharp Score (vdH-S Score) Greater Than Smallest Detectable Change (SDC) at Weeks 24 and 52 |
|-----------------|--|

End point description:

vdH-S score measures structural damage progression as sum of JE and JSNS.JE is summary of erosion(E) severity in 32 of hand(H) and 12 of feet(F) joints, scored as per the surface area- 0(no E) to 5

(complete(CM) collapse of bone); JSN-summary of severity of 30 of H12 of F joints, scored as per sub-luxation(L) from 0(normal) to 4(bony ankylosis or CML). SDC is smallest change in S to be assessed correctly as per limits of agreement. SDC for change from baseline in vdH-SS is determined as: $SDC = 1.96 * SD / (\sqrt{2} * \sqrt{k})$, here SD=standard deviation of difference between 2 readers; k= number of readers. Efficacy FAS population for radiographic assessments included here. Subjects analyzed according to randomized treatment they were assigned to, regardless of treatments they actually received. This score was based on imputed value by EE Rules (set scores after EE to missing for placebo arm) and then missing data rules in all treatment groups (imputed using linear extrapolation

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Weeks 24 and 52 | |

| End point values | Placebo | Sirukumab 50 mg q4w | Sirukumab 100 mg q2w | |
|-------------------------------|-----------------|---------------------|----------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 550 | 553 | 551 | |
| Units: Percentage of Subjects | | | | |
| number (not applicable) | | | | |
| Week 24 | 25.3 | 8.3 | 7.6 | |
| Week 52 | 35.5 | 12.1 | 12.0 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With a Change of Less Than or Equal to 0 From Baseline in van der Heijde Modified Sharp (vdH-S) Score at Weeks 24 and 52

| | |
|-----------------|---|
| End point title | Percentage of Subjects With a Change of Less Than or Equal to 0 From Baseline in van der Heijde Modified Sharp (vdH-S) Score at Weeks 24 and 52 |
|-----------------|---|

End point description:

vdH-S score measures structural damage progression as sum of JE and JSN scores(S).JE is summary of erosion severity in 32 of hands(H) and 12 of feet(F) joints, scored as per surface area-from 0 (no erosion) to 5 (complete(CM) collapse of bone). Maximum (MAX) JES for H-160 (32*5) and MAX JES for F-120 (12*10 [5*2 sides of foot]). MAX JES is 280 whereas JSN is summary of severity of 30 of H and 12 of F joints, scored to subluxation from 0(normal) to 4(bony ankylosis or CM luxation). MAX JSNS for H-120(30*4), and MAX JSS for F-48(12*4). MAX JSNS is 168. Thus MAX JES-280 combined with MAX JSNS-168 gives worst possible vdH-SS of 448. Efficacy FAS population for radiographic assessments included here. Subjects analyzed according to randomized treatment they were assigned to, regardless of treatments they actually received. Imputed value based on EE Rules (set scores after EE to missing for placebo arm) and then missing data rules in all treatment groups (using linear extrapolation method).

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Week 24 and 52 | |

| End point values | Placebo | Sirukumab 50 mg q4w | Sirukumab 100 mg q2w | |
|-------------------------------|-----------------|---------------------|----------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 550 | 553 | 551 | |
| Units: Percentage of Subjects | | | | |
| number (not applicable) | | | | |
| Week 24 | 48.4 | 65.8 | 68.8 | |
| Week 52 | 45.5 | 59.0 | 62.4 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in van der Heijde Modified Sharp Score (vdH-S Score) by Reader at Weeks 24 and 52

| | |
|-----------------|--|
| End point title | Change From Baseline in van der Heijde Modified Sharp Score (vdH-S Score) by Reader at Weeks 24 and 52 |
|-----------------|--|

End point description:

vdH-S score measures structural damage progression as sum of JE and JSN scores(S).JE is summary of erosion severity in 32 of hands(H) and 12 of feet(F) joints,scored as per surface area-from 0 (no erosion) to 5 (complete(CM) collapse of bone). Maximum (MAX) JES for H-160 (32*5) and MAX JES for F-120 (12*10 [5*2 sides of foot]). MAX JES is 280 whereas JSN is summary of severity of 30 of H and 12 of F joints, scored to subluxation from 0(normal) to 4(bony ankylosis or CM luxation). MAX JSNS for H-120(30*4), and MAX JSS for F-48(12*4). MAX JSNS is 168.Thus MAX JES-280 combined with MAX JSNS-168 gives worst possible vdH-SS of 448.Efficacy FAS population for radiographic assessments included here. Subjects analyzed according to randomized treatment they were assigned to, regardless of treatments they actually received. Imputed value based on EE Rules (set scores after EE to missing for placebo arm) then missing data rules in all treatment groups (using linear extrapolation method).

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

End point timeframe:

Baseline, Weeks 24 and 52

| End point values | Placebo | Sirukumab 50 mg q4w | Sirukumab 100 mg q2w | |
|--|-----------------|---------------------|----------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 550 | 553 | 551 | |
| Units: Units on a Scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Reader 1 at Week 24 (n= 550, 551, 550) | 2.06 (± 5.616) | 0.21 (± 2.495) | 0.20 (± 2.773) | |
| Reader 2 at Week 24 (n= 550, 553, 551) | 1.65 (± 5.053) | 0.38 (± 1.969) | 0.33 (± 1.830) | |
| Reader 1 at Week 52 (n= 447, 459, 467) | 2.99 (± 7.940) | 0.54 (± 3.285) | 0.29 (± 3.325) | |
| Reader 2 at Week 52 (n= 447, 460, 467) | 2.65 (± 7.331) | 0.54 (± 2.660) | 0.35 (± 2.184) | |

Statistical analyses

Secondary: Change From Baseline in Serum C-reactive protein (CRP) Levels Through Week 52

| | |
|--|---|
| End point title | Change From Baseline in Serum C-reactive protein (CRP) Levels Through Week 52 |
| End point description: | |
| Serum CRP is a marker of systemic inflammation. A negative change from baseline in CRP represents improvement. FAS included all randomized subjects. Subjects analyzed according to randomized treatment they were assigned to, regardless of treatments they actually received. Last Observation Carried Forward (LOCF) method was used to impute missing values. The last observation at or prior to EE/LE was used to replace the data after EE/LE for subjects who met EE/LE criteria. | |
| End point type | Secondary |
| End point timeframe: | |
| Baseline, Week 2, 4, 6, 8, 12, 16, 18, 20, 24, 28, 32, 36, 40, 44, 48 and 52 | |

| End point values | Placebo | Sirukumab 50 mg q4w | Sirukumab 100 mg q2w | |
|--------------------------------------|---------------------|---------------------|----------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 556 | 557 | 557 | |
| Units: Milligram per Deciliter | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline | 2.5148 (± 3.38577) | 2.4145 (± 2.62179) | 2.3952 (± 2.64241) | |
| Change at Week 2 | -0.1339 (± 2.86946) | -2.2867 (± 2.44604) | -2.3198 (± 2.64772) | |
| Change at Week 4 | -0.2209 (± 2.94279) | -2.2707 (± 2.41525) | -2.3406 (± 2.64584) | |
| Change at Week 6 | -0.3432 (± 2.96865) | -2.3124 (± 2.44604) | -2.3451 (± 2.64678) | |
| Change at Week 8 | -0.3561 (± 3.05281) | -2.2919 (± 2.41368) | -2.3392 (± 2.65864) | |
| Change at Week 12 | -0.4099 (± 3.22085) | -2.3038 (± 2.43828) | -2.3274 (± 2.67383) | |
| Change at Week 16 | -0.4890 (± 3.17554) | -2.2841 (± 2.43707) | -2.3166 (± 2.65115) | |
| Change at Week 18 | -0.4375 (± 3.48359) | -2.3030 (± 2.45255) | -2.3114 (± 2.65919) | |
| Change at Week 20 | -0.4682 (± 3.21483) | -2.2973 (± 2.44855) | -2.2798 (± 2.74939) | |
| Change at Week 24 | -0.4610 (± 3.31445) | -2.2974 (± 2.45343) | -2.2891 (± 2.73480) | |
| Change at Week 28 | -0.5108 (± 3.34288) | -2.2937 (± 2.45419) | -2.2820 (± 2.73435) | |
| Change at Week 32 | -0.5332 (± 3.39542) | -2.2474 (± 2.63824) | -2.2907 (± 2.73375) | |
| Change at Week 36 | -0.5128 (± 3.36374) | -2.2515 (± 2.62647) | -2.3085 (± 2.73396) | |
| Change at Week 40 | -0.4623 (± 3.46179) | -2.2429 (± 2.64450) | -2.3032 (± 2.73402) | |
| Change at Week 44 | -0.4631 (± 4.00446) | -2.2398 (± 2.65898) | -2.2895 (± 2.75035) | |
| Change at Week 48 | -0.4372 (± 4.15311) | -2.2561 (± 2.62491) | -2.2944 (± 2.75776) | |
| Change at Week 52 | -0.3854 (± 3.96633) | -2.2399 (± 2.64267) | -2.2976 (± 2.73878) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in the Duration of Morning Stiffness Through Week 52

| | |
|-----------------|---|
| End point title | Change From Baseline in the Duration of Morning Stiffness Through Week 52 |
|-----------------|---|

End point description:

Duration of morning stiffness was defined as the time elapsed when subject woke up in the morning and was able to resume normal activities without stiffness in minutes (If none was present = 0; If morning stiffness was continuing at the time of assessment or was unusual compared to the recent past, average of duration of stiffness over the past 3 days was reported; If stiffness persisted the entire day, 1440 minutes was recorded). Negative values for this outcome measure represent improvement, i.e. shortening of duration of morning stiffness. FAS was defined as all randomized subjects. Subjects were analyzed according to randomized treatment groups they were assigned to, regardless of treatment they actually received. Here 'N'(number of subject analyzed) signifies subject who were evaluable for this outcome measure. LOCF method was used to impute missing values. The last observation at or prior to EE/LE was used to replace the data after EE/LE for subjects who met EE/LE criteria.

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

End point timeframe:

Baseline, Week 2, 4, 6, 8, 12, 16, 18, 20, 24, 28, 32, 36, 40, 44, 48 and 52

| End point values | Placebo | Sirukumab 50 mg q4w | Sirukumab 100 mg q2w | |
|--------------------------------------|------------------|---------------------|----------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 552 | 552 | 555 | |
| Units: Minutes | | | | |
| arithmetic mean (standard deviation) | | | | |
| Change at Week 2 | -22.5 (± 184.96) | -35.2 (± 212.94) | -24.0 (± 177.41) | |
| Change at Week 4 | -27.2 (± 202.02) | -61.6 (± 213.09) | -45.1 (± 181.13) | |
| Change at Week 6 | -35.3 (± 190.54) | -81.0 (± 207.07) | -70.3 (± 206.41) | |
| Change at Week 8 | -41.7 (± 171.05) | -84.1 (± 232.34) | -79.6 (± 213.42) | |
| Change at Week 12 | -53.2 (± 179.24) | -88.1 (± 220.03) | -89.4 (± 217.48) | |
| Change at Week 16 | -52.2 (± 173.24) | -82.2 (± 241.75) | -84.1 (± 224.72) | |
| Change at Week 18 | -60.2 (± 191.68) | -84.6 (± 239.43) | -88.5 (± 223.95) | |
| Change at Week 20 | -62.0 (± 193.64) | -93.5 (± 234.10) | -90.0 (± 229.08) | |
| Change at Week 24 | -63.7 (± 195.58) | -96.7 (± 228.31) | -95.5 (± 234.19) | |
| Change at Week 28 | -68.3 (± 195.42) | -95.2 (± 230.36) | -98.0 (± 235.03) | |

| | | | | |
|-------------------|------------------|------------------|------------------|--|
| Change at Week 32 | -68.9 (± 196.31) | -96.5 (± 230.46) | -96.5 (± 231.25) | |
| Change at Week 36 | -68.8 (± 196.90) | -96.5 (± 228.71) | -95.2 (± 226.37) | |
| Change at Week 40 | -68.7 (± 68.7) | -95.7 (± 243.78) | -95.9 (± 233.28) | |
| Change at Week 44 | -69.9 (± 197.38) | -96.6 (± 232.42) | -97.0 (± 234.63) | |
| Change at Week 48 | -69.6 (± 195.50) | -97.8 (± 238.36) | -97.0 (± 230.66) | |
| Change at Week 52 | -67.3 (± 196.98) | -99.1 (± 233.82) | -97.7 (± 231.53) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Physical and Mental Component Summary (MCS) Scores of 36-Item Short Form Health Survey (SF-36) at Weeks 24 and 52

| | |
|------------------------|--|
| End point title | Change From Baseline in Physical and Mental Component Summary (MCS) Scores of 36-Item Short Form Health Survey (SF-36) at Weeks 24 and 52 |
| End point description: | SF-36(36 questions),consists of 8 multi-item scales:Limitations(LIM) in physical (PHY) functioning due to health (HEL) problems;LIM in usual role activities due to PHY HEL problems;Bodily pain;General mental HEL(psychological distress/well-being);LIM in usual role activities due to personal/emotional problems;LIM in social functioning due to PHY/mental HEL problems;Vitality;General HEL perception.All 8 scales scored from 0- 100(higher scores(S)=better HEL) Based on scale S,summary S,physical component score (PCS)/MCS will be derived.Scoring is based on algorithm provided by developer.Summary MCS/PCS score is also scaled from 0-100(higher S indicating better HEL).FAS included all randomized subjects.Subjects analyzed according to randomized treatment groups they were assigned to,regardless of treatments they actually received.LOCF method was used to impute missing values.The last observation at/prior to EE/LE was used to replace the data after EE/LE for subjects who met EE/LE criteria |
| End point type | Secondary |
| End point timeframe: | Baseline, Week 24 and 52 |

| End point values | Placebo | Sirukumab 50 mg q4w | Sirukumab 100 mg q2w | |
|--------------------------------------|------------------|---------------------|----------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 556 | 557 | 557 | |
| Units: Units on a Scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| PCS :Change at Week 24 | 2.290 (± 6.2790) | 5.358 (± 7.3312) | 5.850 (± 7.0677) | |
| PCS :Change at Week 52 | 2.423 (± 6.8069) | 5.661 (± 7.7405) | 6.162 (± 7.2277) | |
| MCS :Change at Week 24 | 2.892 (± 9.1766) | 4.898 (± 9.6508) | 4.216 (± 9.4819) | |
| MCS :Change at Week 52 | 2.690 (± 9.5698) | 5.351 (± 9.6397) | 4.767 (± 9.7991) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Greater Than or Equal to 4-Point Change From Baseline in Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-Fatigue) Score at Week 8, 16, 24, 36 and 52

| | |
|-----------------|--|
| End point title | Percentage of Subjects With Greater Than or Equal to 4-Point Change From Baseline in Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-Fatigue) Score at Week 8, 16, 24, 36 and 52 |
|-----------------|--|

End point description:

Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-Fatigue) is a questionnaire that assesses self-reported tiredness, weakness, and difficulty conducting usual activities due to fatigue. The questionnaire consists of 13 questions that assess a subject's level of fatigue and tiredness over the last 7 days. Each question is graded on a 5-point scale (0 - 4); and accordingly, the total FACIT Fatigue scores can range from 0 to 52, with lower score reflecting more fatigue and higher scores reflecting less fatigue. FAS was defined as all randomized subjects. Subjects analyzed according to randomized treatment they were assigned to, regardless of treatments they actually received. Last Observation Carried Forward (LOCF) method was used to impute missing values. The last observation at or prior to EE/LE was used to replace the data after EE/LE for subjects who met EE/LE criteria.

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

End point timeframe:

Week 8, 16, 24, 36 and 52

| End point values | Placebo | Sirukumab 50 mg q4w | Sirukumab 100 mg q2w | |
|-------------------------------|-----------------|---------------------|----------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 556 | 557 | 557 | |
| Units: Percentage of Subjects | | | | |
| number (not applicable) | | | | |
| Week 8 | 41.0 | 55.8 | 54.9 | |
| Week 16 | 42.4 | 58.0 | 58.9 | |
| Week 24 | 43.9 | 61.4 | 59.4 | |
| Week 36 | 39.7 | 57.8 | 56.2 | |
| Week 52 | 41.0 | 59.1 | 60.5 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Total Scores of Work Limitations Questionnaire (WLQ) Week 8, 16, 24, 36 and 52

| | |
|-----------------|--|
| End point title | Change from Baseline in Total Scores of Work Limitations |
|-----------------|--|

End point description:

The Work Limitations Questionnaire (WLQ) was used to measure the impairment in work-related productivity, with reference to the previous two weeks. Each work-related question is scored from 0 to 4 and the total score ranges from 0-100, with lower scores signifying fewer limitations at work. FAS was defined as all randomized subjects. Subjects analyzed according to randomized treatment they were assigned to, regardless of treatments they actually received. Here 'N'(number of subjects analyzed) signifies subjects who were evaluable for this outcome measure. Last Observation Carried Forward (LOCF) method was used to impute missing values. The last observation at or prior to EE/LE was used to replace the data after EE/LE for subjects who met EE/LE criteria.

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

End point timeframe:

Baseline, Week 8, 16, 24, 36 and 52

| End point values | Placebo | Sirukumab 50 mg q4w | Sirukumab 100 mg q2w | |
|--------------------------------------|-------------------|---------------------|----------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 227 | 223 | 223 | |
| Units: Units on a Scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 8 | -0.812 (± 3.6230) | -1.946 (± 3.8040) | -2.202 (± 3.8437) | |
| Week 16 | -0.840 (± 4.6414) | -2.406 (± 4.1403) | -2.600 (± 4.3066) | |
| Week 24 | -1.019 (± 4.5328) | -2.765 (± 4.4381) | -2.884 (± 4.5873) | |
| Week 36 | -0.940 (± 4.7982) | -2.921 (± 4.4205) | -2.952 (± 4.5640) | |
| Week 52 | -0.732 (± 5.0288) | -3.057 (± 4.5290) | -2.936 (± 4.3940) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in EuroQol Health State Visual Analogue Scale (EQ VAS)

| | |
|-----------------|---|
| End point title | Change From Baseline in EuroQol Health State Visual Analogue Scale (EQ VAS) |
|-----------------|---|

End point description:

The EuroQol Health State Visual Analogue Scale (EQ VAS) records the respondent's self-rated health on a vertical line, VAS where the endpoints are labeled as 0= 'Worst imaginable health state' and 100= 'Best imaginable health state'. The EQ VAS can be used as a quantitative measure of health outcome as judged by the individual respondents. FAS included all randomized subjects. Here 'N'(number of subjects analyzed) signifies subjects who were evaluable for this outcome measure. Subjects analyzed according to randomized treatment they were assigned to, regardless of treatments they actually received. Last Observation Carried Forward (LOCF) method was used to impute missing values. The last observation at or prior to EE/LE was used to replace the data after EE/LE for subjects who met EE/LE criteria.

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

End point timeframe:

Baseline, Week 8, 16, 24, and 52

| End point values | Placebo | Sirukumab 50 mg q4w | Sirukumab 100 mg q2w | |
|--------------------------------------|-----------------|---------------------|----------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 554 | 557 | 556 | |
| Units: Units on a Scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Change at Week 8 | 5.61 (± 24.415) | 11.64 (± 26.979) | 12.24 (± 26.025) | |
| Change at Week 16 | 5.83 (± 26.177) | 14.09 (± 28.581) | 14.36 (± 27.884) | |
| Change at Week 24 | 6.71 (± 26.520) | 14.86 (± 28.747) | 16.41 (± 28.830) | |
| Change at Week 36 | 8.30 (± 26.144) | 16.80 (± 28.595) | 17.14 (± 28.329) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in EuroQol EQ-5D-3L Descriptive System

| | |
|-----------------|---|
| End point title | Change From Baseline in EuroQol EQ-5D-3L Descriptive System |
|-----------------|---|

End point description:

The EQ-5D-3L Descriptive System comprises the following 5 dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Each dimension is assessed on a 3-point ordinal scale (1=no problems, 2=some problems, 3=extreme problems). The responses to the five EQ-5D dimensions were scored using a utility-weighted algorithm to derive an EQ-5D health status index score between 0 to 1, with 1.00 indicating "full health" and 0 representing dead. FAS included all randomized subjects. Subjects analyzed according to randomized treatment they were assigned to, regardless of treatments they actually received. LOCF method was used to impute missing values. The last observation at or prior to EE/LE was used to replace the data after EE/LE for subjects who met EE/LE criteria.

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

End point timeframe:

Baseline, Week 8, 16, 24, and 52

| End point values | Placebo | Sirukumab 50 mg q4w | Sirukumab 100 mg q2w | |
|--------------------------------------|--------------------|---------------------|----------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 556 | 557 | 557 | |
| Units: Units on a Scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Change at Week 8 | 0.1041 (± 0.31794) | 0.1734 (± 0.32473) | 0.1647 (± 0.30146) | |
| Change at Week 16 | 0.1131 (± 0.33788) | 0.1831 (± 0.34875) | 0.1899 (± 0.31149) | |
| Change at Week 24 | 0.1263 (± 0.33539) | 0.1885 (± 0.33867) | 0.2057 (± 0.32081) | |
| Change at Week 52 | 0.1255 (± 0.34312) | 0.1950 (± 0.33448) | 0.2007 (± 0.32895) | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Screening up to Week 120

Adverse event reporting additional description:

Safety population included all subjects who received at least 1 partial or complete dose of study agent, analysed in treatment received overtime, regardless randomization. One subject inadvertently received Sirukumab 100 mg instead of Sirukumab 50 mg and therefore reported in Sirukumab 100 mg arm (558) instead of Sirukumab 50 mg (556 subjects).

| | |
|-----------------|----------------|
| Assessment type | Non-systematic |
|-----------------|----------------|

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 17.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|--|
| Reporting group title | W0 to W120-Placebo to Sirukumab 50 mg q4w due to EE/LE or CO |
|-----------------------|--|

Reporting group description:

Subjects who received placebo in the placebo controlled period were rerandomized (due to EE at Week 18 or LE at Week 40 or CO at Week 52) to receive subcutaneous (SC) sirukumab 50 mg q4w dose regimen up to Week 104. Subjects who completed study agent administration up to Week 104 and did not elect for long term extension (LTE) were followed up for safety from Week 104 up to Week 120.

| | |
|-----------------------|----------------------------|
| Reporting group title | Week 0 to Week 120-Placebo |
|-----------------------|----------------------------|

Reporting group description:

Subjects received matching placebo from week 0 to week 52, every 2 weeks (q2w) until either early escape (EE) at Week 18 or late escape (LE) at Week 40 or crossover (CO) at Week 52 and were rerandomized to subcutaneous (SC) sirukumab 50 mg q4w or sirukumab 100 mg q2w dose regimens up to Week 104. Subjects who completed study agent administration up to Week 104 and did not elect for long term extension (LTE) were followed up for safety from Week 104 up to Week 120.

| | |
|-----------------------|--|
| Reporting group title | W0 to W120- Placebo to Sirukumab 100 mg q2w Due to EE/LE or CO |
|-----------------------|--|

Reporting group description:

Subjects who received placebo in the placebo controlled period were rerandomized (due to EE at Week 18 or LE at Week 40 or CO at Week 52) to receive subcutaneous (SC) sirukumab 100 mg q2w dose up to Week 104. Subjects who completed study agent administration up to Week 104 and did not elect for long term extension (LTE) were followed up for safety from Week 104 up to Week 120.

| | |
|-----------------------|---------------------------------|
| Reporting group title | W0 to W120-Sirukumab 100 mg q2w |
|-----------------------|---------------------------------|

Reporting group description:

Subjects received 100 mg of sirukumab SC injections at Weeks 0, 2 and q2w through Week 104. Subjects who completed study agent administration up to Week 104 and did not elect for long term extension (LTE) were followed up for safety from Week 104 up to Week 120.

| | |
|-----------------------|---------------------------------|
| Reporting group title | W0 to W120- Sirukumab 50 mg q4w |
|-----------------------|---------------------------------|

Reporting group description:

Subjects received 50 mg of sirukumab SC injections at Weeks 0, 4, and q4w through Week 104. Subjects who completed study agent administration up to Week 104 and did not elect for long term extension (LTE) were followed up for safety from Week 104 up to Week 120.

| Serious adverse events | W0 to W120-Placebo to Sirukumab 50 mg q4w due to EE/LE or CO | Week 0 to Week 120-Placebo | W0 to W120- Placebo to Sirukumab 100 mg q2w Due to EE/LE or CO |
|---|--|----------------------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 30 / 242 (12.40%) | 40 / 556 (7.19%) | 35 / 241 (14.52%) |

| number of deaths (all causes) number of deaths resulting from adverse events | 5 | 1 | 6 |
|--|-----------------|-----------------|-----------------|
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Acute Myeloid Leukaemia | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Adrenal Adenoma | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Basal Cell Carcinoma | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Benign Neoplasm of Thyroid Gland | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 1 / 556 (0.18%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bladder Cancer | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Bladder Transitional Cell Carcinoma | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Breast Cancer | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 1 / 241 (0.41%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Colon Cancer Metastatic | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Gastric Cancer | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 1 / 241 (0.41%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal Stromal Tumour | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Glioblastoma Multiforme | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 1 / 556 (0.18%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Intraductal Papilloma of Breast | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Invasive Ductal Breast Carcinoma | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Leiomyoma | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 1 / 241 (0.41%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lung Cancer Metastatic | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Lung Neoplasm Malignant | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 1 / 241 (0.41%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| Meningioma | | | |
| subjects affected / exposed | 1 / 242 (0.41%) | 0 / 556 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metastases to Bone | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Metastases to Central Nervous System | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 1 / 241 (0.41%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Neuroendocrine Carcinoma | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Oropharyngeal Squamous Cell Carcinoma | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Ovarian Clear Cell Carcinoma | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Teratoma | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Uterine Cancer | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Uterine Leiomyoma | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 1 / 556 (0.18%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vascular disorders | | | |
| Aortic Aneurysm | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 1 / 241 (0.41%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Aortic Dissection | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 1 / 241 (0.41%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| Axillary Vein Thrombosis | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 1 / 556 (0.18%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Deep Vein Thrombosis | | | |
| subjects affected / exposed | 1 / 242 (0.41%) | 0 / 556 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Extremity Necrosis | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Haematoma | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Hypertension | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 1 / 242 (0.41%) | 1 / 556 (0.18%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 2 / 2 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypotension | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Labile Hypertension | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Necrosis Ischaemic | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Peripheral Arterial Occlusive Disease | | | |
| subjects affected / exposed | 1 / 242 (0.41%) | 0 / 556 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Peripheral Ischaemia | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Shock | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Subclavian Vein Thrombosis | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 1 / 556 (0.18%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Thrombosed Varicose Vein | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Vasculitis | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 1 / 556 (0.18%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Venous Thrombosis Limb | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Pregnancy, puerperium and perinatal conditions | | | |
| Abortion Spontaneous | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Chest Pain | | | |
| subjects affected / exposed | 1 / 242 (0.41%) | 0 / 556 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Death | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 1 / 241 (0.41%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| Influenza Like Illness | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |

| | | | |
|---|-----------------|-----------------|-----------------|
| Medical Device Site Joint Inflammation | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Serositis | | | |
| subjects affected / exposed | 1 / 242 (0.41%) | 0 / 556 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Sudden Cardiac Death | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Immune system disorders | | | |
| Drug Hypersensitivity | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Reproductive system and breast disorders | | | |
| Benign Prostatic Hyperplasia | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 1 / 556 (0.18%) | 1 / 241 (0.41%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Breast Mass | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 1 / 556 (0.18%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cystocele | | | |
| subjects affected / exposed | 1 / 242 (0.41%) | 0 / 556 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Endometriosis | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Ovarian Cyst | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Rectocele | | | |
| subjects affected / exposed | 1 / 242 (0.41%) | 0 / 556 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vaginal Haemorrhage | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Acute Respiratory Distress Syndrome | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 1 / 556 (0.18%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| Acute Respiratory Failure | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 1 / 241 (0.41%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Asthma | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 1 / 241 (0.41%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Chronic Obstructive Pulmonary Disease | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Cough | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 242 (0.00%) | 1 / 556 (0.18%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dyspnoea | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Epistaxis | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Interstitial Lung Disease | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 1 / 556 (0.18%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lung Disorder | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Pleural Effusion | | | |
| subjects affected / exposed | 1 / 242 (0.41%) | 1 / 556 (0.18%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pleurisy | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Pneumonia Aspiration | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Pneumonitis | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Pneumothorax Spontaneous | | | |
| subjects affected / exposed | 1 / 242 (0.41%) | 0 / 556 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary Embolism | | | |
| subjects affected / exposed | 1 / 242 (0.41%) | 0 / 556 (0.00%) | 2 / 241 (0.83%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 2 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary Mass | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 1 / 556 (0.18%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary Necrosis | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 1 / 556 (0.18%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory Failure | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Psychiatric disorders | | | |
| Anxiety | | | |
| subjects affected / exposed | 1 / 242 (0.41%) | 0 / 556 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Mental Status Changes | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Suicidal Ideation | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 242 (0.00%) | 1 / 556 (0.18%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Investigations | | | |
| Alanine Aminotransferase Increased | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 1 / 556 (0.18%) | 1 / 241 (0.41%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Aspartate Aminotransferase Increased | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 1 / 556 (0.18%) | 2 / 241 (0.83%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 2 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood Bilirubin Increased | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 2 / 241 (0.83%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 2 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Chest X-Ray Abnormal | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 1 / 556 (0.18%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatic Enzyme Increased | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Liver Function Test Increased | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 1 / 556 (0.18%) | 1 / 241 (0.41%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Weight Decreased | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Injury, poisoning and procedural complications | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| Abdominal Injury | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 1 / 241 (0.41%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Chemical Peritonitis | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 1 / 241 (0.41%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Concussion | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 1 / 556 (0.18%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Contusion | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 1 / 241 (0.41%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Epiphyseal Fracture | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Facial Bones Fracture | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 1 / 556 (0.18%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Femoral Neck Fracture | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Femur Fracture | | | |
| subjects affected / exposed | 1 / 242 (0.41%) | 1 / 556 (0.18%) | 1 / 241 (0.41%) |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Foot Fracture | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Hand Fracture | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Hip Fracture | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 1 / 556 (0.18%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Humerus Fracture | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 1 / 556 (0.18%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Joint Capsule Rupture | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 1 / 556 (0.18%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Joint Dislocation | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Kidney Rupture | | | |
| subjects affected / exposed | 1 / 242 (0.41%) | 0 / 556 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Laceration | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Ligament Sprain | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Lower Limb Fracture | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Lumbar Vertebral Fracture | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Meniscus Injury | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Multiple Fractures | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Muscle Rupture | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 1 / 556 (0.18%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Post Procedural Complication | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Postoperative Wound Complication | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Procedural Haemorrhage | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Procedural Pain | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Radius Fracture | | | |
| subjects affected / exposed | 1 / 242 (0.41%) | 0 / 556 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Rib Fracture | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 1 / 556 (0.18%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Road Traffic Accident | | | |
| subjects affected / exposed | 2 / 242 (0.83%) | 0 / 556 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| Spinal Compression Fracture | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Tendon Injury | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Tendon Rupture | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 1 / 241 (0.41%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ulna Fracture | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 1 / 242 (0.41%) | 0 / 556 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Upper Limb Fracture | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Wound Dehiscence | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 1 / 556 (0.18%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac disorders | | | |
| Acute Left Ventricular Failure | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 1 / 556 (0.18%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Angina Pectoris | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 1 / 556 (0.18%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Atrial Fibrillation | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 1 / 556 (0.18%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bradycardia | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac Failure Congestive | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 1 / 241 (0.41%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiopulmonary Failure | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Myocardial Infarction | | | |
| subjects affected / exposed | 1 / 242 (0.41%) | 0 / 556 (0.00%) | 1 / 241 (0.41%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 1 / 1 | 0 / 0 | 1 / 1 |
| Sinus Bradycardia | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| Carpal Tunnel Syndrome | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cerebral Infarction | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 1 / 556 (0.18%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cerebral Ischaemia | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Cerebrovascular Accident | | | |
| subjects affected / exposed | 2 / 242 (0.83%) | 0 / 556 (0.00%) | 1 / 241 (0.41%) |
| occurrences causally related to treatment / all | 3 / 3 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| Cervical Myelopathy | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Cervical Radiculopathy | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 1 / 242 (0.41%) | 0 / 556 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Haemorrhagic Stroke | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Headache | | | |
| subjects affected / exposed | 1 / 242 (0.41%) | 1 / 556 (0.18%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypertensive Encephalopathy | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Intracranial Aneurysm | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Ischaemic Stroke | | | |
| subjects affected / exposed | 1 / 242 (0.41%) | 0 / 556 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lumbar Radiculopathy | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Pyramidal Tract Syndrome | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Radiculopathy | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Reversible Cerebral Vasoconstriction Syndrome | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Transient Ischaemic Attack | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Trigeminal Neuralgia | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Ulnar Nerve Palsy | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 1 / 241 (0.41%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vertebrobasilar Insufficiency | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Neutropenia | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Pancytopenia | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Thrombocytopenia | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Eye disorders | | | |
| Amaurosis Fugax | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Cataract | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Keratitis | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Retinal Detachment | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Scleritis | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Ulcerative Keratitis | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| Abdominal Strangulated Hernia | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Colitis | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Diarrhoea | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Diverticular Perforation | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Enterocoele | | | |
| subjects affected / exposed | 1 / 242 (0.41%) | 0 / 556 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Erosive Duodenitis | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Gastric Perforation | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 1 / 556 (0.18%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastric Polyps | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 1 / 556 (0.18%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastric Ulcer | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Gastric Ulcer Haemorrhage | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 1 / 241 (0.41%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastritis Erosive | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal Hypomotility | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal Necrosis | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 1 / 556 (0.18%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal Perforation | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Haemorrhoidal Haemorrhage | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Incarcerated Inguinal Hernia | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Intestinal Obstruction | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Pancreatic Fistula | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 1 / 556 (0.18%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pancreatitis | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Retroperitoneal Haemorrhage | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Vomiting | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 1 / 241 (0.41%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatobiliary disorders | | | |
| Cholecystitis | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 1 / 241 (0.41%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cholecystitis Acute | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Cholelithiasis | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 1 / 241 (0.41%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gallbladder Perforation | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 1 / 241 (0.41%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatic Cyst | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 1 / 556 (0.18%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatic Steatosis | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 1 / 241 (0.41%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Jaundice Cholestatic | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Non-Alcoholic Steatohepatitis | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Skin and subcutaneous tissue disorders | | | |
| Angioedema | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 1 / 556 (0.18%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Decubitus Ulcer | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Dermatitis Allergic | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Dermatitis Bullous | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Dermatitis Contact | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Haemorrhage Subcutaneous | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 1 / 241 (0.41%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hyperkeratosis | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Skin Exfoliation | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Skin Necrosis | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 1 / 241 (0.41%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Skin Ulcer | | | |
| subjects affected / exposed | 1 / 242 (0.41%) | 0 / 556 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Stevens-Johnson Syndrome | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 1 / 241 (0.41%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urticaria | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 242 (0.00%) | 1 / 556 (0.18%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal and urinary disorders | | | |
| Acute Kidney Injury | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Calculus Urinary | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 1 / 556 (0.18%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hydronephrosis | | | |
| subjects affected / exposed | 1 / 242 (0.41%) | 0 / 556 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nephrolithiasis | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 1 / 556 (0.18%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ureterolithiasis | | | |
| subjects affected / exposed | 1 / 242 (0.41%) | 0 / 556 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urinary Tract Obstruction | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Endocrine disorders | | | |
| Basedow's Disease | | | |
| subjects affected / exposed | 1 / 242 (0.41%) | 0 / 556 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Goitre | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Atlantoaxial Instability | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Back Pain | | | |
| subjects affected / exposed | 1 / 242 (0.41%) | 0 / 556 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bursitis | | | |
| subjects affected / exposed | 1 / 242 (0.41%) | 0 / 556 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Chondromalacia | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Fistula | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Fistula Discharge | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Foot Deformity | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 1 / 241 (0.41%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Intervertebral Disc Disorder | | | |
| subjects affected / exposed | 1 / 242 (0.41%) | 0 / 556 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Intervertebral Disc Protrusion | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Lumbar Spinal Stenosis | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 1 / 556 (0.18%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal Chest Pain | | | |
| subjects affected / exposed | 1 / 242 (0.41%) | 0 / 556 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Osteoarthritis | | | |
| subjects affected / exposed | 1 / 242 (0.41%) | 1 / 556 (0.18%) | 1 / 241 (0.41%) |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Rheumatoid Arthritis | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 6 / 556 (1.08%) | 1 / 241 (0.41%) |
| occurrences causally related to treatment / all | 0 / 0 | 6 / 6 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Rheumatoid Nodule | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 1 / 556 (0.18%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Rotator Cuff Syndrome | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Spinal Pain | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Spondylolisthesis | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Synovitis | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 1 / 241 (0.41%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Abdominal Abscess | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Abdominal Sepsis | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 1 / 556 (0.18%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Abscess | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Abscess Limb | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Abscess Soft Tissue | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Appendicitis | | | |
| subjects affected / exposed | 1 / 242 (0.41%) | 0 / 556 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Appendicitis Perforated | | | |
| subjects affected / exposed | 1 / 242 (0.41%) | 0 / 556 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Arthritis Bacterial | | | |
| subjects affected / exposed | 1 / 242 (0.41%) | 0 / 556 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| Bacterial Food Poisoning | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 1 / 556 (0.18%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bacterial Sepsis | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Bronchitis | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 1 / 556 (0.18%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cellulitis | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 1 / 556 (0.18%) | 2 / 241 (0.83%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 3 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cellulitis Staphylococcal | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 1 / 242 (0.41%) | 0 / 556 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| Cytomegalovirus Colitis | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Dengue Fever | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 1 / 241 (0.41%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Device Related Infection | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 1 / 556 (0.18%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diverticulitis | | | |
| subjects affected / exposed | 1 / 242 (0.41%) | 0 / 556 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Endophthalmitis | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Epididymitis | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Erysipelas | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Escherichia Bacteraemia | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Extradural Abscess | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Eye Infection Fungal | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Gangrene | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 1 / 241 (0.41%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastroenteritis | | | |
| subjects affected / exposed | 1 / 242 (0.41%) | 0 / 556 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Herpes Zoster | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Infected Bite | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 1 / 556 (0.18%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infectious Pleural Effusion | | | |
| subjects affected / exposed | 1 / 242 (0.41%) | 1 / 556 (0.18%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infective Spondylitis | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Intervertebral Discitis | | | |
| subjects affected / exposed | 1 / 242 (0.41%) | 0 / 556 (0.00%) | 1 / 241 (0.41%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Localised Infection | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Lung Abscess | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Lymphangitis | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Meningitis | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 1 / 556 (0.18%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Necrotising Fasciitis | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Osteomyelitis | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Osteomyelitis Chronic | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Perirectal Abscess | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Peritonitis | | | |
| subjects affected / exposed | 2 / 242 (0.83%) | 1 / 556 (0.18%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 2 / 2 | 3 / 3 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Peritonsillar Abscess | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Pharyngitis | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Pneumonia | | | |
| subjects affected / exposed | 1 / 242 (0.41%) | 0 / 556 (0.00%) | 1 / 241 (0.41%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| Pneumonia Bacterial | | | |
| subjects affected / exposed | 1 / 242 (0.41%) | 1 / 556 (0.18%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia Necrotising | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 1 / 556 (0.18%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Post Procedural Infection | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Postoperative Wound Infection | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Pulmonary Tuberculosis | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Pyelonephritis | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Pyelonephritis Acute | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Pyoderma | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Pyonephrosis | | | |
| subjects affected / exposed | 1 / 242 (0.41%) | 0 / 556 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Salpingitis | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 1 / 241 (0.41%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Salpingo-Oophoritis | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 242 (0.00%) | 1 / 556 (0.18%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Sepsis | | | |
| subjects affected / exposed | 2 / 242 (0.83%) | 1 / 556 (0.18%) | 1 / 241 (0.41%) |
| occurrences causally related to treatment / all | 2 / 2 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 1 / 1 | 0 / 0 | 1 / 1 |
| Septic Shock | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Skin Infection | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Soft Tissue Infection | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Subcutaneous Abscess | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Urinary Tract Infection | | | |
| subjects affected / exposed | 1 / 242 (0.41%) | 0 / 556 (0.00%) | 1 / 241 (0.41%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Varicella | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Wound Infection | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Hepatitis E | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 1 / 556 (0.18%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolism and nutrition disorders | | | |
| Dehydration | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 1 / 556 (0.18%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diabetes Mellitus | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Hypercalcaemia | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Hyperglycaemia | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | 0 / 556 (0.00%) | 0 / 241 (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 |
| Hypokalaemia | | | |
| subjects affected / exposed | 1 / 242 (0.41%) | 0 / 556 (0.00%) | 0 / 241 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| Serious adverse events | W0 to W120- Sirukumab 100 mg q2w | W0 to W120- Sirukumab 50 mg q4w | |
|---|--|---------------------------------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 97 / 558 (17.38%) | 111 / 556 (19.96%) | |
| number of deaths (all causes) | 5 | 7 | |
| number of deaths resulting from | | | |

| | | | |
|---|-----------------|-----------------|--|
| adverse events | | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Acute Myeloid Leukaemia | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 1 / 556 (0.18%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 1 / 1 | |
| Adrenal Adenoma | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 1 / 556 (0.18%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Basal Cell Carcinoma | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 1 / 556 (0.18%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Benign Neoplasm of Thyroid Gland | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bladder Cancer | | | |
| subjects affected / exposed | 1 / 558 (0.18%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 1 / 1 | 0 / 0 | |
| Bladder Transitional Cell Carcinoma | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 1 / 556 (0.18%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Breast Cancer | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Colon Cancer Metastatic | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 1 / 556 (0.18%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|-----------------|-----------------|--|
| Gastric Cancer | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal Stromal Tumour | | | |
| subjects affected / exposed | 1 / 558 (0.18%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Glioblastoma Multiforme | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Intraductal Papilloma of Breast | | | |
| subjects affected / exposed | 1 / 558 (0.18%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Invasive Ductal Breast Carcinoma | | | |
| subjects affected / exposed | 2 / 558 (0.36%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Leiomyoma | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lung Cancer Metastatic | | | |
| subjects affected / exposed | 1 / 558 (0.18%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 1 / 1 | 0 / 0 | |
| Lung Neoplasm Malignant | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Meningioma | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 558 (0.00%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metastases to Bone | | | |
| subjects affected / exposed | 1 / 558 (0.18%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metastases to Central Nervous System | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Neuroendocrine Carcinoma | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 1 / 556 (0.18%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Oropharyngeal Squamous Cell Carcinoma | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 1 / 556 (0.18%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ovarian Clear Cell Carcinoma | | | |
| subjects affected / exposed | 1 / 558 (0.18%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Teratoma | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 1 / 556 (0.18%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Uterine Cancer | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 1 / 556 (0.18%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Uterine Leiomyoma | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 558 (0.00%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vascular disorders | | | |
| Aortic Aneurysm | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Aortic Dissection | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Axillary Vein Thrombosis | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Deep Vein Thrombosis | | | |
| subjects affected / exposed | 1 / 558 (0.18%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Extremity Necrosis | | | |
| subjects affected / exposed | 1 / 558 (0.18%) | 1 / 556 (0.18%) | |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haematoma | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 1 / 556 (0.18%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypertension | | | |
| subjects affected / exposed | 1 / 558 (0.18%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 1 / 1 | 0 / 0 | |
| Hypotension | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 558 (0.18%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Labile Hypertension | | | |
| subjects affected / exposed | 1 / 558 (0.18%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Necrosis Ischaemic | | | |
| subjects affected / exposed | 1 / 558 (0.18%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Peripheral Arterial Occlusive Disease | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Peripheral Ischaemia | | | |
| subjects affected / exposed | 1 / 558 (0.18%) | 1 / 556 (0.18%) | |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Shock | | | |
| subjects affected / exposed | 1 / 558 (0.18%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Subclavian Vein Thrombosis | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Thrombosed Varicose Vein | | | |
| subjects affected / exposed | 1 / 558 (0.18%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vasculitis | | | |

| | | | |
|--|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 558 (0.00%) | 1 / 556 (0.18%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Venous Thrombosis Limb | | | |
| subjects affected / exposed | 1 / 558 (0.18%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pregnancy, puerperium and perinatal conditions | | | |
| Abortion Spontaneous | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 1 / 556 (0.18%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 1 / 558 (0.18%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Chest Pain | | | |
| subjects affected / exposed | 2 / 558 (0.36%) | 1 / 556 (0.18%) | |
| occurrences causally related to treatment / all | 2 / 2 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Death | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 1 / 556 (0.18%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 1 / 1 | |
| Influenza Like Illness | | | |
| subjects affected / exposed | 1 / 558 (0.18%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Medical Device Site Joint Inflammation | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 558 (0.00%) | 1 / 556 (0.18%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Serositis | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sudden Cardiac Death | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 1 / 556 (0.18%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 1 / 1 | |
| Immune system disorders | | | |
| Drug Hypersensitivity | | | |
| subjects affected / exposed | 1 / 558 (0.18%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Reproductive system and breast disorders | | | |
| Benign Prostatic Hyperplasia | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 1 / 556 (0.18%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Breast Mass | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cystocele | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Endometriosis | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 1 / 556 (0.18%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|-----------------|-----------------|--|
| Ovarian Cyst | | | |
| subjects affected / exposed | 1 / 558 (0.18%) | 1 / 556 (0.18%) | |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Rectocele | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vaginal Haemorrhage | | | |
| subjects affected / exposed | 1 / 558 (0.18%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Acute Respiratory Distress Syndrome | | | |
| subjects affected / exposed | 2 / 558 (0.36%) | 1 / 556 (0.18%) | |
| occurrences causally related to treatment / all | 2 / 2 | 1 / 1 | |
| deaths causally related to treatment / all | 1 / 1 | 0 / 0 | |
| Acute Respiratory Failure | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Asthma | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Chronic Obstructive Pulmonary Disease | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 3 / 556 (0.54%) | |
| occurrences causally related to treatment / all | 0 / 0 | 3 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cough | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|-----------------|-----------------|--|
| Dyspnoea | | | |
| subjects affected / exposed | 1 / 558 (0.18%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Epistaxis | | | |
| subjects affected / exposed | 1 / 558 (0.18%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Interstitial Lung Disease | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 4 / 556 (0.72%) | |
| occurrences causally related to treatment / all | 0 / 0 | 4 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lung Disorder | | | |
| subjects affected / exposed | 1 / 558 (0.18%) | 1 / 556 (0.18%) | |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pleural Effusion | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 1 / 556 (0.18%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pleurisy | | | |
| subjects affected / exposed | 1 / 558 (0.18%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia Aspiration | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 1 / 556 (0.18%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonitis | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 1 / 556 (0.18%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumothorax Spontaneous | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 558 (0.00%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pulmonary Embolism | | | |
| subjects affected / exposed | 2 / 558 (0.36%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pulmonary Mass | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pulmonary Necrosis | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory Failure | | | |
| subjects affected / exposed | 1 / 558 (0.18%) | 1 / 556 (0.18%) | |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 1 / 1 | |
| Psychiatric disorders | | | |
| Anxiety | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 1 / 556 (0.18%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Mental Status Changes | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 1 / 556 (0.18%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Suicidal Ideation | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Investigations | | | |

| | | | |
|---|-----------------|-----------------|--|
| Alanine Aminotransferase Increased | | | |
| subjects affected / exposed | 3 / 558 (0.54%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 3 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Aspartate Aminotransferase Increased | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Blood Bilirubin Increased | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Chest X-Ray Abnormal | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatic Enzyme Increased | | | |
| subjects affected / exposed | 1 / 558 (0.18%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Liver Function Test Increased | | | |
| subjects affected / exposed | 1 / 558 (0.18%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Weight Decreased | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 1 / 556 (0.18%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Injury, poisoning and procedural complications | | | |
| Abdominal Injury | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|-----------------|-----------------|--|
| Chemical Peritonitis | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Concussion | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Contusion | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Epiphyseal Fracture | | | |
| subjects affected / exposed | 1 / 558 (0.18%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Facial Bones Fracture | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Femoral Neck Fracture | | | |
| subjects affected / exposed | 1 / 558 (0.18%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Femur Fracture | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 2 / 556 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Foot Fracture | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 1 / 556 (0.18%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hand Fracture | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 558 (0.00%) | 1 / 556 (0.18%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hip Fracture | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 1 / 556 (0.18%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Humerus Fracture | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 1 / 556 (0.18%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Joint Capsule Rupture | | | |
| subjects affected / exposed | 1 / 558 (0.18%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Joint Dislocation | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 1 / 556 (0.18%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Kidney Rupture | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Laceration | | | |
| subjects affected / exposed | 1 / 558 (0.18%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ligament Sprain | | | |
| subjects affected / exposed | 1 / 558 (0.18%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lower Limb Fracture | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 558 (0.00%) | 1 / 556 (0.18%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lumbar Vertebral Fracture | | | |
| subjects affected / exposed | 1 / 558 (0.18%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Meniscus Injury | | | |
| subjects affected / exposed | 1 / 558 (0.18%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Multiple Fractures | | | |
| subjects affected / exposed | 1 / 558 (0.18%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Muscle Rupture | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Post Procedural Complication | | | |
| subjects affected / exposed | 1 / 558 (0.18%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Postoperative Wound Complication | | | |
| subjects affected / exposed | 1 / 558 (0.18%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Procedural Haemorrhage | | | |
| subjects affected / exposed | 1 / 558 (0.18%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Procedural Pain | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 558 (0.00%) | 1 / 556 (0.18%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Radius Fracture | | | |
| subjects affected / exposed | 5 / 558 (0.90%) | 1 / 556 (0.18%) | |
| occurrences causally related to treatment / all | 5 / 5 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Rib Fracture | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Road Traffic Accident | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Spinal Compression Fracture | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 1 / 556 (0.18%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Tendon Injury | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 1 / 556 (0.18%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Tendon Rupture | | | |
| subjects affected / exposed | 1 / 558 (0.18%) | 1 / 556 (0.18%) | |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ulna Fracture | | | |
| subjects affected / exposed | 1 / 558 (0.18%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Upper Limb Fracture | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 558 (0.18%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Wound Dehiscence | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac disorders | | | |
| Acute Left Ventricular Failure | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Angina Pectoris | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Atrial Fibrillation | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 1 / 556 (0.18%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bradycardia | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 1 / 556 (0.18%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac Failure Congestive | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiopulmonary Failure | | | |
| subjects affected / exposed | 1 / 558 (0.18%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Myocardial Infarction | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 558 (0.18%) | 3 / 556 (0.54%) | |
| occurrences causally related to treatment / all | 1 / 1 | 4 / 4 | |
| deaths causally related to treatment / all | 1 / 1 | 0 / 0 | |
| Sinus Bradycardia | | | |
| subjects affected / exposed | 1 / 558 (0.18%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nervous system disorders | | | |
| Carpal Tunnel Syndrome | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 1 / 556 (0.18%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cerebral Infarction | | | |
| subjects affected / exposed | 1 / 558 (0.18%) | 1 / 556 (0.18%) | |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 1 / 1 | 0 / 0 | |
| Cerebral Ischaemia | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 1 / 556 (0.18%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cerebrovascular Accident | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cervical Myelopathy | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 1 / 556 (0.18%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cervical Radiculopathy | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haemorrhagic Stroke | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 558 (0.00%) | 1 / 556 (0.18%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Headache | | | |
| subjects affected / exposed | 1 / 558 (0.18%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypertensive Encephalopathy | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 1 / 556 (0.18%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Intracranial Aneurysm | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 1 / 556 (0.18%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ischaemic Stroke | | | |
| subjects affected / exposed | 1 / 558 (0.18%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lumbar Radiculopathy | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 2 / 556 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pyramidal Tract Syndrome | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 1 / 556 (0.18%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Radiculopathy | | | |
| subjects affected / exposed | 1 / 558 (0.18%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Reversible Cerebral Vasoconstriction Syndrome | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 558 (0.00%) | 1 / 556 (0.18%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Transient Ischaemic Attack | | | |
| subjects affected / exposed | 2 / 558 (0.36%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Trigeminal Neuralgia | | | |
| subjects affected / exposed | 1 / 558 (0.18%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ulnar Nerve Palsy | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vertebrobasilar Insufficiency | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 1 / 556 (0.18%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 2 / 558 (0.36%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Neutropenia | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 1 / 556 (0.18%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pancytopenia | | | |
| subjects affected / exposed | 1 / 558 (0.18%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Thrombocytopenia | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 2 / 558 (0.36%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Eye disorders | | | |
| Amaurosis Fugax | | | |
| subjects affected / exposed | 1 / 558 (0.18%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cataract | | | |
| subjects affected / exposed | 1 / 558 (0.18%) | 1 / 556 (0.18%) | |
| occurrences causally related to treatment / all | 2 / 2 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Keratitis | | | |
| subjects affected / exposed | 1 / 558 (0.18%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Retinal Detachment | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 1 / 556 (0.18%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Scleritis | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 1 / 556 (0.18%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ulcerative Keratitis | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 2 / 556 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Abdominal Strangulated Hernia | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 1 / 556 (0.18%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Colitis | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 558 (0.18%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diarrhoea | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 1 / 556 (0.18%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diverticular Perforation | | | |
| subjects affected / exposed | 1 / 558 (0.18%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Enterocoele | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Erosive Duodenitis | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 1 / 556 (0.18%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastric Perforation | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastric Polyps | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastric Ulcer | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 1 / 556 (0.18%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastric Ulcer Haemorrhage | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 558 (0.00%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastritis Erosive | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 1 / 556 (0.18%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal Hypomotility | | | |
| subjects affected / exposed | 1 / 558 (0.18%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal Necrosis | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal Perforation | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 1 / 556 (0.18%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haemorrhoidal Haemorrhage | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 1 / 556 (0.18%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Incarcerated Inguinal Hernia | | | |
| subjects affected / exposed | 1 / 558 (0.18%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Intestinal Obstruction | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 1 / 556 (0.18%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pancreatic Fistula | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 558 (0.00%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pancreatitis | | | |
| subjects affected / exposed | 1 / 558 (0.18%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Retroperitoneal Haemorrhage | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 1 / 556 (0.18%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vomiting | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatobiliary disorders | | | |
| Cholecystitis | | | |
| subjects affected / exposed | 3 / 558 (0.54%) | 2 / 556 (0.36%) | |
| occurrences causally related to treatment / all | 3 / 3 | 2 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cholecystitis Acute | | | |
| subjects affected / exposed | 1 / 558 (0.18%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cholelithiasis | | | |
| subjects affected / exposed | 3 / 558 (0.54%) | 2 / 556 (0.36%) | |
| occurrences causally related to treatment / all | 3 / 3 | 2 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gallbladder Perforation | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatic Cyst | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 558 (0.00%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatic Steatosis | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Jaundice Cholestatic | | | |
| subjects affected / exposed | 1 / 558 (0.18%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Non-Alcoholic Steatohepatitis | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 1 / 556 (0.18%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Skin and subcutaneous tissue disorders | | | |
| Angioedema | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Decubitus Ulcer | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 1 / 556 (0.18%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dermatitis Allergic | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 1 / 556 (0.18%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dermatitis Bullous | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 1 / 556 (0.18%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dermatitis Contact | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 558 (0.18%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haemorrhage Subcutaneous | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hyperkeratosis | | | |
| subjects affected / exposed | 1 / 558 (0.18%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Skin Exfoliation | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 1 / 556 (0.18%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Skin Necrosis | | | |
| subjects affected / exposed | 2 / 558 (0.36%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Skin Ulcer | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Stevens-Johnson Syndrome | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urticaria | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 1 / 556 (0.18%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal and urinary disorders | | | |
| Acute Kidney Injury | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 558 (0.18%) | 2 / 556 (0.36%) | |
| occurrences causally related to treatment / all | 1 / 1 | 2 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Calculus Urinary | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hydronephrosis | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nephrolithiasis | | | |
| subjects affected / exposed | 1 / 558 (0.18%) | 3 / 556 (0.54%) | |
| occurrences causally related to treatment / all | 1 / 1 | 3 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ureterolithiasis | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urinary Tract Obstruction | | | |
| subjects affected / exposed | 1 / 558 (0.18%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Endocrine disorders | | | |
| Basedow's Disease | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Goitre | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 1 / 556 (0.18%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal and connective tissue disorders | | | |

| | | | |
|---|-----------------|-----------------|--|
| Arthralgia | | | |
| subjects affected / exposed | 1 / 558 (0.18%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Atlantoaxial Instability | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 1 / 556 (0.18%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Back Pain | | | |
| subjects affected / exposed | 1 / 558 (0.18%) | 1 / 556 (0.18%) | |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bursitis | | | |
| subjects affected / exposed | 1 / 558 (0.18%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Chondromalacia | | | |
| subjects affected / exposed | 1 / 558 (0.18%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Fistula | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 1 / 556 (0.18%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Fistula Discharge | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 1 / 556 (0.18%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Foot Deformity | | | |
| subjects affected / exposed | 2 / 558 (0.36%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Intervertebral Disc Disorder | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 558 (0.00%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Intervertebral Disc Protrusion | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 1 / 556 (0.18%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lumbar Spinal Stenosis | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal Chest Pain | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Osteoarthritis | | | |
| subjects affected / exposed | 2 / 558 (0.36%) | 4 / 556 (0.72%) | |
| occurrences causally related to treatment / all | 2 / 2 | 5 / 5 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Rheumatoid Arthritis | | | |
| subjects affected / exposed | 5 / 558 (0.90%) | 5 / 556 (0.90%) | |
| occurrences causally related to treatment / all | 5 / 5 | 5 / 5 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Rheumatoid Nodule | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Rotator Cuff Syndrome | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 1 / 556 (0.18%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Spinal Pain | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 558 (0.00%) | 1 / 556 (0.18%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Spondylolisthesis | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 1 / 556 (0.18%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Synovitis | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Abdominal Abscess | | | |
| subjects affected / exposed | 1 / 558 (0.18%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Abdominal Sepsis | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Abscess | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 1 / 556 (0.18%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Abscess Limb | | | |
| subjects affected / exposed | 4 / 558 (0.72%) | 3 / 556 (0.54%) | |
| occurrences causally related to treatment / all | 4 / 4 | 3 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Abscess Soft Tissue | | | |
| subjects affected / exposed | 1 / 558 (0.18%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Appendicitis | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 2 / 558 (0.36%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Appendicitis Perforated | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Arthritis Bacterial | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bacterial Food Poisoning | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bacterial Sepsis | | | |
| subjects affected / exposed | 1 / 558 (0.18%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 1 / 1 | 0 / 0 | |
| Bronchitis | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cellulitis | | | |
| subjects affected / exposed | 5 / 558 (0.90%) | 7 / 556 (1.26%) | |
| occurrences causally related to treatment / all | 6 / 6 | 7 / 7 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cellulitis Staphylococcal | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cytomegalovirus Colitis | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 558 (0.00%) | 1 / 556 (0.18%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dengue Fever | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 1 / 556 (0.18%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Device Related Infection | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diverticulitis | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 4 / 556 (0.72%) | |
| occurrences causally related to treatment / all | 0 / 0 | 4 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Endophthalmitis | | | |
| subjects affected / exposed | 1 / 558 (0.18%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Epididymitis | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 1 / 556 (0.18%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Erysipelas | | | |
| subjects affected / exposed | 1 / 558 (0.18%) | 2 / 556 (0.36%) | |
| occurrences causally related to treatment / all | 1 / 1 | 2 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Escherichia Bacteraemia | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 1 / 556 (0.18%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Extradural Abscess | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 558 (0.18%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Eye Infection Fungal | | | |
| subjects affected / exposed | 1 / 558 (0.18%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gangrene | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastroenteritis | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Herpes Zoster | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 1 / 556 (0.18%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infected Bite | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infectious Pleural Effusion | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 2 / 556 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infective Spondylitis | | | |
| subjects affected / exposed | 1 / 558 (0.18%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Intervertebral Discitis | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 558 (0.18%) | 1 / 556 (0.18%) | |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Localised Infection | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 1 / 556 (0.18%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lung Abscess | | | |
| subjects affected / exposed | 1 / 558 (0.18%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lymphangitis | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 1 / 556 (0.18%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Meningitis | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Necrotising Fasciitis | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 1 / 556 (0.18%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 1 / 1 | |
| Osteomyelitis | | | |
| subjects affected / exposed | 2 / 558 (0.36%) | 2 / 556 (0.36%) | |
| occurrences causally related to treatment / all | 2 / 2 | 2 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Osteomyelitis Chronic | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 1 / 556 (0.18%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Perirectal Abscess | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 1 / 558 (0.18%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Peritonitis | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 3 / 556 (0.54%) | |
| occurrences causally related to treatment / all | 0 / 0 | 3 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 1 / 1 | |
| Peritonsillar Abscess | | | |
| subjects affected / exposed | 1 / 558 (0.18%) | 2 / 556 (0.36%) | |
| occurrences causally related to treatment / all | 1 / 1 | 2 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pharyngitis | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 1 / 556 (0.18%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia | | | |
| subjects affected / exposed | 10 / 558 (1.79%) | 11 / 556 (1.98%) | |
| occurrences causally related to treatment / all | 12 / 12 | 11 / 11 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia Bacterial | | | |
| subjects affected / exposed | 1 / 558 (0.18%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia Necrotising | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Post Procedural Infection | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 1 / 556 (0.18%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Postoperative Wound Infection | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 558 (0.18%) | 1 / 556 (0.18%) | |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pulmonary Tuberculosis | | | |
| subjects affected / exposed | 1 / 558 (0.18%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pyelonephritis | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 1 / 556 (0.18%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pyelonephritis Acute | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 1 / 556 (0.18%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pyoderma | | | |
| subjects affected / exposed | 1 / 558 (0.18%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pyonephrosis | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Salpingitis | | | |
| subjects affected / exposed | 1 / 558 (0.18%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Salpingo-Oophoritis | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sepsis | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 5 / 558 (0.90%) | 3 / 556 (0.54%) | |
| occurrences causally related to treatment / all | 5 / 5 | 3 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 1 / 1 | |
| Septic Shock | | | |
| subjects affected / exposed | 1 / 558 (0.18%) | 1 / 556 (0.18%) | |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 1 / 1 | |
| Skin Infection | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 1 / 556 (0.18%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Soft Tissue Infection | | | |
| subjects affected / exposed | 1 / 558 (0.18%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Subcutaneous Abscess | | | |
| subjects affected / exposed | 1 / 558 (0.18%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urinary Tract Infection | | | |
| subjects affected / exposed | 3 / 558 (0.54%) | 1 / 556 (0.18%) | |
| occurrences causally related to treatment / all | 4 / 4 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 1 / 1 | |
| Varicella | | | |
| subjects affected / exposed | 1 / 558 (0.18%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Wound Infection | | | |
| subjects affected / exposed | 1 / 558 (0.18%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatitis E | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 558 (0.00%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metabolism and nutrition disorders | | | |
| Dehydration | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diabetes Mellitus | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 1 / 556 (0.18%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypercalcaemia | | | |
| subjects affected / exposed | 1 / 558 (0.18%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hyperglycaemia | | | |
| subjects affected / exposed | 1 / 558 (0.18%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypokalaemia | | | |
| subjects affected / exposed | 0 / 558 (0.00%) | 0 / 556 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| Non-serious adverse events | W0 to W120-Placebo to Sirukumab 50 mg q4w due to EE/LE or CO | Week 0 to Week 120-Placebo | W0 to W120-Placebo to Sirukumab 100 mg q2w Due to EE/LE or CO |
|---|--|----------------------------|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 113 / 242 (46.69%) | 213 / 556 (38.31%) | 128 / 241 (53.11%) |
| Investigations | | | |

| | | | |
|--|--|--|--|
| Alanine Aminotransferase Increased subjects affected / exposed occurrences (all) | 34 / 242 (14.05%) 45 | 23 / 556 (4.14%) 28 | 41 / 241 (17.01%) 57 |
| Aspartate Aminotransferase Increased subjects affected / exposed occurrences (all) | 20 / 242 (8.26%) 26 | 17 / 556 (3.06%) 18 | 23 / 241 (9.54%) 30 |
| Vascular disorders Hypertension subjects affected / exposed occurrences (all) | 14 / 242 (5.79%) 15 | 21 / 556 (3.78%) 23 | 11 / 241 (4.56%) 11 |
| Nervous system disorders Headache subjects affected / exposed occurrences (all) | 8 / 242 (3.31%) 9 | 22 / 556 (3.96%) 30 | 9 / 241 (3.73%) 11 |
| Blood and lymphatic system disorders Leukopenia subjects affected / exposed occurrences (all) Neutropenia subjects affected / exposed occurrences (all) | 12 / 242 (4.96%) 13 9 / 242 (3.72%) 11 | 7 / 556 (1.26%) 9 5 / 556 (0.90%) 5 | 8 / 241 (3.32%) 11 8 / 241 (3.32%) 12 |
| General disorders and administration site conditions Injection Site Erythema subjects affected / exposed occurrences (all) Injection Site Pruritus subjects affected / exposed occurrences (all) Injection Site Swelling subjects affected / exposed occurrences (all) | 11 / 242 (4.55%) 27 3 / 242 (1.24%) 5 3 / 242 (1.24%) 5 | 6 / 556 (1.08%) 8 1 / 556 (0.18%) 1 0 / 556 (0.00%) 0 | 31 / 241 (12.86%) 126 14 / 241 (5.81%) 33 13 / 241 (5.39%) 38 |
| Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all) | 2 / 242 (0.83%) 2 | 21 / 556 (3.78%) 26 | 9 / 241 (3.73%) 9 |
| Musculoskeletal and connective tissue disorders | | | |

| | | | |
|---|-------------------------|-------------------------|------------------------|
| Rheumatoid Arthritis subjects affected / exposed occurrences (all) | 9 / 242 (3.72%) 11 | 36 / 556 (6.47%) 39 | 10 / 241 (4.15%) 12 |
| Infections and infestations | | | |
| Bronchitis subjects affected / exposed occurrences (all) | 17 / 242 (7.02%) 22 | 27 / 556 (4.86%) 29 | 13 / 241 (5.39%) 14 |
| Nasopharyngitis subjects affected / exposed occurrences (all) | 16 / 242 (6.61%) 26 | 53 / 556 (9.53%) 67 | 19 / 241 (7.88%) 24 |
| Pharyngitis subjects affected / exposed occurrences (all) | 5 / 242 (2.07%) 9 | 13 / 556 (2.34%) 16 | 8 / 241 (3.32%) 14 |
| Upper Respiratory Tract Infection subjects affected / exposed occurrences (all) | 28 / 242 (11.57%) 37 | 63 / 556 (11.33%) 76 | 20 / 241 (8.30%) 31 |
| Urinary Tract Infection subjects affected / exposed occurrences (all) | 8 / 242 (3.31%) 10 | 13 / 556 (2.34%) 15 | 13 / 241 (5.39%) 15 |

| Non-serious adverse events | W0 to W120- Sirukumab 100 mg q2w | W0 to W120- Sirukumab 50 mg q4w | |
|---|--|---------------------------------------|--|
| Total subjects affected by non-serious adverse events subjects affected / exposed | 353 / 558 (63.26%) | 355 / 556 (63.85%) | |
| Investigations | | | |
| Alanine Aminotransferase Increased subjects affected / exposed occurrences (all) | 124 / 558 (22.22%) 192 | 108 / 556 (19.42%) 149 | |
| Aspartate Aminotransferase Increased subjects affected / exposed occurrences (all) | 84 / 558 (15.05%) 132 | 63 / 556 (11.33%) 90 | |
| Vascular disorders | | | |
| Hypertension subjects affected / exposed occurrences (all) | 45 / 558 (8.06%) 55 | 32 / 556 (5.76%) 39 | |
| Nervous system disorders | | | |

| | | | |
|---|--------------------------|--------------------------|--|
| Headache subjects affected / exposed occurrences (all) | 28 / 558 (5.02%) 46 | 38 / 556 (6.83%) 47 | |
| Blood and lymphatic system disorders Leukopenia subjects affected / exposed occurrences (all) | 39 / 558 (6.99%) 67 | 37 / 556 (6.65%) 62 | |
| Neutropenia subjects affected / exposed occurrences (all) | 34 / 558 (6.09%) 61 | 40 / 556 (7.19%) 86 | |
| General disorders and administration site conditions Injection Site Erythema subjects affected / exposed occurrences (all) | 70 / 558 (12.54%) 413 | 50 / 556 (8.99%) 169 | |
| Injection Site Pruritus subjects affected / exposed occurrences (all) | 34 / 558 (6.09%) 135 | 12 / 556 (2.16%) 40 | |
| Injection Site Swelling subjects affected / exposed occurrences (all) | 27 / 558 (4.84%) 66 | 15 / 556 (2.70%) 26 | |
| Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all) | 23 / 558 (4.12%) 28 | 28 / 556 (5.04%) 31 | |
| Musculoskeletal and connective tissue disorders Rheumatoid Arthritis subjects affected / exposed occurrences (all) | 29 / 558 (5.20%) 37 | 46 / 556 (8.27%) 59 | |
| Infections and infestations Bronchitis subjects affected / exposed occurrences (all) | 36 / 558 (6.45%) 46 | 48 / 556 (8.63%) 62 | |
| Nasopharyngitis subjects affected / exposed occurrences (all) | 67 / 558 (12.01%) 99 | 70 / 556 (12.59%) 123 | |
| Pharyngitis | | | |

| | | | |
|-----------------------------------|-------------------|-------------------|--|
| subjects affected / exposed | 24 / 558 (4.30%) | 30 / 556 (5.40%) | |
| occurrences (all) | 28 | 38 | |
| Upper Respiratory Tract Infection | | | |
| subjects affected / exposed | 72 / 558 (12.90%) | 76 / 556 (13.67%) | |
| occurrences (all) | 122 | 123 | |
| Urinary Tract Infection | | | |
| subjects affected / exposed | 23 / 558 (4.12%) | 30 / 556 (5.40%) | |
| occurrences (all) | 31 | 42 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|------------------|---|
| 06 November 2012 | Clarified that in the event of clinically significant decreases in neutrophils or platelet counts, MTX should be temporarily or permanently discontinued |
| 18 February 2014 | Increased the total number of subjects to be enrolled to approximately 1,650 with approximately 550 subjects in each of the 3 treatment groups. The sample size of CNTO136ARA3002 was increased to ensure that the overall safety database size of the Phase 3 RA program for sirukumab was maintained despite a reduction in enrollment in CNTO136ARA3003. Along with the increase in subject enrollment, there was an increase in power of the study. |
| 07 May 2014 | Added acute diverticulitis requiring antibiotic treatment and GI perforation to the list of conditions that would result in the permanent discontinuation of study agent administrations. Power calculations were revised due to an increase in sample size. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

The short pure placebo-controlled period (through Week 18) and the EE at Week 18 and LE at Week 40 for subjects in the placebo group might have affected the ability to directly compare safety between sirukumab and placebo groups through Week 52.

Notes: