



Clinical trial results:

A Long-Term, Open-Label Follow-Up Study of Tofacitinib (CP-690,550) for Treatment of Rheumatoid Arthritis

Summary

| | |
|--------------------------|--|
| EudraCT number | 2006-005035-19 |
| Trial protocol | BE ES AT SE IT HU CZ GR DE SK GB BG FI DK IE |
| Global end of trial date | 26 October 2017 |

Results information

| | |
|--------------------------------|------------------|
| Result version number | v2 (current) |
| This version publication date | 21 October 2018 |
| First version publication date | 03 December 2017 |
| Version creation reason | |

Trial information

Trial identification

| | |
|-----------------------|----------|
| Sponsor protocol code | A3921024 |
|-----------------------|----------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT00413699 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | Pfizer Inc. |
| Sponsor organisation address | 235 East 42nd Street, New York, United States, NY 10017 |
| Public contact | Pfizer ClinicalTrials.gov Call Center, Pfizer Inc., 001 1800-718-1021, ClinicalTrials.gov_Inquiries@pfizer.com |
| Scientific contact | Pfizer ClinicalTrials.gov Call Center, Pfizer Inc., 001 1800-718-1021, ClinicalTrials.gov_Inquiries@pfizer.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 | 25 April 2018 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 26 October 2017 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To determine the long-term safety and tolerability of 5mg twice daily and 10mg twice daily of tofacitinib for treatment of the signs and symptoms of rheumatoid arthritis.

Protection of trial subjects:

The study was conducted in compliance with the ethical principles originating in or derived from the Declaration of Helsinki and in compliance with all International Conference on Harmonization Good Clinical Practice Guidelines. In addition, all local and regulatory requirements were followed, in particular, those affording greater protection to the safety of trial subjects.

Background therapy:

The following DMARDs were allowed in doses consistent with local standards of care: Auranofin (oral gold), aurothioglucose (injectable gold), aurothiomalate (injectable gold); Sulfasalazine, chloroquine, hydroxychloroquine, leflunomide (Arava®), and methotrexate, d-penicillamine and tetracyclines. In Ireland, methotrexate doses higher than 20 mg weekly were not permitted under any circumstances.

Evidence for comparator:

Not applicable

| | |
|---|------------------|
| Actual start date of recruitment | 05 February 2007 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|---------------------------|
| Country: Number of subjects enrolled | Argentina: 60 |
| Country: Number of subjects enrolled | Australia: 99 |
| Country: Number of subjects enrolled | Austria: 31 |
| Country: Number of subjects enrolled | Belgium: 11 |
| Country: Number of subjects enrolled | Bosnia and Herzegovina: 5 |
| Country: Number of subjects enrolled | Brazil: 237 |
| Country: Number of subjects enrolled | Bulgaria: 110 |
| Country: Number of subjects enrolled | Canada: 70 |
| Country: Number of subjects enrolled | Chile: 133 |
| Country: Number of subjects enrolled | China: 192 |
| Country: Number of subjects enrolled | Colombia: 97 |
| Country: Number of subjects enrolled | Costa Rica: 10 |
| Country: Number of subjects enrolled | Croatia: 20 |
| Country: Number of subjects enrolled | Czech Republic: 364 |
| Country: Number of subjects enrolled | Denmark: 3 |

| | |
|--------------------------------------|-------------------------|
| Country: Number of subjects enrolled | Dominican Republic: 22 |
| Country: Number of subjects enrolled | Finland: 10 |
| Country: Number of subjects enrolled | France: 7 |
| Country: Number of subjects enrolled | Germany: 193 |
| Country: Number of subjects enrolled | Greece: 7 |
| Country: Number of subjects enrolled | Hungary: 10 |
| Country: Number of subjects enrolled | India: 115 |
| Country: Number of subjects enrolled | Ireland: 3 |
| Country: Number of subjects enrolled | Italy: 14 |
| Country: Number of subjects enrolled | Korea, Republic of: 210 |
| Country: Number of subjects enrolled | Malaysia: 41 |
| Country: Number of subjects enrolled | Mexico: 212 |
| Country: Number of subjects enrolled | New Zealand: 8 |
| Country: Number of subjects enrolled | Peru: 9 |
| Country: Number of subjects enrolled | Philippines: 44 |
| Country: Number of subjects enrolled | Poland: 267 |
| Country: Number of subjects enrolled | Puerto Rico: 7 |
| Country: Number of subjects enrolled | Romania: 7 |
| Country: Number of subjects enrolled | Russian Federation: 140 |
| Country: Number of subjects enrolled | Slovakia: 90 |
| Country: Number of subjects enrolled | Spain: 117 |
| Country: Number of subjects enrolled | Sweden: 15 |
| Country: Number of subjects enrolled | Taiwan: 28 |
| Country: Number of subjects enrolled | Thailand: 55 |
| Country: Number of subjects enrolled | Turkey: 3 |
| Country: Number of subjects enrolled | Ukraine: 201 |
| Country: Number of subjects enrolled | United Kingdom: 14 |
| Country: Number of subjects enrolled | United States: 1190 |
| Worldwide total number of subjects | 4481 |
| EEA total number of subjects | 1293 |

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) | 3754 |
| From 65 to 84 years | 724 |
| 85 years and over | 3 |

Subject disposition

Recruitment

Recruitment details:

Initial period (IP): conducted at multiple sites, subjects were assigned to Tofacitinib 5 mg and 10 mg BID. Extension period (EP): subjects who took part initially in IP, completed 2 years of lymphocyte assessment in IP, given consent, were enrolled in EP and assigned to "Extension Period: Tofacitinib 5 mg". EP was conducted in 2 countries.

Pre-assignment

Screening details:

Subjects had previously participated in qualifying studies (A3921019, A3921025, A3921032, A3921035, A3921044, A3921045, A3921046, A3921064, A3921068, A3921069, A3921073, A3921109, A3921129, A3921130, A3921152, A3921237) prior to enrollment in initial period.

Period 1

| | |
|------------------------------|-----------------------------|
| Period 1 title | Initial Period |
| Is this the baseline period? | Yes |
| Allocation method | Non-randomised - controlled |
| Blinding used | Not blinded |

Arms

| | |
|------------------------------|---|
| Are arms mutually exclusive? | Yes |
| Arm title | Initial Period: Tofacitinib 5 milligram(mg) twice daily (BID) |

Arm description:

Tofacitinib 5 mg BID. Participants with non-zero average total daily dose across study <15 were assigned to 5 mg BID.

avg=average; BID=twice daily; mg=milligram; ppts=participants; tofa=tofacitinib

| | |
|--|--------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Tofacitinib |
| Investigational medicinal product code | CP-690550-10 |
| Other name | |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

5 mg BID

| | |
|------------------|---------------------------------------|
| Arm title | Initial Period: Tofacitinib 10 mg BID |
|------------------|---------------------------------------|

Arm description:

Tofacitinib 10 mg BID. Participants with non-zero average total daily dose across study ≥ 15 were assigned to 10 mg BID.

avg=average; BID=twice daily; mg=milligram; ppts=participants; tofa=tofacitinib

| | |
|--|--------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Tofacitinib |
| Investigational medicinal product code | CP-690550-10 |
| Other name | |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

10 mg BID

| Number of subjects in period 1 | Initial Period: Tofacitinib 5 milligram(mg) twice daily (BID) | Initial Period: Tofacitinib 10 mg BID |
|---|--|---|
| Started | 1123 | 3358 |
| Completed | 484 | 1653 |
| Not completed | 639 | 1705 |
| Adverse event, serious fatal | 25 | 30 |
| Did not meet entrance criteria | 2 | 2 |
| Study terminated by Sponsor | - | 1 |
| Not specified | 67 | 211 |
| Missing end of study page | - | 4 |
| Medication error without adverse event | - | 1 |
| No longer willing to participate | 116 | 368 |
| Adverse event not related to study drug | 113 | 248 |
| Pregnancy | 10 | 8 |
| Lost to follow-up | 31 | 101 |
| Adverse event related to study drug | 178 | 527 |
| Lack of efficacy | 59 | 115 |
| Protocol deviation | 38 | 89 |

Period 2

| | |
|------------------------------|------------------|
| Period 2 title | Extension Period |
| Is this the baseline period? | No |
| Allocation method | Not applicable |
| Blinding used | Not blinded |

Arms

| | |
|---|------------------------------------|
| Arm title | Extension Period: Tofacitinib 5 mg |
| Arm description: | |
| Subjects who completed 2 years of lymphocyte assessment in Initial period and enrolled for Extension period received Tofacitinib (CP-690,550) 5 mg orally, twice daily up to 12 months. | |
| Arm type | Experimental |
| Investigational medicinal product name | Tofacitinib |
| Investigational medicinal product code | CP-690,550 |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Subjects received Tofacitinib (CP-690,550) 5 mg orally, twice daily up to 12 months.

| Number of subjects in period 2 ^[1] | Extension Period: Tofacitinib 5 mg |
|---|---------------------------------------|
| | |
| Started | 48 |
| Completed | 43 |
| Not completed | 5 |
| Adverse Event | 2 |
| No longer willing to participate | 2 |
| Protocol deviation | 1 |

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: Only those subjects who enrolled in extension period are reported

Baseline characteristics

Reporting groups

| | |
|--|---|
| Reporting group title | Initial Period: Tofacitinib 5 milligram(mg) twice daily (BID) |
| Reporting group description: Tofacitinib 5 mg BID. Participants with non-zero average total daily dose across study <15 were assigned to 5 mg BID. avg=average; BID=twice daily; mg=milligram; ppts=participants; tofa=tofacitinib | |
| Reporting group title | Initial Period: Tofacitinib 10 mg BID |
| Reporting group description: Tofacitinib 10 mg BID. Participants with non-zero average total daily dose across study ≥15 were assigned to 10 mg BID. avg=average; BID=twice daily; mg=milligram; ppts=participants; tofa=tofacitinib | |

| Reporting group values | Initial Period: Tofacitinib 5 milligram(mg) twice daily (BID) | Initial Period: Tofacitinib 10 mg BID | Total |
|---|--|---|-------|
| Number of subjects | 1123 | 3358 | 4481 |
| Age Categorical | | | |
| The subject analysis set groups for tofacitinib 10mg BID continuous and interrupted are from the vaccine sub-study. Age and gender characteristics are presented for the main study only. | | | |
| Units: Subjects | | | |
| <18 years | 0 | 0 | 0 |
| 18 to 64 years | 916 | 2838 | 3754 |
| ≥65 years | 207 | 520 | 727 |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 54.0 | 53.0 | |
| standard deviation | ± 12.1 | ± 11.5 | - |
| Gender, Male/Female | | | |
| The subject analysis set groups for tofacitinib 10mg BID continuous and interrupted are from the vaccine sub-study. Age and gender characteristics are presented for the main study only. | | | |
| Units: Subjects | | | |
| Female | 927 | 2744 | 3671 |
| Male | 196 | 614 | 810 |

Subject analysis sets

| | |
|--|--|
| Subject analysis set title | All Tofacitinib |
| Subject analysis set type | Full analysis |
| Subject analysis set description: All participants treated with tofacitinib from 5 mg BID and 10 mg BID groups | |
| Subject analysis set title | Tofacitinib 5 milligram (mg) twice daily (BID) |
| Subject analysis set type | Full analysis |
| Subject analysis set description: Participants with non-zero average total daily dose across study <15 were assigned to 5 mg BID | |
| Subject analysis set title | Tofacitinib 10 mg BID |
| Subject analysis set type | Full analysis |
| Subject analysis set description: Participants with non-zero average total daily dose across study ≥15 were assigned to 10 mg BID | |
| Subject analysis set title | Tofacitinib 10 mg BID Continuous Visit 3 |

| | |
|--|---|
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: | |
| Participants receiving continuous tofacitinib treatment | |
| Subject analysis set title | Tofacitinib 10 mg BID Interrupted Visit 3 |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: | |
| Participants whose treatment with tofacitinib was interrupted for 2 weeks post-randomization | |
| Subject analysis set title | Tofacitinib 10 mg BID Continuous Visit 4 |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: | |
| Participants receiving continuous tofacitinib treatment | |
| Subject analysis set title | Tofacitinib 10 mg BID Interrupted Visit 4 |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: | |
| Participants whose treatment with tofacitinib was interrupted for 2 weeks post-randomization | |
| Subject analysis set title | Tofacitinib 10 mg BID Continuous |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: | |
| Participants receiving continuous tofacitinib treatment | |
| Subject analysis set title | Tofacitinib 10 mg BID Interrupted |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: | |
| Participants whose treatment with tofacitinib was interrupted for 2 weeks post-randomization | |
| Subject analysis set title | Tofacitinib 10 mg Continuous |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: | |
| Participants receiving continuous tofacitinib treatment | |
| Subject analysis set title | Tofacitinib 10 mg BID Continuous Visit 2 |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: | |
| Participants receiving continuous tofacitinib treatment | |
| Subject analysis set title | Tofacitinib 10 mg BID Interrupted Visit 2 |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: | |
| Participants whose treatment with tofacitinib was interrupted for 2 weeks post-randomization | |
| Subject analysis set title | Tofacitinib 10 mg BID Continuous Visit 3 |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: | |
| Participants receiving continuous tofacitinib treatment | |
| Subject analysis set title | Tofacitinib 10 mg BID Interrupted Visit 4 |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: | |
| Patients whose treatment with tofacitinib was interrupted for 2 weeks post-randomization | |

| Reporting group values | All Tofacitinib | Tofacitinib 5 milligram (mg) twice daily (BID) | Tofacitinib 10 mg BID |
|---|-----------------|--|-----------------------|
| Number of subjects | 4481 | 1123 | 3358 |
| Age Categorical | | | |
| The subject analysis set groups for tofacitinib 10mg BID continuous and interrupted are from the vaccine sub-study. Age and gender characteristics are presented for the main study only. | | | |
| Units: Subjects | | | |
| <18 years | 0 | 0 | 0 |

| | | | |
|----------------|------|-----|------|
| 18 to 64 years | 3754 | 916 | 2838 |
| >=65 years | 727 | 207 | 520 |

| | | | |
|---|--------|--------|--------|
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 53.3 | 54.0 | 53.0 |
| standard deviation | ± 11.6 | ± 12.1 | ± 11.5 |
| Gender, Male/Female | | | |
| The subject analysis set groups for tofacitinib 10mg BID continuous and interrupted are from the vaccine sub-study. Age and gender characteristics are presented for the main study only. | | | |
| Units: Subjects | | | |
| Female | 3671 | 927 | 2744 |
| Male | 810 | 196 | 614 |

| Reporting group values | Tofacitinib 10 mg BID Continuous Visit 3 | Tofacitinib 10 mg BID Interrupted Visit 3 | Tofacitinib 10 mg BID Continuous Visit 4 |
|---|--|---|--|
| Number of subjects | 91 | 91 | 92 |
| Age Categorical | | | |
| The subject analysis set groups for tofacitinib 10mg BID continuous and interrupted are from the vaccine sub-study. Age and gender characteristics are presented for the main study only. | | | |
| Units: Subjects | | | |
| <18 years | | | |
| 18 to 64 years | | | |
| >=65 years | | | |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 0 | 0 | 0 |
| standard deviation | ± 0 | ± 0 | ± 0 |
| Gender, Male/Female | | | |
| The subject analysis set groups for tofacitinib 10mg BID continuous and interrupted are from the vaccine sub-study. Age and gender characteristics are presented for the main study only. | | | |
| Units: Subjects | | | |
| Female | | | |
| Male | | | |

| Reporting group values | Tofacitinib 10 mg BID Interrupted Visit 4 | Tofacitinib 10 mg BID Continuous | Tofacitinib 10 mg BID Interrupted |
|---|---|-------------------------------------|--------------------------------------|
| Number of subjects | 91 | 92 | 91 |
| Age Categorical | | | |
| The subject analysis set groups for tofacitinib 10mg BID continuous and interrupted are from the vaccine sub-study. Age and gender characteristics are presented for the main study only. | | | |
| Units: Subjects | | | |
| <18 years | | | |
| 18 to 64 years | | | |
| >=65 years | | | |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 0 | 0 | 0 |
| standard deviation | ± 0 | ± 0 | ± 0 |
| Gender, Male/Female | | | |
| The subject analysis set groups for tofacitinib 10mg BID continuous and interrupted are from the vaccine sub-study. Age and gender characteristics are presented for the main study only. | | | |
| Units: Subjects | | | |

| | | | |
|--------|--|--|--|
| Female | | | |
| Male | | | |

| Reporting group values | Tofacitinib 10 mg Continuous | Tofacitinib 10 mg BID Continuous Visit 2 | Tofacitinib 10 mg BID Interrupted Visit 2 |
|---|---------------------------------|--|---|
| Number of subjects | 92 | 92 | 91 |
| Age Categorical | | | |
| The subject analysis set groups for tofacitinib 10mg BID continuous and interrupted are from the vaccine sub-study. Age and gender characteristics are presented for the main study only. | | | |
| Units: Subjects | | | |
| <18 years | | | |
| 18 to 64 years | | | |
| >=65 years | | | |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 0 | 0 | 0 |
| standard deviation | ± 0 | ± 0 | ± 0 |
| Gender, Male/Female | | | |
| The subject analysis set groups for tofacitinib 10mg BID continuous and interrupted are from the vaccine sub-study. Age and gender characteristics are presented for the main study only. | | | |
| Units: Subjects | | | |
| Female | | | |
| Male | | | |

| Reporting group values | Tofacitinib 10 mg BID Continuous Visit 3 | Tofacitinib 10 mg BID Interrupted Visit 4 | |
|---|--|---|--|
| Number of subjects | 92 | 91 | |
| Age Categorical | | | |
| The subject analysis set groups for tofacitinib 10mg BID continuous and interrupted are from the vaccine sub-study. Age and gender characteristics are presented for the main study only. | | | |
| Units: Subjects | | | |
| <18 years | | | |
| 18 to 64 years | | | |
| >=65 years | | | |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 0 | 0 | |
| standard deviation | ± 0 | ± 0 | |
| Gender, Male/Female | | | |
| The subject analysis set groups for tofacitinib 10mg BID continuous and interrupted are from the vaccine sub-study. Age and gender characteristics are presented for the main study only. | | | |
| Units: Subjects | | | |
| Female | | | |
| Male | | | |

End points

End points reporting groups

| | |
|--|---|
| Reporting group title | Initial Period: Tofacitinib 5 milligram(mg) twice daily (BID) |
| Reporting group description: Tofacitinib 5 mg BID. Participants with non-zero average total daily dose across study <15 were assigned to 5 mg BID. avg=average; BID=twice daily; mg=milligram; ppts=participants; tofa=tofacitinib | |
| Reporting group title | Initial Period: Tofacitinib 10 mg BID |
| Reporting group description: Tofacitinib 10 mg BID. Participants with non-zero average total daily dose across study ≥15 were assigned to 10 mg BID. avg=average; BID=twice daily; mg=milligram; ppts=participants; tofa=tofacitinib | |
| Reporting group title | Extension Period: Tofacitinib 5 mg |
| Reporting group description: Subjects who completed 2 years of lymphocyte assessment in Initial period and enrolled for Extension period received Tofacitinib (CP-690,550) 5 mg orally, twice daily up to 12 months. | |
| Subject analysis set title | All Tofacitinib |
| Subject analysis set type | Full analysis |
| Subject analysis set description: All participants treated with tofacitinib from 5 mg BID and 10 mg BID groups | |
| Subject analysis set title | Tofacitinib 5 milligram (mg) twice daily (BID) |
| Subject analysis set type | Full analysis |
| Subject analysis set description: Participants with non-zero average total daily dose across study <15 were assigned to 5 mg BID | |
| Subject analysis set title | Tofacitinib 10 mg BID |
| Subject analysis set type | Full analysis |
| Subject analysis set description: Participants with non-zero average total daily dose across study ≥15 were assigned to 10 mg BID | |
| Subject analysis set title | Tofacitinib 10 mg BID Continuous Visit 3 |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: Participants receiving continuous tofacitinib treatment | |
| Subject analysis set title | Tofacitinib 10 mg BID Interrupted Visit 3 |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: Participants whose treatment with tofacitinib was interrupted for 2 weeks post-randomization | |
| Subject analysis set title | Tofacitinib 10 mg BID Continuous Visit 4 |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: Participants receiving continuous tofacitinib treatment | |
| Subject analysis set title | Tofacitinib 10 mg BID Interrupted Visit 4 |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: Participants whose treatment with tofacitinib was interrupted for 2 weeks post-randomization | |
| Subject analysis set title | Tofacitinib 10 mg BID Continuous |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: Participants receiving continuous tofacitinib treatment | |
| Subject analysis set title | Tofacitinib 10 mg BID Interrupted |
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

Participants whose treatment with tofacitinib was interrupted for 2 weeks post-randomization

| | |
|----------------------------|------------------------------|
| Subject analysis set title | Tofacitinib 10 mg Continuous |
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

Participants receiving continuous tofacitinib treatment

| | |
|----------------------------|--|
| Subject analysis set title | Tofacitinib 10 mg BID Continuous Visit 2 |
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

Participants receiving continuous tofacitinib treatment

| | |
|----------------------------|---|
| Subject analysis set title | Tofacitinib 10 mg BID Interrupted Visit 2 |
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

Participants whose treatment with tofacitinib was interrupted for 2 weeks post-randomization

| | |
|----------------------------|--|
| Subject analysis set title | Tofacitinib 10 mg BID Continuous Visit 3 |
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

Participants receiving continuous tofacitinib treatment

| | |
|----------------------------|---|
| Subject analysis set title | Tofacitinib 10 mg BID Interrupted Visit 4 |
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

Patients whose treatment with tofacitinib was interrupted for 2 weeks post-randomization

Primary: Initial Period: Primary endpoints were standard laboratory safety data (chemistry, hematology, etc.) and adverse event (AE) reports

| | |
|-----------------|---|
| End point title | Initial Period: Primary endpoints were standard laboratory safety data (chemistry, hematology, etc.) and adverse event (AE) reports |
|-----------------|---|

End point description:

Treatment-emergent non serious AEs by System Organ Class (SOC) (all causalities) and Laboratory Test Abnormalities (without regard to baseline).

The stated number of participants analyzed was the total number of participants in each group. The actual number of participants analyzed for each laboratory parameter varied, and is provided for each. Abs=absolute; ALT=alanine aminotransferase; AST=aspartate aminotransferase; ESR=erythrocyte sedimentation rate; GGT=gamma glutamyl transferase; hgb=hemoglobin; HDL=high density lipids; LDL=low density lipids; LLN=lower limit of normal; qual=qualitative; Tot=total; ULN=upper limit of normal; WBC=white blood cell

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Includes laboratory test abnormality data for all visits and AE data up to 999 days after last dose of study drug

| End point values | Initial Period: Tofacitinib 5 milligram(mg) twice daily (BID) | Initial Period: Tofacitinib 10 mg BID | All Tofacitinib | |
|--------------------------------------|---|---|----------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 1123 | 3358 | 4481 | |
| Units: Number of participants | | | | |
| Participants with non-serious AEs | 991 | 2963 | 3954 | |
| Blood and lymphatic system disorders | 159 | 395 | 554 | |
| Cardiac disorders | 93 | 185 | 278 | |

| | | | | |
|---|------|------|------|--|
| Congenital, familial and genetic disorders | 6 | 16 | 22 | |
| Ear and labyrinth disorders | 67 | 138 | 205 | |
| Endocrine disorders | 29 | 94 | 123 | |
| Eye disorders | 117 | 259 | 376 | |
| Gastrointestinal disorders | 393 | 1011 | 1404 | |
| General disorders and admin site conditions | 169 | 477 | 646 | |
| Hepatobiliary disorders | 60 | 176 | 236 | |
| Immune system disorders | 18 | 87 | 105 | |
| Infections and infestations | 704 | 2200 | 2904 | |
| Injury, poisoning and procedural complications | 244 | 721 | 965 | |
| Investigations | 402 | 995 | 1397 | |
| Metabolism and nutrition disorders | 184 | 562 | 746 | |
| Musculoskeletal and connective tissue disorders | 425 | 1314 | 1739 | |
| Neoplasms benign, malignant and unspecified | 80 | 219 | 299 | |
| Nervous system disorders | 222 | 639 | 861 | |
| Pregnancy, puerperium and perinatal conditions | 1 | 0 | 1 | |
| Product issues | 2 | 8 | 10 | |
| Psychiatric disorders | 97 | 280 | 377 | |
| Renal and urinary disorders | 123 | 265 | 388 | |
| Reproductive system and breast disorders | 89 | 206 | 295 | |
| Respiratory, thoracic and mediastinal disorders | 208 | 634 | 842 | |
| Skin and subcutaneous tissue disorders | 201 | 682 | 883 | |
| Social circumstances | 1 | 5 | 6 | |
| Surgical and medical procedures | 2 | 4 | 6 | |
| Vascular disorders | 207 | 468 | 675 | |
| Participants evaluable for lab abnormalities | 1118 | 3346 | 4464 | |
| Participants with laboratory abnormalities | 1095 | 3208 | 4303 | |
| Hemoglobin <0.8x LLN (N=1117,3343,4460) | 57 | 148 | 205 | |
| Hematocrit <0.8x LLN (N=1117,3343,4460) | 29 | 67 | 96 | |
| Red blood cell count <0.8x LLN (N=1049,3343,4392) | 32 | 142 | 174 | |
| Reticulocytes (Abs) <0.5x LLN (N=570,75,645) | 44 | 5 | 49 | |
| Reticulocytes (Abs) >1.5x ULN (N=570,75,645) | 49 | 9 | 58 | |
| Platelets <0.5x LLN (N=1116,3343,4459) | 5 | 2 | 7 | |
| Platelets >1.75x ULN (N=1116,3343,4459) | 5 | 25 | 30 | |
| Reticulocyte count (%) <0.5x LLN (N=46,34,80) | 1 | 1 | 2 | |
| Reticulocyte count (%) >1.5x ULN (N=46,34,80) | 24 | 17 | 41 | |
| WBC count <0.6x LLN (N=1117,3343,4460) | 21 | 33 | 54 | |
| WBC count >1.5x ULN (N=1117,3343,4460) | 29 | 71 | 100 | |

| | | | |
|---|-----|------|------|
| Lymphocytes (Abs) <0.8x LLN (N=1117,3343,4460) | 254 | 789 | 1043 |
| Lymphocytes (Abs) >1.2x ULN (N=1117,3343,4460) | 23 | 94 | 117 |
| Lymphocytes (%) <0.8x LLN (N=1043,3343,4386) | 401 | 1267 | 1668 |
| Lymphocytes (%) >1.2x ULN (N=1043,3343,4386) | 23 | 75 | 98 |
| Tot neutrophils (Abs) <0.8x LLN (N=1117,3343,4460) | 105 | 305 | 410 |
| Tot neutrophils (Abs) >1.2x ULN (N=1117,3343,4460) | 239 | 617 | 856 |
| Neutrophils (%) <0.8x LLN (N=1042,3343,4385) | 23 | 75 | 98 |
| Neutrophils (%) >1.2x ULN (N=1042,3343,4385) | 29 | 93 | 122 |
| Basophils (Abs) >1.2x ULN (N=1117,3343,4460) | 19 | 10 | 29 |
| Basophils (%) >1.2x ULN (N=1043,3343,4386) | 76 | 221 | 297 |
| Eosinophils (Abs) >1.2x ULN (N=1117,3343,4460) | 24 | 58 | 82 |
| Eosinophils (%) >1.2x ULN (N=1043,3343,4386) | 36 | 118 | 154 |
| Monocytes (Abs) >1.2x ULN (N=1117,3343,4460) | 65 | 107 | 172 |
| Monocytes (%) >1.2x ULN (N=1043,3343,4386) | 128 | 405 | 533 |
| ESR >1.5x ULN (N=1113,3343,4456) | 872 | 2411 | 3283 |
| Total bilirubin >1.5x ULN (N=1117,3345,4462) | 18 | 38 | 56 |
| Direct bilirubin >1.5x ULN (N=1088,3344,4432) | 5 | 14 | 19 |
| Indirect bilirubin >1.5x ULN (N=1041,3344,4385) | 4 | 18 | 22 |
| AST >3.0x ULN (N=1117,3343,4461) | 52 | 111 | 163 |
| ALT >3.0x ULN (N=1117,3345,4462) | 87 | 189 | 276 |
| GGT >3.0x ULN (N=1118,3345,4463) | 82 | 239 | 321 |
| Alkaline phosphatase >3.0x ULN (N=1118,3345,4463) | 3 | 10 | 13 |
| Total protein <0.8x LLN (N=1118,3345,4463) | 1 | 0 | 1 |
| Total protein >1.2x ULN (N=1118,3345,4463) | 2 | 4 | 6 |
| Albumin <0.8x LLN (N=1118,3345,4463) | 11 | 28 | 39 |
| Albumin >1.2x ULN (N=1118,3345,4463) | 0 | 0 | 0 |
| Blood urea nitrogen >1.3x ULN (N=1118,3345,4463) | 87 | 126 | 213 |
| Creatinine >1.3x ULN (N=1118,3345,4463) | 52 | 95 | 147 |
| Cholesterol >1.3x ULN (N=1104,3345,4449) | 42 | 130 | 172 |
| HDL Cholesterol <0.8x LLN (N=1097,3301,4398) | 32 | 59 | 91 |
| LDL Cholesterol >1.2x ULN (N=1094,3293,4387) | 69 | 145 | 214 |
| Triglycerides >1.3x ULN (N=1096,3300,4396) | 196 | 373 | 569 |

| | | | | |
|--|-----|------|------|--|
| Sodium <0.95x LLN (N=1118,3345,4463) | 6 | 19 | 25 | |
| Sodium >1.05x ULN (N=1118,3345,4463) | 11 | 18 | 29 | |
| Potassium <0.9x LLN (N=1118,3345,4463) | 28 | 62 | 90 | |
| Potassium >1.1x ULN (N=1118,3345,4463) | 11 | 25 | 36 | |
| Chloride <0.9x LLN (N=1118,3345,4463) | 3 | 5 | 8 | |
| Chloride >1.1x ULN (N=1118,3345,4463) | 0 | 1 | 1 | |
| Calcium <0.9x LLN (N=1041,3345,4386) | 2 | 8 | 10 | |
| Calcium >1.1x ULN (N=1041,3345,4386) | 6 | 9 | 15 | |
| Bicarbonate (venous) <0.9x LLN (N=1117,3345,4462) | 106 | 277 | 383 | |
| Bicarbonate (venous) >1.1x ULN (N=1117,3345,4462) | 1 | 5 | 6 | |
| Glucose <0.6x LLN (N=1118,3345,4463) | 3 | 4 | 7 | |
| Glucose >1.5x ULN (N=1118,3345,4463) | 125 | 345 | 470 | |
| Creatine Kinase >2.0x ULN (N=1041,3345,4386) | 203 | 908 | 1111 | |
| C-reactive protein >1.25x ULN (N=697,242,939) | 365 | 106 | 471 | |
| Urine specific gravity <1.003 (N=1098,3319,4417) | 2 | 7 | 9 | |
| Urine specific gravity >1.030 (N=1098,3319,4417) | 203 | 303 | 506 | |
| Urine pH <4.5 (N=1098,3319,4417) | 0 | 0 | 0 | |
| Urine pH >8 (N=1098,3319,4417) | 20 | 17 | 37 | |
| Urine glucose (qual) ≥1 (N=1095,3319,4414) | 60 | 148 | 208 | |
| Urine ketones (qual) ≥1 (N=686,103,789) | 2 | 1 | 3 | |
| Urine protein (qual) ≥1 (N=1097,3319,4416) | 65 | 222 | 287 | |
| Urine blood/hgb (qual) ≥1 (N=1098,3319,4417) | 444 | 1260 | 1704 | |
| Urine leukocyte esterase ≥1 (N=687,132,819) | 158 | 23 | 181 | |
| Urine red blood cells ≥20 (N=678,1498,2176) | 198 | 491 | 689 | |
| Urine WBC ≥20 (N=689,1603,2292) | 219 | 507 | 726 | |
| Urine epithelial cells ≥6 (N=422,38,460) | 205 | 20 | 225 | |
| Urine casts >1 (N=420,38,458) | 0 | 0 | 0 | |
| Urine granular casts >1 (N=0,2,2) | 0 | 0 | 0 | |
| Urine hyaline casts >1 (N=14,60,74) | 0 | 0 | 0 | |
| Urine bacteria >20 (N=384,35,419) | 0 | 0 | 0 | |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Descriptive statistics only performed |
| Comparison groups | Initial Period: Tofacitinib 5 milligram(mg) twice daily (BID) v Initial Period: Tofacitinib 10 mg BID |
| Number of subjects included in analysis | 4481 |
| Analysis specification | Post-hoc |
| Analysis type | other ^[1] |
| P-value | = 0 |
| Method | Not applicable |
| Parameter estimate | Not applicable |

Notes:

[1] - Arbitrary analysis specification entered as only descriptive statistics performed for this endpoint

Primary: Extension Period: Number of Subjects with Treatment Emergent Adverse Events (AEs), Serious Adverse Events (SAEs)

| | |
|-----------------|---|
| End point title | Extension Period: Number of Subjects with Treatment Emergent Adverse Events (AEs), Serious Adverse Events (SAEs) ^[2] |
|-----------------|---|

End point description:

An AE was any untoward medical occurrence in a subject who received study drug without regard to possibility of causal relationship. SAE was an AE resulting in any of the following outcomes or deemed significant for any other reason: death; initial or prolonged inpatient hospitalization; life-threatening experience (immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly. A treatment emergent AE was defined as an event that emerged during the treatment period that was absent before treatment, or worsened during the treatment period relative to the pretreatment state. AEs included both serious and non-serious adverse events. Safety analysis set included all subjects who enrolled for extension period and received at least 1 dose of open label study medication in extension period.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Baseline (Entry of Extension Period) up to 28 days after last study drug dose in Extension Period (13 Months)

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Only descriptive data was planned to be analyzed for this endpoint

| | | | | |
|-----------------------------|---------------------------------------|--|--|--|
| End point values | Extension Period: Tofacitinib 5 mg | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 48 | | | |
| Units: Subjects | | | | |
| Subjects with AEs | 16 | | | |
| Subjects with SAEs | 5 | | | |

Statistical analyses

No statistical analyses for this end point

Primary: Extension Period: Number of Subjects with Laboratory Test Abnormalities

| | |
|-----------------|--|
| End point title | Extension Period: Number of Subjects with Laboratory Test Abnormalities ^[3] |
|-----------------|--|

End point description:

Criteria for laboratory abnormalities: hemoglobin (Hg), hematocrit, red blood cell (RBC), high density lipoprotein (HDL) cholesterol: <0.8*lower limit of normal (LLN), platelet <0.5*LLN/>1.75*upper limit of normal (ULN), white blood cell (WBC) <0.6*LLN/>1.5*ULN, lymphocyte, neutrophil, protein, albumin <0.8*LLN/>1.2*ULN, basophil, eosinophil, monocyte, low density lipoprotein (LDL) cholesterol: >1.2*ULN; bilirubin >1.5*ULN, aspartate amino transferase(AT), alanine AT, gammaglutamyl transferase, alkaline phosphatase: >3.0*ULN; blood urea nitrogen, creatinine, cholesterol, triglyceride: >1.3*ULN; sodium <0.95*LLN/>1.05*ULN, potassium, chloride, calcium, bicarbonate: <0.9*LLN/>1.1*ULN; glucose <0.6*LLN/>1.5*ULN; Urine (specific gravity <1.003/>1.030, pH <4.5/>8, glucose, ketone, protein, blood/Hg(>=1; RBC, WBC>=20; creatinine kinase >2*ULN). Safety analysis set included all subjects who enrolled for extension period and received at least 1 dose of open label study medication in extension period.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Baseline (Day 1 at Entry of Extension Period) up to 28 days after last study drug dose in Extension Period (13 Months)

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Only descriptive data was planned to be analyzed for this endpoint

| | | | | |
|-----------------------------|---------------------------------------|--|--|--|
| End point values | Extension Period: Tofacitinib 5 mg | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 48 | | | |
| Units: Subjects | 30 | | | |

Statistical analyses

No statistical analyses for this end point

Primary: Initial Period: The long-term safety and tolerability of CP-690,550 5 milligrams (mg) twice daily (BID) and 10 mg BID for the treatment of rheumatoid arthritis

| | |
|-----------------|---|
| End point title | Initial Period: The long-term safety and tolerability of CP-690,550 5 milligrams (mg) twice daily (BID) and 10 mg BID for the treatment of rheumatoid arthritis |
|-----------------|---|

End point description:

Treatment-emergent AEs by SOC (all causalities) - all patients, by time. Data presented for Post Month 96 includes data up to and including Month 114.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Every visit until last observation

| End point values | Initial Period: Tofacitinib 5 milligram(mg) twice daily (BID) | Initial Period: Tofacitinib 10 mg BID | All Tofacitinib | |
|---|---|---|----------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 1123 | 3358 | 4481 | |
| Units: Number of participants | | | | |
| number (not applicable) | | | | |
| Evaluable for AEs at Months 0 to 6 | 1123 | 3358 | 4481 | |
| Percent with AEs at Months 0 to 6 | 59.4 | 61.8 | 61.2 | |
| Percent discontinued due to AEs at Months 0 to 6 | 4.2 | 4.0 | 4.0 | |
| Evaluable for AEs at Months 6 to 12 | 1033 | 3121 | 4154 | |
| Percent with AEs at Months 6 to 12 | 45.1 | 47.7 | 47.1 | |
| Percent discontinued due to AEs at Months 6 to 12 | 2.1 | 3.7 | 3.3 | |
| Evaluable for AEs at Months 12 to 18 | 969 | 2865 | 3834 | |
| Percent with AEs at Months 12 to 18 | 41.2 | 46.8 | 45.4 | |
| Percent discontinued due to AEs at Months 12 to 18 | 3.2 | 3.4 | 3.3 | |
| Evaluable at Months 18 to 24 | 896 | 2660 | 3556 | |
| Percent with AEs at Months 18 to 24 | 38.1 | 43.2 | 41.9 | |
| Percent discontinued due to AEs at Months 18 to 24 | 2.8 | 2.9 | 2.9 | |
| Evaluable for AEs at Months 24 to 30 | 820 | 2461 | 3281 | |
| Percent with AEs at Months 24 to 30 | 40.7 | 44.5 | 43.5 | |
| Percent discontinued due to AEs at Months 24 to 30 | 3.2 | 2.8 | 2.9 | |
| Evaluable for AEs at Months 30 to 36 | 774 | 2288 | 3062 | |
| Percent with AEs at Months 30 to 36 | 39.0 | 40.7 | 40.3 | |
| Percent discontinued due to AEs at Months 30 to 36 | 2.6 | 2.5 | 2.5 | |
| Evaluable for AEs at Months 36 to 42 | 729 | 2162 | 2891 | |
| Percent with AEs at Months 36 to 42 | 38.1 | 37.5 | 37.6 | |
| Percent discontinued due to AEs at Months 36 to 42 | 2.5 | 2.5 | 2.5 | |
| Evaluable for AEs at Months 42 to 48 | 652 | 1843 | 2495 | |
| Percent with AEs at Months 42 to 48 | 37.9 | 34.3 | 35.3 | |
| Percent discontinued due to AEs at Months 42 to 48 | 2.8 | 2.9 | 2.9 | |
| Evaluable for AEs at Months 48 to 54 | 558 | 1471 | 2029 | |
| Percent with AEs at Months 48 to 54 | 36.0 | 36.4 | 36.3 | |
| Percent discontinued due to AEs at Months 48 to 54 | 2.0 | 2.5 | 2.4 | |
| Evaluable for AEs at Months 54 to 60 | 466 | 1172 | 1638 | |
| Percent with AEs at Months 54 to 60 | 37.1 | 35.4 | 35.9 | |
| Percent discontinued due to AEs at Months 54 to 60 | 3.6 | 2.7 | 3.0 | |
| Evaluable for AEs at Months 60 to 66 | 414 | 918 | 1332 | |
| Percent with AEs at Months 60 to 66 | 33.8 | 31.4 | 32.1 | |
| Percent discontinued due to AEs at Months 60 to 66 | 2.4 | 1.9 | 2.0 | |
| Evaluable for AEs at Months 66 to 72 | 379 | 670 | 1049 | |
| Percent with AEs at Months 66 to 72 | 33.5 | 21.6 | 25.9 | |
| Percent discontinued due to AEs at Months 66 to 72 | 3.2 | 0.7 | 1.6 | |

| | | | | |
|--|------|------|------|--|
| Evaluable for AEs at Months 72 to 78 | 336 | 262 | 598 | |
| Percent with AEs at Months 72 to 78 | 33.6 | 22.5 | 28.8 | |
| Percent discontinued due to AEs at Months 72 to 78 | 0.9 | 0.4 | 0.7 | |
| Evaluable for AEs at Months 78 to 84 | 302 | 86 | 388 | |
| Percent with AEs at Months 78 to 84 | 36.8 | 26.7 | 34.5 | |
| Percent discontinued due to AEs at Months 78 to 84 | 3.3 | 1.2 | 2.8 | |
| Evaluable for AEs at Months 84 to 90 | 273 | 42 | 315 | |
| Percent with AEs at Months 84 to 90 | 30.8 | 35.7 | 31.4 | |
| Percent discontinued due to AEs at Months 84 to 90 | 1.8 | 0 | 1.6 | |
| Evaluable for AEs at Months 90 to 96 | 234 | 34 | 268 | |
| Percent with AEs at Months 90 to 96 | 21.8 | 29.4 | 22.8 | |
| Percent discontinued due to AEs at Months 90 to 96 | 0.9 | 0 | 0.7 | |
| Evaluable for AEs post Month 96 | 130 | 15 | 145 | |
| Percent with AEs post Month 96 | 20.8 | 46.7 | 23.4 | |
| Percent discontinued due to AEs post Month 96 | 1.5 | 0 | 1.4 | |

Statistical analyses

| Statistical analysis title | Descriptive statistics only performed |
|---|---|
| Comparison groups | Initial Period: Tofacitinib 5 milligram(mg) twice daily (BID) v Initial Period: Tofacitinib 10 mg BID |
| Number of subjects included in analysis | 4481 |
| Analysis specification | Post-hoc |
| Analysis type | other ^[4] |
| P-value | = 0 |
| Method | Not applicable |
| Parameter estimate | Not applicable |

Notes:

[4] - Arbitrary analysis specification entered as descriptive statistics only performed for this endpoint

Primary: Extension Period: Percentage of Subjects With Adverse Events and who Discontinued Treatment Due to Adverse Events to Assess Long-term Safety and Tolerability of Tofacitinib

| | |
|-----------------|---|
| End point title | Extension Period: Percentage of Subjects With Adverse Events and who Discontinued Treatment Due to Adverse Events to Assess Long-term Safety and Tolerability of Tofacitinib ^[5] |
|-----------------|---|

End point description:

Long term safety and tolerability of Tofacitinib was measured as following: percentage (%) of subjects with AEs, percentage of subjects who discontinued due to AEs. An AE is any untoward medical occurrence in subject who received study drug without regard to possibility of causal relationship. Safety analysis set included all subjects who enrolled for extension period and received at least 1 dose of open label study medication in extension period. Here, "n" signifies number of subjects evaluable for specified categories.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Baseline (Day 1 at Entry of Extension Period) up to Month 6 of Extension Period; Month 6 of Extension Period to Month 12 of Extension Period

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Only descriptive data was planned to be analyzed for this endpoint

| End point values | Extension Period: Tofacitinib 5 mg | | | |
|--|---------------------------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 48 | | | |
| Units: Percentage of subjects | | | | |
| number (not applicable) | | | | |
| Baseline to Month 6: % of Subjects with AEs (n=48) | 31.3 | | | |
| Baseline-Month 6:%of Subjects Discontinued(n=48) | 4.2 | | | |
| Month 6 to 12: % of Subjects with AEs (n=17) | 17.6 | | | |
| Month 6 to 12: % of Subjects Discontinued (n=17) | 0.0 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Initial Period: Percent of patients with American College of Rheumatology (ACR) 20, 50, and 70 responses

| | |
|-----------------|--|
| End point title | Initial Period: Percent of patients with American College of Rheumatology (ACR) 20, 50, and 70 responses |
|-----------------|--|

End point description:

The stated number of participants analyzed was the total number of participants in each group. The actual number of participants analyzed on each occasion varied, and is provided for each visit presented.

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

End point timeframe:

Every visit until last observation

| End point values | Initial Period: Tofacitinib 5 milligram(mg) twice daily (BID) | Initial Period: Tofacitinib 10 mg BID | All Tofacitinib | |
|--------------------------------------|--|--|----------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 1123 | 3358 | 4481 | |
| Units: Percent of participants | | | | |
| number (not applicable) | | | | |
| ACR20 at Month 1 (N=1114,3307,4421) | 70.65 | 73.60 | 72.86 | |
| ACR20 at Month 2 (N=1080,3254,4334) | 74.81 | 76.06 | 75.75 | |
| ACR20 at Month 3 (N=1069, 3228,4297) | 75.68 | 78.00 | 77.43 | |
| ACR20 at Month 6 (N=1040,3132,4172) | 75.58 | 77.36 | 76.92 | |

| | | | | |
|---------------------------------------|--------|--------|--------|--|
| ACR20 at Month 9 (N=1003,3022,4025) | 76.57 | 77.53 | 77.29 | |
| ACR20 at Month 12 (N=972,2891,3863) | 77.88 | 78.24 | 78.15 | |
| ACR20 at Month 15 (N=938,2775,3713) | 76.76 | 78.67 | 78.18 | |
| ACR20 at Month 18 (N=910,2665,3575) | 77.91 | 78.46 | 78.32 | |
| ACR20 at Month 21 (N=860,2565,3425) | 77.91 | 79.42 | 79.04 | |
| ACR20 at Month 24 (N=824, 2464, 3288) | 79.61 | 78.37 | 78.68 | |
| ACR20 at Month 27 (N=796,2361,3157) | 79.15 | 79.16 | 79.16 | |
| ACR20 at Month 30 (N=770,2288,3058) | 80.00 | 79.90 | 79.92 | |
| ACR20 at Month 33 (N=749,2219,2968) | 80.51 | 79.81 | 79.99 | |
| ACR20 at Month 36 (N=730, 2157, 2887) | 81.78 | 79.37 | 79.98 | |
| ACR20 at Month 39 (N=690,2073,2763) | 78.55 | 81.23 | 80.56 | |
| ACR20 at Month 42 (N=657,1907,2564) | 78.69 | 80.49 | 80.03 | |
| ACR20 at Month 45 (N=616,1658,2274) | 82.14 | 79.55 | 80.26 | |
| ACR20 at Month 48 (N=581,1486,2067) | 78.31 | 80.69 | 80.02 | |
| ACR20 at Month 51 (N=490,1355,1845) | 83.47 | 80.30 | 81.14 | |
| ACR20 at Month 54 (N=471,1208,1679) | 79.19 | 78.97 | 79.04 | |
| ACR20 at Month 57 (N=441,1021,1462) | 80.73 | 82.37 | 81.87 | |
| ACR20 at Month 60 (N=411,920,1331) | 81.75 | 82.39 | 82.19 | |
| ACR20 at Month 63 (N=396,692,1010) | 80.30 | 82.97 | 82.11 | |
| ACR20 at Month 66 (N=382,705,1087) | 79.84 | 81.42 | 80.86 | |
| ACR20 at Month 69 (N=358,486,844) | 82.68 | 83.54 | 83.18 | |
| ACR20 at Month 72 (N=339, 287, 626) | 82.01 | 82.58 | 82.27 | |
| ACR20 at Month 75 (N=309,171,480) | 82.20 | 78.95 | 81.04 | |
| ACR20 at Month 78 (N=295,91,386) | 81.69 | 80.22 | 81.35 | |
| ACR20 at Month 81 (N=286,54,340) | 82.52 | 79.63 | 82.06 | |
| ACR20 at Month 84 (N=271,44,315) | 82.66 | 81.82 | 82.54 | |
| ACR20 at Month 87 (N=264,41,305) | 84.47 | 70.73 | 82.62 | |
| ACR20 at Month 90 (N=241,39,280) | 82.57 | 74.36 | 81.43 | |
| ACR20 at Month 93 (N=196,28,224) | 82.14 | 78.57 | 81.70 | |
| ACR20 at Month 96 (N=144,16,160) | 78.47 | 81.25 | 78.75 | |
| ACR20 at Month 99 (N=65,11,76) | 83.08 | 90.91 | 84.21 | |
| ACR20 at Month 102 (N=22,4,26) | 77.27 | 50.00 | 73.08 | |
| ACR20 at Month 105 (N=15,3,18) | 73.33 | 66.67 | 72.22 | |
| ACR20 at Month 108 (N=8,1,9) | 62.50 | 100.00 | 66.67 | |
| ACR20 at Month 111 (N=3,1,4) | 100.00 | 100.00 | 100.00 | |
| ACR20 at Month 114 (N=1,0,1) | 100.00 | 0 | 100.00 | |
| ACR50 at Month 1 (N=1114,3307,4421) | 47.67 | 49.56 | 49.08 | |
| ACR50 at Month 2 (N=1080,3254,4334) | 50.19 | 53.29 | 52.51 | |
| ACR50 at Month 3 (N=1069,3228,4297) | 51.45 | 54.52 | 53.76 | |
| ACR50 at Month 6 (N=1040,3132,4172) | 52.79 | 55.75 | 55.01 | |
| ACR50 at Month 9 (N=1003,3022,4025) | 53.24 | 55.96 | 55.28 | |
| ACR50 at Month 12 (N=972,2891,3863) | 52.98 | 56.73 | 55.79 | |
| ACR50 at Month 15 (N=938,2775,3713) | 55.76 | 56.61 | 56.40 | |
| ACR50 at Month 18 (N=910,2665,3575) | 55.16 | 57.30 | 56.76 | |
| ACR50 at Month 21 (N=860,2565,3425) | 54.77 | 59.10 | 58.01 | |
| ACR50 at Month 24 (N=824,2464,3288) | 57.77 | 57.67 | 57.69 | |
| ACR50 at Month 27 (N=796,2361,3157) | 56.91 | 58.58 | 58.16 | |
| ACR50 at Month 30 (N=770,2288,3058) | 58.83 | 58.65 | 58.70 | |
| ACR50 at Month 33 (N=749,2219,2968) | 57.68 | 59.31 | 58.89 | |
| ACR50 at Month 36 (N=730,2157,2887) | 58.49 | 58.51 | 58.50 | |

| | | | | |
|-------------------------------------|--------|-------|--------|--|
| ACR50 at Month 39 (N=690,2073,2763) | 59.28 | 59.29 | 59.28 | |
| ACR50 at Month 42 (N=657,1907,2564) | 58.60 | 59.99 | 59.63 | |
| ACR50 at Month 45 (N=616,1658,2274) | 59.42 | 60.07 | 59.89 | |
| ACR50 at Month 48 (N=581,1486,2067) | 58.00 | 57.60 | 57.72 | |
| ACR50 at Month 51 (N=490,1355,1845) | 62.45 | 59.19 | 60.05 | |
| ACR50 at Month 54 (N=471,1355,1845) | 58.60 | 59.44 | 59.20 | |
| ACR50 at Month 57 (N=441,1021,1462) | 61.45 | 61.12 | 61.22 | |
| ACR50 at Month 60 (N=411,920,1331) | 62.53 | 60.65 | 61.23 | |
| ACR50 at Month 63 (N=396,834,1230) | 64.39 | 61.99 | 62.76 | |
| ACR50 at Month 66 (N=382,705,1087) | 60.73 | 60.85 | 60.81 | |
| ACR50 at Month 69 (N=358,486,844) | 58.10 | 61.11 | 59.83 | |
| ACR50 at Month 72 (N=339,287,626) | 62.54 | 59.93 | 61.34 | |
| ACR50 at Month 75 (N=309,171,480) | 61.49 | 56.14 | 59.58 | |
| ACR50 at Month 78 (N=295,91,386) | 60.00 | 58.24 | 59.59 | |
| ACR50 at Month 81 (N=286,54,340) | 63.99 | 51.85 | 62.06 | |
| ACR50 at Month 84 (N=271,44,315) | 63.10 | 54.55 | 61.90 | |
| ACR50 at Month 87 (N=264,41,305) | 67.05 | 43.90 | 63.93 | |
| ACR50 at Month 90 (N=241,39,280) | 61.00 | 46.15 | 58.93 | |
| ACR50 at Month 93 (N=196,28,224) | 61.22 | 57.14 | 60.71 | |
| ACR50 at Month 96 (N=144,16,160) | 61.11 | 56.25 | 60.63 | |
| ACR50 at Month 99 (N=65,11,76) | 53.85 | 54.55 | 53.95 | |
| ACR50 at Month 102 (N=22,4,26) | 54.55 | 25.00 | 50.00 | |
| ACR50 at Month 105 (N=15,3,18) | 66.67 | 33.33 | 61.11 | |
| ACR50 at Month 108 (N=8,1,9) | 50.00 | 0.00 | 44.44 | |
| ACR50 at Month 111 (N=3,1,4) | 100.00 | 0.00 | 75.00 | |
| ACR50 at Month 114 (N=1,0,1) | 100.00 | 0.00 | 100.00 | |
| ACR70 at Month 1 (N=1114,3307,4421) | 26.66 | 28.82 | 28.27 | |
| ACR70 at Month 2 (N=1080,3254,4334) | 27.78 | 31.53 | 30.60 | |
| ACR70 at Month 3 (N=1069,3228,4297) | 29.37 | 33.09 | 32.16 | |
| ACR70 at Month 6 (N=1040,3132,4172) | 31.06 | 33.75 | 33.08 | |
| ACR70 at Month 9 (N=1003,3022,4025) | 31.80 | 34.91 | 34.14 | |
| ACR70 at Month 12 (N=972,2891,3863) | 31.38 | 35.84 | 34.71 | |
| ACR70 at Month 15 (N=937,2775,3713) | 32.94 | 36.54 | 35.63 | |
| ACR70 at Month 18 (N=910,2665,3575) | 35.82 | 36.40 | 36.25 | |
| ACR70 at Month 21 (N=860,2565,3425) | 33.49 | 37.66 | 36.61 | |
| ACR70 at Month 24 (N=824,2464,3288) | 35.44 | 38.15 | 37.47 | |
| ACR70 at Month 27 (N=796,2361,3157) | 36.06 | 38.33 | 37.76 | |
| ACR70 at Month 30 (N=770,2288,3058) | 37.27 | 38.99 | 38.55 | |
| ACR70 at Month 33 (N=749,2219,2968) | 33.64 | 38.26 | 37.10 | |
| ACR70 at Month 36 (N=730,2157,2887) | 36.71 | 37.41 | 37.24 | |
| ACR70 at Month 39 (N=690,2073,2763) | 38.41 | 38.88 | 38.76 | |
| ACR70 at Month 42 (N=657,1907,2564) | 35.77 | 38.91 | 38.10 | |
| ACR70 at Month 45 (N=616,1658,2274) | 36.69 | 38.18 | 37.77 | |
| ACR70 at Month 48 (N=581,1486,2067) | 35.97 | 37.01 | 36.72 | |
| ACR70 at Month 51 (N=490,1355,1845) | 39.59 | 37.34 | 37.94 | |
| ACR70 at Month 54 (N=471,1208,1679) | 36.73 | 39.32 | 38.59 | |
| ACR70 at Month 57 (N=441,1021,1462) | 38.78 | 39.47 | 39.26 | |
| ACR70 at Month 60 (N=411,920,1331) | 37.96 | 38.91 | 38.62 | |
| ACR70 at Month 63 (N=396,834,1230) | 38.64 | 39.33 | 39.11 | |
| ACR70 at Month 66 (N=.146,283,429) | 38.22 | 40.14 | 39.47 | |
| ACR70 at Month 69 (N=358,486,844) | 38.55 | 41.56 | 40.28 | |
| ACR70 at Month 72 (N=339,287,626) | 40.12 | 36.59 | 38.50 | |

| | | | | |
|-----------------------------------|--------|-------|--------|--|
| ACR70 at Month 75 (N=309,171,480) | 40.13 | 36.84 | 38.96 | |
| ACR70 at Month 78 (N=295,91,386) | 42.37 | 32.97 | 40.16 | |
| ACR70 at Month 81 (N=286,54,340) | 41.26 | 35.19 | 40.29 | |
| ACR70 at Month 84 (N=271,44,315) | 42.07 | 31.82 | 40.63 | |
| ACR70 at Month 87 (N=264,41,305) | 42.80 | 21.95 | 40.00 | |
| ACR70 at Month 90 (N=241,39,280) | 38.17 | 25.64 | 36.43 | |
| ACR70 at Month 93 (N=196,28,224) | 41.84 | 39.29 | 41.52 | |
| ACR70 at Month 96 (N=144,16,160) | 43.75 | 31.25 | 42.50 | |
| ACR70 at Month 99 (N=65,11,76) | 40.00 | 18.18 | 36.84 | |
| ACR70 at Month 102 (N=22,4,26) | 40.91 | 25.00 | 38.46 | |
| ACR70 at Month 105 (N=15,3,18) | 46.67 | 33.33 | 44.44 | |
| ACR70 at Month 108 (N=8,1,9) | 25.00 | 0.00 | 22.22 | |
| ACR70 at Month 111 (N=3,1,4) | 100.00 | 0.00 | 75.00 | |
| ACR70 at Month 114 (N=1,0,1) | 100.00 | 0.00 | 100.00 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Extension Period: Percentage of Subjects With American College of Rheumatology (ACR) 20, 50, and 70 Responses

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|-----------------|---|
| End point title | Extension Period: Percentage of Subjects With American College of Rheumatology (ACR) 20, 50, and 70 Responses |
|-----------------|---|

End point description:

ACR20=20 percent (%) improvement from baseline (Month 0 at entry of Initial Period) in tender/painful joint count (JC), swollen JC, and in at least 3 of 5 variables: subject's global assessment of arthritis (SGA), physician's global assessment of arthritis (PGA), subject's assessment of arthritis pain (SA), HAQ-DI, CRP. ACR50 is a 50% improvement and ACR70 a 70% improvement in these variables. SGA:subject assessed overall disease activity, score: 0 (no arthritis) to 10 (extreme arthritis), higher score=more arthritis. PGA: physician judged subject's overall disease activity, score: 0 (no arthritis) to 10 (extreme arthritis), higher score=more arthritis. SA: subject assessed arthritis pain by 100 millimeter (mm) visual analogue scale, score: 0 mm (no pain) to 100 mm (extreme pain), higher score=more pain. HAQ-DI:functional disability evaluation, score: 0 (no difficulty) to 3 (extreme difficulty), higher score=more disability. FAS for extension. "n"=subjects evaluable for categories.

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

End point timeframe:

Month 3, 6, 9 and 12 of Extension Period

| End point values | Extension Period: Tofacitinib 5 mg | | | |
|-------------------------------|------------------------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 48 | | | |
| Units: Percentage of subjects | | | | |
| number (not applicable) | | | | |
| ACR20 at Month 3 (n =47) | 70.21 | | | |
| ACR20 at Month 6 (n =36) | 66.67 | | | |
| ACR20 at Month 9 (n =15) | 86.67 | | | |
| ACR20 at Month 12 (n =2) | 50.00 | | | |

| | | | | |
|--------------------------|-------|--|--|--|
| ACR50 at Month 3 (n =47) | 48.94 | | | |
| ACR50 at Month 6 (n =36) | 55.56 | | | |
| ACR50 at Month 9 (n =15) | 60.00 | | | |
| ACR50 at Month 12 (n =2) | 50.00 | | | |
| ACR70 at Month 3 (n =47) | 23.40 | | | |
| ACR70 at Month 6 (n =36) | 36.11 | | | |
| ACR70 at Month 9 (n =15) | 40.00 | | | |
| ACR70 at Month 12 (n =2) | 50.00 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Area under American College of Rheumatology (ACR) n curve

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|--|---|
| End point title | Area under American College of Rheumatology (ACR) n curve |
| End point description: No data was analyzed for this endpoint because it was removed from the protocol in a previous amendment. | |
| End point type | Secondary |
| End point timeframe: Every visit until last observation | |

| End point values | Initial Period: Tofacitinib 5 milligram(mg) twice daily (BID) | Initial Period: Tofacitinib 10 mg BID | | |
|---|---|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 0 ^[6] | 0 ^[7] | | |
| Units: Not applicable | | | | |
| arithmetic mean (confidence interval 95%) | (to) | (to) | | |

Notes:

[6] - No data analyzed for this endpoint as it was removed in a previous protocol amendment.

[7] - No data analyzed for this endpoint as it was removed in a previous protocol amendment.

Statistical analyses

No statistical analyses for this end point

Secondary: Initial Period: Disease Activity Score (DAS)28 (C-reactive protein [CRP]) and DAS28 (erythrocyte sedimentation rate [ESR])

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|--|--|
| End point title | Initial Period: Disease Activity Score (DAS)28 (C-reactive protein [CRP]) and DAS28 (erythrocyte sedimentation rate [ESR]) |
| End point description: Descriptive statistics for DAS28-3 (CRP) and DAS28-4 (ESR). The stated number of participants analyzed was the total number of participants in each group. The actual number of participants analyzed on each occasion varied, and is provided for each visit presented. | |
| End point type | Secondary |

End point timeframe:

Every visit until last observation

| End point values | Initial Period: Tofacitinib 5 milligram(mg) twice daily (BID) | Initial Period: Tofacitinib 10 mg BID | All Tofacitinib | |
|--|---|---|----------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 1123 | 3358 | 4481 | |
| Units: Score | | | | |
| arithmetic mean (standard deviation) | | | | |
| DAS28-4 (ESR) Baseline (N=1002,3296,4298) | 6.27 (± 1.02) | 6.39 (± 1.04) | 6.36 (± 1.04) | |
| DAS28-4 (ESR) Month 1 (N=1036,3254,4290) | 3.81 (± 1.32) | 3.78 (± 1.36) | 3.79 (± 1.35) | |
| DAS28-4 (ESR) Month 2 (N=1026,3222,4248) | 3.72 (± 1.27) | 3.66 (± 1.32) | 3.68 (± 1.31) | |
| DAS28-4 (ESR) Month 3 (N=1033,3203,4236) | 3.75 (± 1.32) | 3.61 (± 1.30) | 3.65 (± 1.31) | |
| DAS28-4 (ESR) Month 6 (N=1015,3110,4125) | 3.67 (± 1.33) | 3.61 (± 1.30) | 3.62 (± 1.31) | |
| DAS28-4 (ESR) Month 9 (N=992,3003,3995) | 3.60 (± 1.31) | 3.58 (± 1.32) | 3.59 (± 1.31) | |
| DAS28-4 (ESR) Month 12 (N=967,2862,3829) | 3.61 (± 1.26) | 3.56 (± 1.30) | 3.57 (± 1.29) | |
| DAS28-4 (ESR) Month 15 (N=922,2759,3681) | 3.54 (± 1.26) | 3.53 (± 1.30) | 3.53 (± 1.29) | |
| DAS28-4 (ESR) Month 18 (N=899,2655,3554) | 3.57 (± 1.26) | 3.50 (± 1.28) | 3.52 (± 1.28) | |
| DAS28-4 (ESR) Month 21 (N=850,2547,3397) | 3.58 (± 1.25) | 3.45 (± 1.27) | 3.48 (± 1.26) | |
| DAS28-4 (ESR) Month 24 (N=818,2441,3259) | 3.54 (± 1.21) | 3.46 (± 1.26) | 3.48 (± 1.25) | |
| DAS28-4 (ESR) Month 27 (N=787,2343,3130) | 3.52 (± 1.20) | 3.44 (± 1.25) | 3.46 (± 1.24) | |
| DAS28-4 (ESR) Month 30 (N=764,2257,3021) | 3.54 (± 1.23) | 3.43 (± 1.25) | 3.46 (± 1.24) | |
| DAS28-4 (ESR) Month 33 (N=746,2199,2945) | 3.51 (± 1.22) | 3.42 (± 1.27) | 3.45 (± 1.26) | |
| DAS28-4 (ESR) Month 36 (N=720,2141,2861) | 3.51 (± 1.23) | 3.42 (± 1.27) | 3.44 (± 1.26) | |
| DAS28-4 (ESR) Month 39 (N=679,2056,2735) | 3.56 (± 1.27) | 3.39 (± 1.24) | 3.43 (± 1.25) | |
| DAS28-4 (ESR) Month 42 (N=642,1890,2532) | 3.53 (± 1.26) | 3.40 (± 1.26) | 3.43 (± 1.26) | |
| DAS28-4 (ESR) Month 45 (N=609,1641,2250) | 3.45 (± 1.20) | 3.37 (± 1.21) | 3.39 (± 1.20) | |
| DAS28-4 (ESR) Month 48 (N=570,1471,2041) | 3.46 (± 1.16) | 3.36 (± 1.21) | 3.39 (± 1.20) | |
| DAS28-4 (ESR) Month 51 (N=481,1344,1825) | 3.43 (± 1.20) | 3.39 (± 1.24) | 3.40 (± 1.23) | |
| DAS28-4 (ESR) Month 54 (N=467,1194,1661) | 3.54 (± 1.23) | 3.38 (± 1.25) | 3.42 (± 1.25) | |
| DAS28-4 (ESR) Month 57 (N=438,1006,1444) | 3.48 (± 1.19) | 3.36 (± 1.21) | 3.40 (± 1.20) | |
| DAS28-4 (ESR) Month 60 (N=408,908,1316) | 3.51 (± 1.27) | 3.34 (± 1.20) | 3.39 (± 1.22) | |

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|--|---------------|---------------|---------------|
| DAS28-4 (ESR) Month 63 (N=388,825,1213) | 3.51 (± 1.15) | 3.30 (± 1.16) | 3.37 (± 1.16) |
| DAS28-4 (ESR) Month 66 (N=379,700,1079) | 3.58 (± 1.12) | 3.34 (± 1.17) | 3.42 (± 1.15) |
| DAS28-4 (ESR) Month 69 (N=355,483,838) | 3.51 (± 1.18) | 3.35 (± 1.20) | 3.41 (± 1.19) |
| DAS28-4 (ESR) Month 72 (N=338,284,622) | 3.45 (± 1.20) | 3.42 (± 1.19) | 3.44 (± 1.20) |
| DAS28-4 (ESR) Month 75 (N=299,169,468) | 3.43 (± 1.11) | 3.41 (± 1.14) | 3.43 (± 1.12) |
| DAS28-4 (ESR) Month 78 (N=291,91,382) | 3.44 (± 1.14) | 3.32 (± 1.20) | 3.41 (± 1.16) |
| DAS28-4 (ESR) Month 81 (N=284,54,338) | 3.40 (± 1.11) | 3.56 (± 1.24) | 3.42 (± 1.13) |
| DAS28-4 (ESR) Month 84 (N=271,44,315) | 3.32 (± 1.13) | 3.42 (± 1.37) | 3.34 (± 1.16) |
| DAS28-4 (ESR) Month 87 (N=263,41,304) | 3.33 (± 1.13) | 3.19 (± 1.15) | 3.31 (± 1.13) |
| DAS28-4 (ESR) Month 90 (N=237,39,276) | 3.34 (± 1.14) | 3.28 (± 1.10) | 3.33 (± 1.13) |
| DAS28-4 (ESR) Month 93 (N=191,28,219) | 3.33 (± 1.14) | 3.23 (± 1.12) | 3.32 (± 1.13) |
| DAS28-4 (ESR) Month 96 (N=142,16,158) | 3.30 (± 1.12) | 3.48 (± 1.06) | 3.32 (± 1.11) |
| DAS28-4 (ESR) Month 99 (N=65,11,76) | 3.26 (± 1.07) | 3.04 (± 1.24) | 3.23 (± 1.09) |
| DAS28-4 (ESR) Month 102 (N=22,4,26) | 3.34 (± 1.47) | 3.10 (± 1.76) | 3.30 (± 1.48) |
| DAS28-4 (ESR) Month 105 (N=14,3,17) | 3.64 (± 1.52) | 2.65 (± 0.97) | 3.46 (± 1.46) |
| DAS28-4 (ESR) Month 108 (N=8,1,9) | 3.36 (± 1.76) | 4.65 (± 0) | 3.51 (± 1.70) |
| DAS28-4 (ESR) Month 111 (N=3,1,4) | 2.03 (± 0.69) | 3.59 (± 0) | 2.42 (± 0.96) |
| DAS28-4 (ESR) Month 114 (N=1,0,1) | 1.28 (± 0) | 0 (± 0) | 1.28 (± 0) |
| DAS28-3 (CRP) Baseline (N=1112,3340,4452) | 5.31 (± 0.95) | 5.34 (± 0.98) | 5.33 (± 0.97) |
| DAS28-3 (CRP) Month 1 (N=1096,3234,4330) | 3.10 (± 1.19) | 2.96 (± 1.22) | 2.99 (± 1.21) |
| DAS28-3 (CRP) Month 2 (N=1070,3180,4250) | 3.01 (± 1.15) | 2.87 (± 1.17) | 2.90 (± 1.17) |
| DAS28-3 (CRP) Month 3 (N=1057,3190,4247) | 2.98 (± 1.15) | 2.81 (± 1.15) | 2.85 (± 1.15) |
| DAS28-3 (CRP) Month 6 (N=1026,3106,4132) | 2.89 (± 1.16) | 2.79 (± 1.15) | 2.81 (± 1.16) |
| DAS28-3 (CRP) Month 9 (N=993,3008,4001) | 2.82 (± 1.12) | 2.74 (± 1.16) | 2.76 (± 1.15) |
| DAS28-3 (CRP) Month 12 (N=962,2874,3836) | 2.81 (± 1.11) | 2.72 (± 1.13) | 2.74 (± 1.13) |
| DAS28-3 (CRP) Month 15 (N=923,2761,3684) | 2.73 (± 1.10) | 2.69 (± 1.13) | 2.70 (± 1.12) |
| DAS28-3 (CRP) Month 18 (N=899,2654,3553) | 2.72 (± 1.11) | 2.66 (± 1.11) | 2.68 (± 1.11) |
| DAS28-3 (CRP) Month 21 (N=856,2556,3412) | 2.75 (± 1.12) | 2.62 (± 1.09) | 2.65 (± 1.09) |
| DAS28-3 (CRP) Month 24 (N=813,2456,3269) | 2.96 (± 1.07) | 2.63 (± 1.11) | 2.64 (± 1.10) |
| DAS28-3 (CRP) Month 27 (N=793,2345,3138) | 2.66 (± 1.06) | 2.60 (± 1.09) | 2.62 (± 1.08) |
| DAS28-3 (CRP) Month 30 (N=766,2271,3037) | 2.65 (± 1.07) | 2.59 (± 1.09) | 2.60 (± 1.08) |
| DAS28-3 (CRP) Month 33 (N=745,2209,2954) | 2.64 (± 1.06) | 2.58 (± 1.10) | 2.60 (± 1.09) |
| DAS28-3 (CRP) Month 36 (N=724,2142,2866) | 2.64 (± 1.07) | 2.59 (± 1.08) | 2.60 (± 1.08) |

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|---|---------------|---------------|---------------|--|
| DAS28-3 (CRP) Month 39 (N=686,2057,2743) | 2.65 (± 1.10) | 2.57 (± 1.07) | 2.59 (± 1.08) | |
| DAS28-3 (CRP) Month 42 (N=653,1893,2546) | 2.63 (± 1.09) | 2.57 (± 1.09) | 2.59 (± 1.09) | |
| DAS28-3 (CRP) Month 45 (N=611,1644,2255) | 2.57 (± 1.04) | 2.53 (± 1.03) | 2.54 (± 1.03) | |
| DAS28-3 (CRP) Month 48 (N=579,1469,2048) | 2.59 (± 1.03) | 2.54 (± 1.05) | 2.56 (± 1.04) | |
| DAS28-3 (CRP) Month 51 (N=487,1348,1835) | 2.59 (± 0.99) | 2.57 (± 1.07) | 2.57 (± 1.05) | |
| DAS28-3 (CRP) Month 54 (N=468,1198,1666) | 2.68 (± 1.07) | 2.56 (± 1.05) | 2.59 (± 1.06) | |
| DAS28-3 (CRP) Month 57 (N=439,1011,1450) | 2.63 (± 1.03) | 2.54 (± 1.04) | 2.56 (± 1.03) | |
| DAS28-3 (CRP) Month 60 (N=407,913,1320) | 2.66 (± 1.09) | 2.53 (± 1.03) | 2.57 (± 1.05) | |
| DAS28-3 (CRP) Month 63 (N=390,824,1214) | 2.67 (± 1.01) | 2.51 (± 0.98) | 2.56 (± 0.99) | |
| DAS28-3 (CRP) Month 66 (N=376,702,1078) | 2.70 (± 1.02) | 2.53 (± 1.01) | 2.59 (± 1.02) | |
| DAS28-3 (CRP) Month 69 (N=355,483,838) | 2.67 (± 1.06) | 2.55 (± 1.00) | 2.60 (± 1.03) | |
| DAS28-3 (CRP) Month 72 (N=337,285,622) | 2.65 (± 1.04) | 2.64 (± 1.03) | 2.64 (± 1.04) | |
| DAS28-3 (CRP) Month 75 (N=304,170,474) | 2.63 (± 1.05) | 2.59 (± 1.02) | 2.61 (± 1.04) | |
| DAS28-3 (CRP) Month 78 (N=292,91,383) | 2.59 (± 1.02) | 2.68 (± 1.01) | 2.61 (± 1.02) | |
| DAS28-3 (CRP) Month 81 (N=285,54,339) | 2.54 (± 0.96) | 2.82 (± 1.13) | 2.59 (± 0.99) | |
| DAS28-3 (CRP) Month 84 (N=269,44,313) | 2.49 (± 0.94) | 2.84 (± 1.20) | 2.54 (± 0.99) | |
| DAS28-3 (CRP) Month 87 (N=264,41,305) | 2.52 (± 0.97) | 2.56 (± 0.91) | 2.52 (± 0.96) | |
| DAS28-3 (CRP) Month 90 (N=240,39,279) | 2.55 (± 1.00) | 2.58 (± 0.95) | 2.55 (± 0.99) | |
| DAS28-3 (CRP) Month 93 (N=196,28,224) | 2.59 (± 1.00) | 2.59 (± 0.85) | 2.59 (± 0.98) | |
| DAS28-3 (CRP) Month 96 (N=144,16,160) | 2.59 (± 0.93) | 2.68 (± 0.80) | 2.60 (± 0.92) | |
| DAS28-3 (CRP) Month 99 (N=64,11,75) | 2.58 (± 0.89) | 2.49 (± 1.12) | 2.57 (± 0.92) | |
| DAS28-3 (CRP) Month 102 (N=13,3,16) | 2.66 (± 0.78) | 2.29 (± 1.01) | 2.59 (± 0.81) | |
| DAS28-3 (CRP) Month 105 (N=12,2,14) | 3.31 (± 1.23) | 1.76 (± 0.34) | 3.09 (± 1.26) | |
| DAS28-3 (CRP) Month 108 (N=7,1,8) | 3.46 (± 1.59) | 3.70 (± 0) | 3.49 (± 1.47) | |
| DAS28-3 (CRP) Month 111 (N=3,1,4) | 1.82 (± 0.50) | 2.49 (± 0) | 1.98 (± 0.53) | |
| DAS28-3 (CRP) Month 114 (N=1,0,1) | 2.67 (± 0) | 0 (± 0) | 2.67 (± 0) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Extension Period: Change From Baseline in Disease Activity Score (DAS) 28-3 C-reactive Protein [CRP](DAS28-3 CRP) and DAS28-4 Erythrocyte Sedimentation Rate (ESR)(DAS28-4 ESR) at Month 3, 6, 9 and 12

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|-----------------|---|
| End point title | Extension Period: Change From Baseline in Disease Activity Score (DAS) 28-3 C-reactive Protein [CRP](DAS28-3 CRP) and DAS28-4 Erythrocyte Sedimentation Rate (ESR)(DAS28-4 ESR) |
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End point description:

DAS28 is composite score, derived from: 1) tender/painful joints count, out of 28 joints (TJC28), 2) swollen joints count, out of 28 joints (SJC28), 3) blood marker of inflammation (ESR [millimeter per hour] or CRP [milligram per liter]). DAS28-4 also include score of general health (GH). GH is general health or subjects' global assessment of disease activity on 100 mm VAS (score: 0 mm=very well to 100 mm=extremely bad, higher scores=worse health condition). $DAS28-3(CRP) = (0.56 * \sqrt{TJC28} + 0.28 * \sqrt{SJC28} + 0.36 * \ln[CRP+1]) * 1.10 + 1.15$ and $DAS28-4(ESR) = (0.56 * \sqrt{TJC28} + 0.28 * \sqrt{SJC28} + 0.70 * \ln[ESR] + 0.014 * GH)$, where sqrt=square root, ln=natural logarithm. DAS28-4 ESR and DAS28-3 CRP:score range is 0 (none) to 9.4 (extreme disease activity), higher score = more disease activity. Score of ≤ 3.2 : low disease activity; score of < 2.6 : disease remission. FAS. "n"=subjects evaluable for specified categories. 99999=standard deviation not estimable as 1 subject

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| End point type | Secondary |
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End point timeframe:

Baseline (Month 0 at the entry of Initial period); Month 3, 6, 9 and 12 of Extension Period

| End point values | Extension Period: Tofacitinib 5 mg | | | |
|--|---------------------------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 48 | | | |
| Units: units on score | | | | |
| arithmetic mean (standard deviation) | | | | |
| DAS28-4 (ESR) Baseline (n =47) | 5.68 (± 1.26) | | | |
| DAS28-4 (ESR): Change at Month 3 (n =43) | -2.82 (± 1.52) | | | |
| DAS28-4 (ESR): Change at Month 6 (n =34) | -3.02 (± 1.50) | | | |
| DAS28-4 (ESR): Change at Month 9 (n =15) | -3.13 (± 1.66) | | | |
| DAS28-4 (ESR): Change at Month 12 (n =2) | -2.55 (± 3.70) | | | |
| DAS28-3 (CRP): Baseline (n =48) | 4.67 (± 1.24) | | | |
| DAS28-3 (CRP): Change at Month 3 (n =42) | -2.36 (± 1.25) | | | |
| DAS28-3 (CRP): Change at Month 6 (n =34) | -2.49 (± 1.30) | | | |
| DAS28-3 (CRP): Change at Month 9 (n =15) | -3.04 (± 1.49) | | | |
| DAS28-3 (CRP): Change at Month 12 (n =1) | 0.29 (± 99999) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Initial Period: Number (%) of participants with DAS28-4 (ESR) and DAS28-3 (CRP) < 2.6 and ≤ 3.2

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| End point title | Initial Period: Number (%) of participants with DAS28-4 (ESR) and DAS28-3 (CRP) < 2.6 and ≤ 3.2 |
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End point description:

Percent participants with DAS28-4 (ESR) < 2.6 and ≤ 3.2 and percent participants with DAS28-3 (CRP)

<2.6 and ≤3.2. The stated number of participants analyzed was the total number of participants in each group. The actual number of participants analyzed on each occasion varied, and is provided for each visit presented.

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| End point type | Secondary |
| End point timeframe: | |
| Every visit until last observation | |

| End point values | Initial Period: Tofacitinib 5 milligram(mg) twice daily (BID) | Initial Period: Tofacitinib 10 mg BID | All Tofacitinib | |
|---|---|---|----------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 1123 | 3358 | 4481 | |
| Units: Percent of participants | | | | |
| number (not applicable) | | | | |
| DAS28-4 (ESR) <2.6 Baseline (N=1002,3296,4298) | 0.2 | 0.3 | 0.3 | |
| DAS28-4 (ESR) <2.6 Month 1 (N=1036,3254,4290) | 19.9 | 20.4 | 20.3 | |
| DAS28-4 (ESR) <2.6 Month 2 (N=1026,3222,4248) | 20.5 | 22.5 | 22.0 | |
| DAS28-4 (ESR) <2.6 Month 3 (N=1033,3203,4236) | 20.0 | 22.9 | 22.2 | |
| DAS28-4 (ESR) <2.6 Month 6 (N=1015,3110,4125) | 22.9 | 23.4 | 23.3 | |
| DAS28-4 (ESR) <2.6 Month 9 (N=992,3003,3995) | 24.4 | 25.1 | 24.9 | |
| DAS28-4 (ESR) <2.6 Month 12 (N=967,2862,3829) | 22.3 | 24.4 | 23.9 | |
| DAS28-4 (ESR) <2.6 Month 15 (N=922,2759,3681) | 23.8 | 25.7 | 25.2 | |
| DAS28-4 (ESR) <2.6 Month 18 (N=899,2655,3554) | 25.3 | 26.9 | 26.4 | |
| DAS28-4 (ESR) <2.6 Month 21 (N=850,2547,3397) | 22.2 | 27.1 | 25.9 | |
| DAS28-4 (ESR) <2.6 Month 24 (N=818,2441,3259) | 22.7 | 26.8 | 25.8 | |
| DAS28-4 (ESR) <2.6 Month 27 (N=787,2343,3130) | 22.6 | 27.9 | 26.5 | |
| DAS28-4 (ESR) <2.6 Month 30 (N=764,2257,3021) | 24.6 | 27.7 | 26.9 | |
| DAS28-4 (ESR) <2.6 Month 33 (N=746,2199,2945) | 23.7 | 28.3 | 27.1 | |
| DAS28-4 (ESR) <2.6 Month 36 (N=720,2141,2861) | 25.6 | 28.9 | 28.1 | |
| DAS28-4 (ESR) <2.6 Month 39 (N=679,2056,2735) | 23.9 | 28.4 | 27.3 | |
| DAS28-4 (ESR) <2.6 Month 42 (N=642,1890,2532) | 24.3 | 27.9 | 27.0 | |
| DAS28-4 (ESR) <2.6 Month 45 (N=609,1641,2250) | 24.1 | 27.5 | 26.6 | |
| DAS28-4 (ESR) <2.6 Month 48 (N=570,1471,2041) | 23.5 | 28.0 | 26.8 | |
| DAS28-4 (ESR) <2.6 Month 51 (N=481,1344,1825) | 28.3 | 27.3 | 27.6 | |

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| DAS28-4 (ESR) <2.6 Month 54 (N=467,1194,1661) | 21.4 | 28.3 | 26.4 |
| DAS28-4 (ESR) <2.6 Month 57 (N=438,1006,1444) | 23.1 | 28.0 | 26.5 |
| DAS28-4 (ESR) <2.6 Month 60 (N=408,908,1316) | 24.0 | 28.6 | 27.2 |
| DAS28-4 (ESR) <2.6 Month 63 (N=388,825,1213) | 22.4 | 29.5 | 27.2 |
| DAS28-4 (ESR) <2.6 Month 66 (N=379,700,1079) | 19.5 | 26.9 | 24.3 |
| DAS28-4 (ESR) <2.6 Month 69 (N=355,483,838) | 23.9 | 26.3 | 25.3 |
| DAS28-4 (ESR) <2.6 Month 72 (N=338,284,622) | 25.7 | 25.0 | 25.4 |
| DAS28-4 (ESR) <2.6 Month 75 (N=299,169,468) | 23.7 | 26.0 | 24.6 |
| DAS28-4 (ESR) <2.6 Month 78 (N=291,91,382) | 24.7 | 33.0 | 26.7 |
| DAS28-4 (ESR) <2.6 Month 81 (N=284,54,338) | 24.6 | 22.2 | 24.3 |
| DAS28-4 (ESR) <2.6 Month 84 (N=271,44,315) | 27.3 | 27.3 | 27.3 |
| DAS28-4 (ESR) <2.6 Month 87 (N=263,41,304) | 31.2 | 31.7 | 31.3 |
| DAS28-4 (ESR) <2.6 Month 90 (N=237,39,276) | 28.7 | 25.6 | 28.3 |
| DAS28-4 (ESR) <2.6 Month 93 (N=191,28,219) | 28.3 | 28.6 | 28.3 |
| DAS28-4 (ESR) <2.6 Month 96 (N=142,16,158) | 25.4 | 18.8 | 24.7 |
| DAS28-4 (ESR) <2.6 Month 99 (N=65,11,76) | 27.7 | 36.4 | 28.9 |
| DAS28-4 (ESR) <2.6 Month 102 (N=22,4,26) | 31.8 | 50.0 | 34.6 |
| DAS28-4 (ESR) <2.6 Month 105 (N=14,3,17) | 28.6 | 33.3 | 29.4 |
| DAS28-4 (ESR) <2.6 Month 108 (N=8,1,9) | 25.0 | 0 | 22.2 |
| DAS28-4 (ESR) <=3.2 Baseline (N=1002,3296,4298) | 0.4 | 0.7 | 0.6 |
| DAS28-4 (ESR) <=3.2 Month 1 (N=1036,3254,4290) | 34.2 | 37.6 | 36.8 |
| DAS28-4 (ESR) <=3.2 Month 2 (N=1026,3222,4248) | 36.7 | 40.5 | 39.6 |
| DAS28-4 (ESR) <=3.2 Month 3 (N=1033,3203,4236) | 36.6 | 41.6 | 40.4 |
| DAS28-4 (ESR) <=3.2 Month 6 (N=1015,3110,4125) | 39.8 | 42.5 | 41.9 |
| DAS28-4 (ESR) <=3.2 Month 9 (N=992,3003,3995) | 41.3 | 43.8 | 43.2 |
| DAS28-4 (ESR) <=3.2 Month 12 (N=967,2862,3829) | 42.1 | 42.5 | 42.4 |
| DAS28-4 (ESR) <=3.2 Month 18 (N=899,2655,3554) | 42.7 | 45.0 | 44.4 |
| DAS28-4 (ESR) <=3.2 Month 21 (N=850,2547,3397) | 41.9 | 47.2 | 45.9 |
| DAS28-4 (ESR) <=3.2 Month 24 (N=818,2441,3259) | 42.5 | 46.5 | 45.5 |
| DAS28-4 (ESR) <=3.2 Month 27 (N=787,2343,3130) | 44.9 | 46.9 | 46.4 |
| DAS28-4 (ESR) <=3.2 Month 30 (N=764,2257,3021) | 42.8 | 47.4 | 46.2 |

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|--|------|------|------|--|
| DAS28-4 (ESR) \leq 3.2 Month 33 (N=746,2199,2945) | 42.8 | 47.5 | 46.3 | |
| DAS28-4 (ESR) \leq 3.2 Month 36 (N=720,2141,2861) | 44.6 | 48.4 | 47.5 | |
| DAS28-4 (ESR) \leq 3.2 Month 39 (N=679,2056,2735) | 42.6 | 48.3 | 46.9 | |
| DAS28-4 (ESR) \leq 3.2 Month 42 (N=642,1890,2532) | 45.8 | 49.2 | 48.3 | |
| DAS28-4 (ESR) \leq 3.2 Month 45 (N=609,1641,2250) | 45.3 | 48.4 | 47.6 | |
| DAS28-4 (ESR) \leq 3.2 Month 48 (N=570,1471,2041) | 46.1 | 49.4 | 48.5 | |
| DAS28-4 (ESR) \leq 3.2 Month 51 (N=481,1344,1825) | 44.9 | 49.0 | 47.9 | |
| DAS28-4 (ESR) \leq 3.2 Month 54 (N=467,1194,1661) | 43.7 | 49.4 | 47.8 | |
| DAS28-4 (ESR) \leq 3.2 Month 57 (N=438,1006,1444) | 45.2 | 50.3 | 48.8 | |
| DAS28-4 (ESR) \leq 3.2 Month 60 (N=408,908,1316) | 46.3 | 49.9 | 48.8 | |
| DAS28-4 (ESR) \leq 3.2 Month 63 (N=388,825,1213) | 41.0 | 49.9 | 47.1 | |
| DAS28-4 (ESR) \leq 3.2 Month 66 (N=379,700,1079) | 38.8 | 49.7 | 45.9 | |
| DAS28-4 (ESR) \leq 3.2 Month 69 (N=355,483,838) | 45.6 | 50.3 | 48.3 | |
| DAS28-4 (ESR) \leq 3.2 Month 72 (N=338,284,622) | 44.7 | 48.2 | 46.3 | |
| DAS28-4 (ESR) \leq 3.2 Month 75 (N=299,169,458) | 43.1 | 48.5 | 45.1 | |
| DAS28-4 (ESR) \leq 3.2 Month 78 (N=291,91,382) | 44.7 | 45.1 | 44.8 | |
| DAS28-4 (ESR) \leq 3.2 Month 81 (N=284,54,338) | 49.3 | 48.1 | 49.1 | |
| DAS28-4 (ESR) \leq 3.2 Month 84 (N=271,44,315) | 47.2 | 45.5 | 47.0 | |
| DAS28-4 (ESR) \leq 3.2 Month 87 (N=263,41,304) | 47.9 | 46.3 | 47.7 | |
| DAS28-4 (ESR) \leq 3.2 Month 90 (N=237,39,276) | 46.0 | 46.2 | 46.0 | |
| DAS28-4 (ESR) \leq 3.2 Month 93 (N=191,28,219) | 48.2 | 50.0 | 48.4 | |
| DAS28-4 (ESR) \leq 3.2 Month 96 (N=142,16,158) | 47.2 | 43.8 | 46.8 | |
| DAS28-4 (ESR) \leq 3.2 Month 99 (N=142,16,158) | 43.1 | 54.5 | 44.7 | |
| DAS28-4 (ESR) \leq 3.2 Month 102 (N=22,4,26) | 45.5 | 50.0 | 46.2 | |
| DAS28-4 (ESR) \leq 3.2 Month 105 (N=14,3,17) | 42.9 | 66.7 | 47.1 | |
| DAS28-4 (ESR) \leq 3.2 Month 108 (N=8,1,9) | 50.0 | 0 | 44.4 | |
| DAS28-3 (CRP) $<$ 2.6 Baseline 1 (N=1112,3340,4452) | 0.5 | 0.9 | 0.8 | |
| DAS28-3 (CRP) $<$ 2.6 Month 1 (N=1096,3234,4330) | 38.0 | 43.0 | 41.7 | |
| DAS28-3 (CRP) $<$ 2.6 Month 2 (N=1070,3180,4250) | 39.7 | 47.1 | 45.2 | |
| DAS28-3 (CRP) $<$ 2.6 Month 3 (N=1057,3190,4247) | 42.3 | 47.5 | 46.2 | |
| DAS28-3 (CRP) $<$ 2.6 Month 6 (N=1026,3106,4132) | 45.2 | 49.0 | 48.1 | |

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|--|------|------|------|--|
| DAS28-3 (CRP) <2.6 Month 9 (N=993,3008,4001) | 47.1 | 50.7 | 49.8 | |
| DAS28-3 (CRP) <2.6 Month 12 (N=962,2874,3836) | 47.8 | 51.8 | 50.8 | |
| DAS28-3 (CRP) <2.6 Month 15 (N=923,2761,3684) | 50.6 | 52.3 | 51.9 | |
| DAS28-3 (CRP) <2.6 Month 18 (N=899,2654,3553) | 51.3 | 54.1 | 53.4 | |
| DAS28-3 (CRP) <2.6 Month 21 (N=856,2556,3412) | 51.1 | 55.5 | 54.4 | |
| DAS28-3 (CRP) <2.6 Month 24 (N=813,2456,3269) | 51.9 | 55.3 | 54.4 | |
| DAS28-3 (CRP) <2.6 Month 27 (N=793,2345,3138) | 53.2 | 55.8 | 55.2 | |
| DAS28-3 (CRP) <2.6 Month 30 (N=766,2271,3037) | 53.3 | 56.8 | 55.9 | |
| DAS28-3 (CRP) <2.6 Month 33 (N=745,2209,2954) | 54.1 | 56.0 | 55.6 | |
| DAS28-3 (CRP) <2.6 Month 36 (N=724,2142,2866) | 52.9 | 55.6 | 54.9 | |
| DAS28-3 (CRP) <2.6 Month 39 (N=686,2057,2743) | 54.2 | 56.9 | 56.2 | |
| DAS28-3 (CRP) <2.6 Month 42 (N=653,1893,2546) | 54.2 | 56.8 | 56.2 | |
| DAS28-3 (CRP) <2.6 Month 45 (N=611,1644,2255) | 56.3 | 58.6 | 58.0 | |
| DAS28-3 (CRP) <2.6 Month 48 (N=579,1469,2048) | 55.4 | 59.3 | 58.2 | |
| DAS28-3 (CRP) <2.6 Month 51 (N=487,1348,1835) | 56.1 | 57.3 | 56.9 | |
| DAS28-3 (CRP) <2.6 Month 54 (N=468,1198,1666) | 52.6 | 57.8 | 56.3 | |
| DAS28-3 (CRP) <2.6 Month 57 (N=439,1011,1450) | 55.6 | 57.7 | 57.0 | |
| DAS28-3 (CRP) <2.6 Month 60 (N=407,913,1320) | 55.0 | 57.9 | 57.0 | |
| DAS28-3 (CRP) <2.6 Month 63 (N=390,824,1214) | 51.0 | 58.1 | 55.8 | |
| DAS28-3 (CRP) <2.6 Month 66 (N=376,702,1078) | 51.9 | 59.3 | 56.7 | |
| DAS28-3 (CRP) <2.6 Month 69 (N=355,483,838) | 53.5 | 57.8 | 56.0 | |
| DAS28-3 (CRP) <2.6 Month 72 (N=337,285,622) | 52.2 | 55.4 | 53.7 | |
| DAS28-3 (CRP) <2.6 Month 75 (N=304,170,474) | 53.9 | 53.5 | 53.8 | |
| DAS28-3 (CRP) <2.6 Month 78 (N=292,91,383) | 58.2 | 51.6 | 56.7 | |
| DAS28-3 (CRP) <2.6 Month 81 (N=285,54,339) | 58.6 | 51.9 | 57.5 | |
| DAS28-3 (CRP) <2.6 Month 84 (N=269,44,313) | 61.7 | 43.2 | 59.1 | |
| DAS28-3 (CRP) <2.6 Month 87 (N=264,41,305) | 60.2 | 48.8 | 58.7 | |
| DAS28-3 (CRP) <2.6 Month 90 (N=240,39,279) | 60.8 | 46.2 | 58.8 | |
| DAS28-3 (CRP) <2.6 Month 93 (N=196,28,224) | 56.1 | 53.6 | 55.8 | |
| DAS28-3 (CRP) <2.6 Month 96 (N=144,16,160) | 56.3 | 37.5 | 54.4 | |
| DAS28-3 (CRP) <2.6 Month 99 (N=64,11,75) | 50.0 | 63.6 | 52.0 | |

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| DAS28-3 (CRP) <2.6 Month 102 (N=13,3,16) | 46.2 | 66.7 | 50.0 |
| DAS28-3 (CRP) <2.6 Month 105 (N=12,2,14) | 33.3 | 100 | 42.9 |
| DAS28-3 (CRP) <2.6 Month 108 (N=7,1,8) | 42.9 | 0 | 37.5 |
| DAS28-3 (CRP) <2.6 Month 111 (N=3,1,4) | 100 | 100 | 100 |
| DAS28-3 (CRP) <=3.2 Month 1 (N=1096,3234,4330) | 55.3 | 61.9 | 60.2 |
| DAS28-3 (CRP) <=3.2 Month 2 (N=1070,3180,4250) | 60.7 | 64.5 | 63.6 |
| DAS28-3 (CRP) <=3.2 Month 3 (N=1057,3190,4247) | 60.6 | 66.3 | 64.9 |
| DAS28-3 (CRP) <=3.2 Month 6 (N=1026,3106,4132) | 64.4 | 67.1 | 66.4 |
| DAS28-3 (CRP) <=3.2 Month 9 (N=993,3008,4001) | 66.4 | 68.3 | 67.8 |
| DAS28-3 (CRP) <=3.2 Month 12 (N=962,2874,3836) | 66.1 | 70.0 | 69.0 |
| DAS28-3 (CRP) <=3.2 Month 15 (N=923,2761,3684) | 70.0 | 70.0 | 70.0 |
| DAS28-3 (CRP) <=3.2 Month 18 (N=899,2654,3553) | 69.2 | 71.7 | 71.1 |
| DAS28-3 (CRP) <=3.2 Month 21 (N=856,2556,3412) | 69.5 | 72.5 | 71.8 |
| DAS28-3 (CRP) <=3.2 Month 24 (N=813,2456,3269) | 71.7 | 72.5 | 72.3 |
| DAS28-3 (CRP) <=3.2 Month 27 (N=793,2345,3138) | 72.6 | 73.0 | 72.9 |
| DAS28-3 (CRP) <=3.2 Month 30 (N=766,2271,3037) | 73.0 | 73.8 | 73.6 |
| DAS28-3 (CRP) <=3.2 Month 33 (N=745,2209,2954) | 72.2 | 74.5 | 73.9 |
| DAS28-3 (CRP) <=3.2 Month 36 (N=724,2142,2866) | 73.8 | 73.4 | 73.5 |
| DAS28-3 (CRP) <=3.2 Month 39 (N=686,2057,2743) | 73.2 | 74.6 | 74.2 |
| DAS28-3 (CRP) <=3.2 Month 42 (N=653,1893,2546) | 73.8 | 74.7 | 74.5 |
| DAS28-3 (CRP) <=3.2 Month 45 (N=611,1644,2255) | 74.6 | 75.2 | 75.1 |
| DAS28-3 (CRP) <=3.2 Month 48 (N=579,1469,2048) | 74.6 | 75.0 | 74.9 |
| DAS28-3 (CRP) <=3.2 Month 51 (N=487,1348,1835) | 74.3 | 75.1 | 74.9 |
| DAS28-3 (CRP) <=3.2 Month 54 (N=468,1198,1666) | 71.4 | 76.4 | 75.0 |
| DAS28-3 (CRP) <=3.2 Month 57 (N=439,1011,1450) | 73.6 | 75.2 | 74.7 |
| DAS28-3 (CRP) <=3.2 Month 60 (N=407,913,1320) | 72.5 | 77.0 | 75.6 |
| DAS28-3 (CRP) <=3.2 Month 63 (N=390,824,1214) | 72.8 | 76.5 | 75.3 |
| DAS28-3 (CRP) <=3.2 Month 66 (N=376,702,1078) | 71.5 | 78.1 | 75.8 |
| DAS28-3 (CRP) <=3.2 Month 69 (N=355,483,838) | 69.9 | 77.0 | 74.0 |
| DAS28-3 (CRP) <=3.2 Month 72 (N=337,285,622) | 74.8 | 73.3 | 74.1 |
| DAS28-3 (CRP) <=3.2 Month 75 (N=304,170,474) | 77.0 | 72.9 | 75.5 |

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|---|------|------|------|--|
| DAS28-3 (CRP) \leq 3.2 Month 78 (N=292,91,383) | 74.3 | 70.3 | 73.4 | |
| DAS28-3 (CRP) \leq 3.2 Month 81 (N=285,54,339) | 75.8 | 68.5 | 74.6 | |
| DAS28-3 (CRP) \leq 3.2 Month 84 (N=269,44,313) | 79.2 | 68.2 | 77.6 | |
| DAS28-4 (CRP) \leq 3.2 Month 87 (N=264,41,305) | 81.1 | 70.7 | 79.7 | |
| DAS28-3 (CRP) \leq 3.2 Month 90 (N=240,39,279) | 77.1 | 74.4 | 76.7 | |
| DAS28-3 (CRP) \leq 3.2 Month 93 (N=196,28,224) | 75.0 | 67.9 | 74.1 | |
| DAS28-3 (CRP) \leq 3.2 Month 96 (N=144,16,160) | 77.1 | 87.5 | 78.1 | |
| DAS28-3 (CRP) \leq 3.2 Month 99 (N=64,11,75) | 76.6 | 81.8 | 77.3 | |
| DAS28-3 (CRP) \leq 3.2 Month 102 (N=13,3,16) | 84.6 | 66.7 | 81.3 | |
| DAS28-3 (CRP) \leq 3.2 Month 105 (N=12,2,14) | 50.0 | 100 | 57.1 | |
| DAS28-3 (CRP) \leq 3.2 Month 108 (N=7,1,8) | 42.9 | 0 | 37.5 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Extension Period: Percentage of Subjects With DAS28-4 (ESR) and DAS28-3 (CRP) Less Than ($<$) 2.6 and Less Than or (\leq) 3.2

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| End point title | Extension Period: Percentage of Subjects With DAS28-4 (ESR) and DAS28-3 (CRP) Less Than ($<$) 2.6 and Less Than or (\leq) 3.2 |
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End point description:

DAS28 is composite score, derived from: 1) tender/painful joints count, out of 28 joints (TJC28), 2) swollen joints count, out of 28 joints (SJC28), 3) blood marker of inflammation (ESR [millimeter per hour] or CRP [milligram per liter]). DAS28-4 also include score of GH. GH is general health or subjects' global assessment of disease activity on 100 mm VAS (score: 0 mm=very well to 100 mm=extremely bad, higher scores=worse health condition). $DAS28-3(CRP) = (0.56 * \sqrt{TJC28} + 0.28 * \sqrt{SJC28} + 0.36 * \ln[CRP+1]) * 1.10 + 1.15$ and $DAS28-4(ESR) = (0.56 * \sqrt{TJC28} + 0.28 * \sqrt{SJC28} + 0.70 * \ln[ESR] + 0.014 * GH)$, where $\sqrt{\text{ }}$ =square root, \ln =natural logarithm. DAS28-4 ESR and DAS28-3 CRP:score range is 0 (none) to 9.4 (extreme disease activity), higher score = more disease activity. Score of ≤ 3.2 : low disease activity; score of < 2.6 : disease remission. FAS analysis set. "n"=subjects evaluable for specified categories.

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

End point timeframe:

Baseline (Day 1 at the entry of Extension period); Month 3, 6, 9 and 12 of Extension Period

| | | | | |
|---------------------------------------|---|--|--|--|
| End point values | Extension Period: Tofacitinib 5 mg | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 48 | | | |
| Units: Percentage of subjects | | | | |
| number (not applicable) | | | | |
| DAS28-4 (ESR) <2.6: Baseline (n =48) | 12.5 | | | |
| DAS28-4 (ESR) <2.6: Month 3 (n =44) | 40.9 | | | |
| DAS28-4 (ESR) <2.6: Month 6 (n =35) | 45.7 | | | |
| DAS28-4 (ESR) <2.6: Month 9 (n =15) | 46.7 | | | |
| DAS28-4 (ESR) <2.6: Month 12 (n =2) | 50.0 | | | |
| DAS28-4 (ESR) <=3.2: Baseline (n =48) | 29.2 | | | |
| DAS28-4 (ESR) <=3.2: Month 3 (n =44) | 68.2 | | | |
| DAS28-4 (ESR) <=3.2: Month 6 (n =35) | 68.6 | | | |
| DAS28-4 (ESR) <=3.2: Month 9 (n =15) | 66.7 | | | |
| DAS28-4 (ESR) <=3.2: Month 12 (n =2) | 50.0 | | | |
| DAS28-3 (CRP) <2.6: Baseline (n =47) | 27.7 | | | |
| DAS28-3 (CRP) <2.6: Month 3 (n =42) | 61.9 | | | |
| DAS28-3 (CRP) <2.6: Month 6 (n =34) | 67.6 | | | |
| DAS28-3 (CRP) <2.6: Month 9 (n =15) | 80.0 | | | |
| DAS28-3 (CRP) <2.6: Month 12 (n =1) | 0.0 | | | |
| DAS28-3 (CRP) <=3.2: Baseline (n =47) | 53.2 | | | |
| DAS28-3 (CRP) <=3.2: Month 3 (n =42) | 85.7 | | | |
| DAS28-3 (CRP) <=3.2: Month 6 (n =34) | 85.3 | | | |
| DAS28-3 (CRP) <=3.2: Month 9 (n =15) | 80.0 | | | |
| DAS28-3 (CRP) <=3.2: Month 12 (n =1) | 0.0 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Initial Period: Health Assessment Questionnaire – Disability Index (HAQ-DI) Score

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|-----------------|---|
| End point title | Initial Period: Health Assessment Questionnaire – Disability Index (HAQ-DI) Score |
|-----------------|---|

End point description:

Change from baseline by visit. The stated number of participants analyzed was the total number of participants in each group. The actual number of participants analyzed on each occasion varied, and is provided for each visit presented.

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

End point timeframe:

Every visit until last observation

| End point values | Initial Period: Tofacitinib 5 milligram(mg) twice daily (BID) | Initial Period: Tofacitinib 10 mg BID | All Tofacitinib | |
|--------------------------------------|---|---|----------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 1123 | 1123 | 4481 | |
| Units: Score | | | | |
| arithmetic mean (standard deviation) | | | | |
| Month 1 (N=1098,3264,4362) | -0.57 (± 0.62) | -0.61 (± 0.63) | -0.60 (± 0.63) | |
| Month 2 (N=1067,3213,4280) | -0.58 (± 0.62) | -0.65 (± 0.65) | -0.63 (± 0.65) | |
| Month 3 (N=1057,3196,4253) | -0.58 (± 0.63) | -0.66 (± 0.65) | -0.64 (± 0.65) | |
| Month 6 (N=1029,3105,4134) | -0.58 (± 0.65) | -0.65 (± 0.66) | -0.64 (± 0.66) | |
| Month 9 (N=990,2992,3982) | -0.58 (± 0.64) | -0.66 (± 0.66) | -0.64 (± 0.66) | |
| Month 12 (N=960,2866,3826) | -0.58 (± 0.65) | -0.66 (± 0.67) | -0.64 (± 0.67) | |
| Month 15 (N=926,2756,3682) | -0.61 (± 0.65) | -0.68 (± 0.68) | -0.66 (± 0.67) | |
| Month 18 (N=898,2646,3544) | -0.60 (± 0.65) | -0.68 (± 0.67) | -0.66 (± 0.67) | |
| Month 21 (N=849,2542,3391) | -0.60 (± 0.67) | -0.69 (± 0.68) | -0.67 (± 0.68) | |
| Month 24 (N=815,2443,3258) | -0.60 (± 0.65) | -0.69 (± 0.68) | -0.67 (± 0.67) | |
| Month 27 (N=789,2341,3130) | -0.62 (± 0.65) | -0.69 (± 0.68) | -0.67 (± 0.67) | |
| Month 30 (N=757,2258,3015) | -0.58 (± 0.66) | -0.68 (± 0.69) | -0.66 (± 0.68) | |
| Month 33 (N=741,2194,2935) | -0.60 (± 0.66) | -0.67 (± 0.69) | -0.66 (± 0.68) | |
| Month 36 (N=720,2136,2856) | -0.63 (± 0.66) | -0.67 (± 0.68) | -0.66 (± 0.67) | |
| Month 39 (N=683,2053,2736) | -0.59 (± 0.67) | -0.68 (± 0.69) | -0.66 (± 0.69) | |
| Month 42 (N=649,1884,2533) | -0.59 (± 0.67) | -0.66 (± 0.68) | -0.65 (± 0.68) | |
| Month 45 (N=609,1636,2245) | -0.59 (± 0.69) | -0.64 (± 0.69) | -0.63 (± 0.69) | |
| Month 48 (N=575,1468,2043) | -0.58 (± 0.69) | -0.64 (± 0.68) | -0.62 (± 0.68) | |
| Month 51 (N=482,1332,1814) | -0.59 (± 0.67) | -0.63 (± 0.66) | -0.62 (± 0.67) | |
| Month 54 (N=463,1191,1654) | -0.57 (± 0.68) | -0.65 (± 0.67) | -0.63 (± 0.67) | |
| Month 57 (N=434,1011,1445) | -0.57 (± 0.69) | -0.66 (± 0.68) | -0.63 (± 0.68) | |
| Month 60 (N=405,916,1321) | -0.59 (± 0.68) | -0.66 (± 0.69) | -0.64 (± 0.69) | |
| Month 63 (N=392,828,1220) | -0.57 (± 0.68) | -0.68 (± 0.70) | -0.64 (± 0.69) | |
| Month 66 (N=375,702,1077) | -0.54 (± 0.70) | -0.67 (± 0.69) | -0.63 (± 0.70) | |
| Month 69 (N=353,484,837) | -0.55 (± 0.70) | -0.66 (± 0.71) | -0.61 (± 0.71) | |
| Month 72 (N=335,286,621) | -0.57 (± 0.71) | -0.62 (± 0.73) | -0.59 (± 0.72) | |
| Month 75 (N=303,171,474) | -0.57 (± 0.72) | -0.58 (± 0.73) | -0.57 (± 0.72) | |
| Month 78 (N=289,91,380) | -0.54 (± 0.73) | -0.61 (± 0.78) | -0.56 (± 0.74) | |
| Month 81 (N=282,54,336) | -0.55 (± 0.73) | -0.64 (± 0.68) | -0.56 (± 0.72) | |
| Month 84 (N=269,44,313) | -0.53 (± 0.73) | -0.56 (± 0.68) | -0.53 (± 0.72) | |
| Month 87 (N=262,41,303) | -0.53 (± 0.70) | -0.53 (± 0.60) | -0.53 (± 0.69) | |
| Month 90 (240,39,279) | -0.52 (± 0.72) | -0.54 (± 0.61) | -0.52 (± 0.70) | |
| Month 93 (194,28,222) | -0.52 (± 0.75) | -0.50 (± 0.60) | -0.52 (± 0.73) | |
| Month 96 (N=143,16,159) | -0.54 (± 0.77) | -0.48 (± 0.58) | -0.53 (± 0.75) | |
| Month 99 (N=64,11,75) | -0.53 (± 0.80) | -0.44 (± 0.51) | -0.52 (± 0.76) | |
| Month 102 (N=22,3,25) | -0.61 (± 0.82) | -0.29 (± 0.85) | -0.58 (± 0.81) | |
| Month 105 (N=15,3,18) | -0.65 (± 0.91) | -0.50 (± 0.99) | -0.63 (± 0.90) | |
| Month 108 (N=8,1,9) | -0.89 (± 0.97) | 0.13 (± 0) | -0.78 (± 0.97) | |
| Month 111 (N=3,1,4) | -1.29 (± 1.34) | 0.25 (± 0) | -0.91 (± 1.34) | |
| Month 114 (N=1,0,1) | -0.13 (± 0) | 0 (± 0) | -0.13 (± 0) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Extension Period: Change From Baseline in Health Assessment Questionnaire - Disability Index (HAQ-DI) Score at Month 3, 6, 9 and 12

| | |
|-----------------|---|
| End point title | Extension Period: Change From Baseline in Health Assessment Questionnaire - Disability Index (HAQ-DI) Score at Month 3, 6, 9 and 12 |
|-----------------|---|

End point description:

HAQ-DI assesses the degree of difficulty a subject has experienced during the past week in 8 categories of daily living activities: dressing/grooming; arising; eating; walking; reach; grip; hygiene and other activities. Each activity category consisted of 2-3 questionnaire. Each questionnaire was scored on a 4-point scale from 0 to 3: 0=no difficulty; 1=some difficulty; 2=much difficulty; 3=unable to do. Any activity that required the use of an assistive device was adjusted to a score of 2 to represent a more limited functional status. Overall score was the sum of total scores divided by the number of questionnaire answered. Total possible HAQ-DI score range: 0 and 3, where higher scores indicate more difficulty while performing daily living activities. Full analysis set included all subjects who enrolled for extension period and received at least 1 dose of open label study medication. Here, "n" signifies number of subjects who were evaluable at the specified time points.

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

End point timeframe:

Baseline (Month 0 at the entry of Initial Period); Month 3, 6, 9, and 12 of Extension Period

| End point values | Extension Period: Tofacitinib 5 mg | | | |
|--------------------------------------|---------------------------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 48 | | | |
| Units: units on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (n= 48) | 1.35 (± 0.63) | | | |
| Change at Month 3 (n= 46) | -0.48 (± 0.58) | | | |
| Change at Month 6 (n= 35) | -0.55 (± 0.65) | | | |
| Change at Month 9 (n= 15) | -0.58 (± 0.70) | | | |
| Change at Month 12 (n= 2) | -1.50 (± 1.94) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Initial Period: Short-Form-36 Health Survey (SF-36) score

| | |
|-----------------|---|
| End point title | Initial Period: Short-Form-36 Health Survey (SF-36) score |
|-----------------|---|

End point description:

Change from Baseline for Physical Component and Mental Component Scores by visit. The stated number of participants analyzed was the total number of participants in each group. The actual number of participants analyzed on each occasion varied, and is provided for each visit presented.

| | |
|------------------------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Every visit until last observation | |

| End point values | Initial Period: Tofacitinib 5 milligram(mg) twice daily (BID) | Initial Period: Tofacitinib 10 mg BID | All Tofacitinib | |
|--|---|---|----------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 1123 | 3358 | 4481 | |
| Units: Score | | | | |
| arithmetic mean (standard deviation) | | | | |
| Physical Component Month 3 (N=983,2693,3676) | 7.90 (± 8.70) | 8.85 (± 8.92) | 8.60 (± 8.87) | |
| Physical Component Month 6 (N=961,2629,3590) | 8.10 (± 8.94) | 9.02 (± 9.11) | 8.77 (± 9.07) | |
| Physical Component Month 9 (N=534,2499,3033) | 8.60 (± 9.07) | 8.80 (± 9.20) | 8.77 (± 9.18) | |
| Physical Component Month 12 (N=903,2449,3352) | 8.44 (± 8.53) | 8.78 (± 9.26) | 8.69 (± 9.07) | |
| Physical Component Month 15 (N=733,2324,3057) | 8.43 (± 8.88) | 8.98 (± 9.05) | 8.85 (± 9.01) | |
| Physical Component Month 18 (N=855,2188,3043) | 8.14 (± 8.89) | 8.99 (± 9.18) | 8.75 (± 9.11) | |
| Physical Component Month 21 (N=767,2005,2772) | 8.00 (± 8.70) | 8.85 (± 8.96) | 8.62 (± 8.90) | |
| Physical Component Month 24(N=797,2102,2899) | 8.28 (± 8.73) | 9.00 (± 9.30) | 8.80 (± 9.15) | |
| Physical Component Month 27(N=739,1663,2402) | 8.41 (± 8.84) | 8.64 (± 9.16) | 8.57 (± 9.06) | |
| Physical Component Month 30 (N=708,1566,2274) | 7.78 (± 8.81) | 8.56 (± 9.06) | 8.32 (± 8.99) | |
| Physical Component Month 33 (N=682,1444,2126) | 8.17 (± 8.87) | 8.39 (± 9.31) | 8.32 (± 9.17) | |
| Physical Component Month 36 (N=676,1530,2206) | 8.31 (± 8.97) | 8.43 (± 9.22) | 8.40 (± 9.14) | |
| Physical Component Month 39 (N=609,1176,1785) | 8.05 (± 9.26) | 8.13 (± 9.14) | 8.10 (± 9.18) | |
| Physical Component Month 42 (N=573,923,1496) | 7.81 (± 9.32) | 8.07 (± 9.13) | 7.97 (± 9.21) | |
| Physical Component Month 45 (N=540,652,1192) | 8.40 (± 9.87) | 8.33 (± 9.40) | 8.36 (± 9.61) | |
| Physical Component Month 48 (N=537,1044,1581) | 8.12 (± 9.56) | 8.27 (± 9.23) | 8.22 (± 9.34) | |
| Physical Component Month 51 (N=417,304,721) | 7.88 (± 9.69) | 8.55 (± 9.70) | 8.16 (± 9.69) | |
| Physical Component Month 54 (N=396,175,571) | 7.72 (± 9.41) | 8.82 (± 9.47) | 8.06 (± 9.43) | |
| Physical Component Month 57 (N=372,105,477) | 7.57 (± 9.72) | 8.12 (± 9.69) | 7.69 (± 9.71) | |
| Physical Component Month 60 (N=371,259,630) | 7.94 (± 9.74) | 9.29 (± 9.43) | 8.49 (± 9.63) | |

| | | | |
|--|-----------------|----------------|-----------------|
| Physical Component Month 63 (N=345,68,413) | 7.73 (± 9.76) | 7.90 (± 8.98) | 7.76 (± 9.63) |
| Physical Component Month 66 (N=327,56,383) | 7.92 (± 9.41) | 7.58 (± 7.88) | 7.87 (± 9.20) |
| Physical Component Month 69 (N=267,40,307) | 7.68 (± 9.32) | 9.12 (± 7.06) | 7.87 (± 9.06) |
| Physical Component Month 72 (N=316,54,370) | 7.90 (± 9.93) | 8.70 (± 10.24) | 8.02 (± 9.97) |
| Physical Component Month 75 (N=84,12,96) | 9.03 (± 10.96) | 5.75 (± 9.05) | 8.62 (± 10.75) |
| Physical Component Month 78 (N=55,7,62) | 10.22 (± 11.10) | 7.39 (± 7.09) | 9.90 (± 10.72) |
| Physical Component Month 81 (N=49,4,53) | 10.51 (± 10.17) | 7.90 (± 13.05) | 10.31 (± 10.28) |
| Physical Component Month 84 (N=93,11,104) | 8.93 (± 11.56) | 7.14 (± 8.01) | 8.74 (± 11.22) |
| Physical Component Month 87 (N=26,2,28) | 11.92 (± 10.49) | 15.23 (± 3.64) | 12.16 (± 10.15) |
| Physical Component Month 90 (N=12,1,13) | 13.50 (± 10.98) | 16.50 (± 0) | 13.73 (± 10.55) |
| Physical Component Month 93 (N=1,0,1) | 26.71 (± 0) | 0 (± 0) | 26.71 (± 0) |
| Physical Component Month 96 (N=5,0,5) | 4.61 (± 9.75) | 0 (± 0) | 4.61 (± 9.75) |
| Physical Component Month 99 (N=1,0,1) | -8.26 (± 0) | 0 (± 0) | -8.26 (± 0) |
| Mental Component Month 3 (N=983,2693,3676) | 4.37 (± 10.88) | 4.91 (± 11.18) | 4.77 (± 11.10) |
| Mental Component Month 6 (N=961,2629,3590) | 3.94 (± 10.85) | 4.81 (± 11.12) | 4.58 (± 11.06) |
| Mental Component Month 9 (N=534,2499,3033) | 4.65 (± 10.78) | 5.04 (± 11.17) | 4.97 (± 11.10) |
| Mental Component Month 12 (N=903,2449,3352) | 3.77 (± 11.03) | 4.81 (± 11.43) | 4.53 (± 11.33) |
| Mental Component Month 15 (N=733,2324,3057) | 4.14 (± 11.21) | 4.79 (± 11.52) | 4.63 (± 11.45) |
| Mental Component Month 18 (N=855,2188,3043) | 4.12 (± 11.11) | 4.87 (± 11.41) | 4.66 (± 11.33) |
| Mental Component Month 21 (N=767,2005,2772) | 4.21 (± 11.08) | 4.87 (± 11.22) | 4.68 (± 11.18) |
| Mental Component Month 24 (N=797,2102,2899) | 4.12 (± 11.06) | 5.08 (± 11.32) | 4.82 (± 11.26) |
| Mental Component Month 27 (N=739,1663,2402) | 3.67 (± 10.53) | 4.91 (± 11.28) | 4.53 (± 11.07) |
| Mental Component Month 30 (N=708,1566,2274) | 3.58 (± 11.14) | 4.68 (± 11.71) | 4.34 (± 11.54) |
| Mental Component Month 33 (N=682,1444,2126) | 3.91 (± 10.65) | 4.82 (± 11.74) | 4.53 (± 11.40) |
| Mental Component Month 36 (N=676,1530,2206) | 3.83 (± 10.94) | 4.81 (± 11.60) | 4.51 (± 11.40) |
| Mental Component Month 39 (N=609,1176,1785) | 3.60 (± 11.02) | 4.59 (± 11.75) | 4.25 (± 11.51) |
| Mental Component Month 42 (N=573,923,1496) | 3.23 (± 11.40) | 4.55 (± 11.63) | 4.04 (± 11.56) |
| Mental Component Month 45 (N=540,652,1192) | 3.16 (± 11.63) | 4.40 (± 11.64) | 3.83 (± 11.56) |
| Mental Component Month 48 (N=537,1044,1581) | 3.48 (± 11.71) | 4.73 (± 11.83) | 4.31 (± 11.80) |
| Mental Component Month 51 (N=417,304,721) | 3.61 (± 12.12) | 4.83 (± 11.82) | 4.13 (± 12.00) |
| Mental Component Month 54 (N=396,175,571) | 3.44 (± 11.77) | 6.49 (± 12.67) | 4.38 (± 12.12) |

| | | | |
|---|----------------|-----------------|----------------|
| Mental Component Month 57 (N=372,105,477) | 3.24 (± 12.24) | 5.10 (± 11.74) | 3.65 (± 12.15) |
| Mental Component Month 60 (N=371,259,630) | 3.05 (± 12.06) | 5.18 (± 12.22) | 3.93 (± 12.16) |
| Mental Component Month 63 (N=345,68,413) | 3.04 (± 11.61) | 4.22 (± 10.32) | 3.23 (± 11.40) |
| Mental Component Month 66 (N=327,56,383) | 2.96 (± 11.32) | 3.47 (± 8.33) | 3.04 (± 10.93) |
| Mental Component Month 69 (N=267,40,307) | 3.90 (± 12.35) | 4.90 (± 9.84) | 4.03 (± 12.04) |
| Mental Component Month 72 (N=316,54,370) | 3.78 (± 11.48) | 5.32 (± 12.80) | 4.00 (± 11.68) |
| Mental Component Month 75 (N=84,12,96) | 5.04 (± 12.22) | 1.52 (± 11.38) | 4.60 (± 12.12) |
| Mental Component Month 78 (N=55,7,62) | 4.12 (± 13.37) | 1.05 (± 13.28) | 3.77 (± 13.29) |
| Mental Component Month 81 (N=49,4,53) | 6.09 (± 10.40) | 2.60 (± 14.75) | 5.83 (± 10.64) |
| Mental Component Month 84 (N=93,11,104) | 5.73 (± 13.07) | -2.36 (± 11.63) | 4.87 (± 13.11) |
| Mental Component Month 87 (N=26,2,28) | 7.52 (± 13.03) | 16.93 (± 2.66) | 8.19 (± 12.79) |
| Mental Component Month 90 (N=12,1,13) | 4.61 (± 11.75) | 18.75 (± 0) | 5.65 (± 11.86) |
| Mental Component Month 93 (N=1,0,1) | 14.03 (± 0) | 0 (± 0) | 14.03 (± 0) |
| Mental Component Month 96 (N=5,0,5) | 7.58 (± 9.73) | 0 (± 0) | 7.58 (± 9.73) |
| Mental Component Month 99 (N=1,0,1) | 22.28 (± 0) | 0 (± 0) | 22.28 (± 0) |

Statistical analyses

No statistical analyses for this end point

Secondary: Initial Period: FACIT Fatigue Scale, EuroQol EQ 5D, Work Limitations Questionnaire, and RA Healthcare Resource Utilization Questionnaire (RA-HCRU)

| | |
|---|--|
| End point title | Initial Period: FACIT Fatigue Scale, EuroQol EQ 5D, Work Limitations Questionnaire, and RA Healthcare Resource Utilization Questionnaire (RA-HCRU) |
| End point description: Change from Baseline Scores for FACIT Fatigue Scale, EuroQol EQ 5D, Work Limitations (WL) Physical Demands, and RA Healthcare Resource Utilization Work Performance in Past 3 Months on Days Bothered by RA. The stated number of participants analyzed was the total number of participants in each group. The actual number of participants analyzed on each occasion varied, and is provided for each visit presented. | |
| End point type | Secondary |
| End point timeframe: Every visit until last observation | |

| End point values | Initial Period: Tofacitinib 5 milligram(mg) twice daily (BID) | Initial Period: Tofacitinib 10 mg BID | All Tofacitinib | |
|---|---|---|----------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 1123 | 3358 | 4481 | |
| Units: Score | | | | |
| arithmetic mean (standard deviation) | | | | |
| FACIT Month 6 (N=370,2544,2914) | 6.29 (± 8.98) | 7.33 (± 10.57) | 7.19 (± 10.39) | |
| FACIT Month 12 (N=582,2396,2978) | 5.98 (± 9.74) | 7.33 (± 10.56) | 7.06 (± 10.41) | |
| FACIT Month 18 (N=729,2168,2897) | 6.14 (± 10.06) | 7.40 (± 10.65) | 7.09 (± 10.51) | |
| FACIT Month 24 (N=704,2053,2757) | 5.90 (± 9.76) | 7.42 (± 10.56) | 7.03 (± 10.38) | |
| FACIT Month 30 (N=618,1525,2143) | 5.36 (± 10.08) | 7.00 (± 10.91) | 6.52 (± 10.70) | |
| FACIT Month 36 (N=589,1497,2086) | 5.95 (± 9.87) | 6.87 (± 10.94) | 6.61 (± 10.66) | |
| FACIT Month 42 (N=491,898,1389) | 5.35 (± 10.36) | 6.83 (± 10.86) | 6.31 (± 10.71) | |
| FACIT Month 48 (N=464,1025,1489) | 6.01 (± 10.33) | 6.88 (± 10.95) | 6.61 (± 10.77) | |
| FACIT Month 54 (N=330,169,499) | 6.16 (± 10.49) | 8.51 (± 11.58) | 6.96 (± 10.92) | |
| FACIT Month 60 (N=318,256,574) | 5.96 (± 10.69) | 8.88 (± 11.65) | 7.27 (± 11.21) | |
| FACIT Month 66 (N=277,55,332) | 5.64 (± 10.93) | 6.67 (± 10.58) | 5.81 (± 10.86) | |
| FACIT Month 72 (N=272,51,323) | 5.73 (± 11.10) | 8.63 (± 10.71) | 6.18 (± 11.07) | |
| FACIT Month 78 (N=32,7,39) | 12.06 (± 11.15) | 0.71 (± 14.84) | 10.03 (± 12.48) | |
| FACIT Month 84 (N=74,11,85) | 9.13 (± 12.88) | 2.91 (± 12.36) | 8.32 (± 12.91) | |
| FACIT Month 90 (N=6,1,7) | 18.67 (± 9.14) | 10.00 (± 0) | 17.43 (± 8.96) | |
| FACIT Month 96 (N=3,0,3) | 6.00 (± 2.65) | 0 (± 0) | 6.00 (± 2.65) | |
| EuroQol Month 6 (N=323,2021,2344) | 0.20 (± 0.31) | 0.22 (± 0.32) | 0.22 (± 0.32) | |
| EuroQol Month 12 (N=538,1897,2435) | 0.22 (± 0.30) | 0.22 (± 0.33) | 0.22 (± 0.32) | |
| EuroQol Month 18 (N=684,1748,2432) | 0.20 (± 0.32) | 0.23 (± 0.33) | 0.22 (± 0.33) | |
| EuroQol Month 24 (N=664,1619,2283) | 0.20 (± 0.31) | 0.23 (± 0.33) | 0.22 (± 0.32) | |
| EuroQol Month 30 (N=616,1456,2072) | 0.19 (± 0.31) | 0.22 (± 0.33) | 0.21 (± 0.32) | |
| EuroQol Month 36 (N=582,1397,1979) | 0.21 (± 0.30) | 0.23 (± 0.33) | 0.22 (± 0.32) | |
| EuroQol Month 42 (N=483,874,1357) | 0.18 (± 0.31) | 0.24 (± 0.33) | 0.22 (± 0.32) | |
| EuroQol Month 48 (N=464,1010,1474) | 0.19 (± 0.31) | 0.23 (± 0.33) | 0.22 (± 0.32) | |
| EuroQol Month 54 (N=330,167,497) | 0.22 (± 0.32) | 0.32 (± 0.36) | 0.22 (± 0.32) | |
| EuroQol Month 60 (N=317,255,572) | 0.20 (± 0.33) | 0.27 (± 0.35) | 0.23 (± 0.34) | |
| EuroQol Month 66 (N=276,53,329) | 0.21 (± 0.33) | 0.24 (± 0.34) | 0.21 (± 0.33) | |
| EuroQol Month 72 (N=273,50,323) | 0.22 (± 0.32) | 0.28 (± 0.35) | 0.23 (± 0.32) | |
| EuroQol Month 78 (N=32,7,39) | 0.36 (± 0.37) | 0.10 (± 0.51) | 0.31 (± 0.40) | |
| EuroQol Month 84 (N=75,11,86) | 0.27 (± 0.35) | 0.21 (± 0.43) | 0.27 (± 0.36) | |
| EuroQol Month 90 (N=6,1,7) | 0.47 (± 0.32) | 0.84 (± 0) | 0.52 (± 0.32) | |
| EuroQol Month 96 (N=3,0,3) | 0.09 (± 0.04) | 0 (± 0) | 0.09 (± 0.04) | |
| WL: Physical Demands Month 6 (N=109,900,1009) | -5.34 (± 39.81) | -3.67 (± 38.17) | -3.85 (± 38.33) | |
| WL: Physical Demands Month 12 (N=96,808,904) | -5.31 (± 37.81) | -4.02 (± 39.25) | -4.16 (± 39.08) | |
| WL: Physical Demands Month 18 (N=83,706,789) | -7.97 (± 35.46) | -2.29 (± 37.48) | -2.89 (± 37.29) | |
| WL: Physical Demands Month 24 (N=63,544,607) | -2.62 (± 36.05) | -4.46 (± 37.54) | -4.27 (± 37.36) | |
| WL: Physical Demands Month 30 (N=51,444,495) | -10.12 (± 37.17) | -3.75 (± 37.67) | -4.41 (± 37.63) | |
| WL: Physical Demands Month 36 (N=35,350,385) | -7.31 (± 34.69) | -3.95 (± 39.58) | -4.25 (± 39.14) | |

| | | | | |
|--|------------------|------------------|------------------|--|
| WL: Physical Demands Month 42 (N=24,245,270) | -13.51 (± 33.91) | -4.81 (± 38.98) | -5.58 (± 38.58) | |
| WL: Physical Demands Month 48 (N=19,126,145) | -25.86 (± 34.47) | 0.73 (± 38.68) | -2.76 (± 39.09) | |
| WL: Physical Demands Month 54 (N=2,20,22) | -39.17 (± 62.46) | -13.27 (± 45.69) | -15.63 (± 46.18) | |
| WL: Physical Demands Month 60 (N=0,3,3) | 0 (± 0) | -27.78 (± 34.94) | -27.78 (± 34.94) | |
| WL: Physical Demands Month 66 (N=0,1,1) | 0 (± 0) | 8.33 (± 0) | 8.33 (± 0) | |
| RA-HCRU Month 6 (N=189,1419,1608) | -2.01 (± 6.20) | -2.08 (± 4.15) | -2.07 (± 4.44) | |
| RA-HCRU Month 12 (N=180,1329,1509) | -2.41 (± 6.43) | -2.26 (± 3.76) | -2.28 (± 4.17) | |
| RA-HCRU Month 18 (N=161,1162,1323) | -1.88 (± 2.93) | -2.24 (± 3.90) | -2.19 (± 3.80) | |
| RA-HCRU Month 24 (N=162,1101,1263) | -2.03 (± 3.18) | -2.22 (± 3.26) | -2.19 (± 3.25) | |
| RA-HCRU Month 30 (N=126,785,911) | -1.67 (± 3.02) | -2.16 (± 4.17) | -2.10 (± 4.04) | |
| RA-HCRU Month 36 (N=106,759,865) | -2.38 (± 2.91) | -2.32 (± 4.14) | -2.33 (± 4.01) | |
| RA-HCRU Month 42 (N=68,455,523) | -1.68 (± 2.84) | -2.18 (± 4.70) | -2.11 (± 4.51) | |
| RA-HCRU Month 48 (N=66,527,593) | -1.88 (± 3.24) | -2.15 (± 4.67) | -2.12 (± 4.53) | |
| RA-HCRU Month 54 (N=3,39,42) | -2.00 (± 1.00) | -2.59 (± 3.42) | -2.55 (± 3.30) | |
| RA-HCRU Month 60 (N=4,94,98) | -2.00 (± 3.56) | -2.88 (± 2.85) | -2.85 (± 2.87) | |
| RA-HCRU Month 66 (N=0,0,0) | 0 (± 0) | 0 (± 0) | 0 (± 0) | |
| RA-HCRU Month 72 (N=0,4,4) | 0 (± 0) | -1.25 (± 6.70) | -1.25 (± 6.70) | |
| RA-HCRU Month 78 (0,0,0) | 0 (± 0) | 0 (± 0) | 0 (± 0) | |
| RA-HCRU Month 84 (0,0,0) | 0 (± 0) | 0 (± 0) | 0 (± 0) | |
| RA-HCRU Month 90 (0,0,0) | 0 (± 0) | 0 (± 0) | 0 (± 0) | |
| RA-HCRU Month 96 (0,0,0) | 0 (± 0) | 0 (± 0) | 0 (± 0) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Initial Period: Preservation of joint structure in participants who had baseline radiographs obtained in their qualifying index study

| | |
|-----------------|---|
| End point title | Initial Period: Preservation of joint structure in participants who had baseline radiographs obtained in their qualifying index study |
|-----------------|---|

End point description:

Modified Total Sharp Score per visit. Baseline score was the last available assessment from the index study. The stated number of participants analyzed was the total number of participants in each group. The actual number of participants analyzed on each occasion varied, and is provided for each visit presented. TSS=Total Sharp Score

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

End point timeframe:

Every 6 months until last observation

| End point values | Initial Period: Tofacitinib 5 milligram(mg) twice daily (BID) | Initial Period: Tofacitinib 10 mg BID | All Tofacitinib | |
|---|---|---|----------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 1123 | 3358 | 4481 | |
| Units: Score | | | | |
| arithmetic mean (standard deviation) | | | | |
| Modified TSS Baseline (N=95,1061,1156) | 20.55 (± 33.37) | 24.13 (± 43.57) | 23.84 (± 42.83) | |
| Modified TSS Month 6 (N=82,937,1019) | 22.58 (± 35.10) | 25.12 (± 44.42) | 24.91 (± 43.74) | |
| Modified TSS Month 12 (N=85,918,1003) | 21.26 (± 33.75) | 24.73 (± 44.08) | 24.44 (± 43.30) | |
| Modified TSS Month 24 (N=77,801,878) | 22.07 (± 35.85) | 24.85 (± 43.21) | 24.61 (± 42.61) | |
| Modified TSS Month 36 (N=35,379,414) | 25.88 (± 37.74) | 28.22 (± 44.95) | 28.02 (± 44.35) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Vaccine sub-study. Percent achieving a satisfactory humoral response to the pneumococcal vaccine as defined by ≥ 2-fold increase in antibody concentrations

| | |
|-----------------|---|
| End point title | Vaccine sub-study. Percent achieving a satisfactory humoral response to the pneumococcal vaccine as defined by ≥ 2-fold increase in antibody concentrations |
|-----------------|---|

End point description:

Number (%) of participants achieving a satisfactory humoral response to the pneumococcal vaccine as defined by ≥2-fold increase in antibody concentration from vaccine sub-study visit 2 (vaccination baseline) in ≥6 of 12 anti-pneumococcal antigens (serotypes 1, 3, 4, 5, 6B, 7F, 9V, 14, 18C, 19A, 19F, 23F) The number of participants was the number with a determinate antibody titer to the given vaccine antigen within the population. 95% CI is based on Clopper-Pearson exact method for response rate. Evaluable immunogenicity population.

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

End point timeframe:

From vaccine sub-study visit 2 (baseline) to sub-study visit 4

| End point values | Tofacitinib 10 mg BID Continuous Visit 3 | Tofacitinib 10 mg BID Interrupted Visit 3 | Tofacitinib 10 mg BID Continuous Visit 4 | Tofacitinib 10 mg BID Interrupted Visit 4 |
|----------------------------------|---|--|---|--|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 91 | 91 | 92 | 91 |
| Units: Percent of participants | | | | |
| number (confidence interval 95%) | 18.7 (11.3 to 28.2) | 38.5 (28.4 to 49.2) | 75.0 (64.9 to 83.4) | 84.6 (75.5 to 91.3) |

Statistical analyses

No statistical analyses for this end point

Secondary: Vaccine sub-study. Percent achieving a satisfactory humoral response to the seasonal influenza vaccine as defined by ≥ 4 -fold increase in antibody titers

| | |
|-----------------|---|
| End point title | Vaccine sub-study. Percent achieving a satisfactory humoral response to the seasonal influenza vaccine as defined by ≥ 4 -fold increase in antibody titers |
|-----------------|---|

End point description:

Number of participants achieving a satisfactory humoral response to the seasonal influenza vaccine as defined by ≥ 4 -fold increase in antibody titers from visit 2 (vaccination baseline) in ≥ 2 of 3 influenza antigens (HAI B, HAI H1N1, and HAI H3N2) The number of participants was the number with a determinate antibody titer to the given vaccine antigen within the population. 95% CI is based on Clopper-Pearson exact method for response rate.
Evaluable immunogenicity population.

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

End point timeframe:

From vaccine sub-study visit 2 (baseline) to sub-study visit 4

| End point values | Tofacitinib 10 mg BID Continuous Visit 3 | Tofacitinib 10 mg BID Interrupted Visit 3 | Tofacitinib 10 mg BID Continuous Visit 4 | Tofacitinib 10 mg BID Interrupted Visit 4 |
|----------------------------------|--|---|--|---|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 91 | 91 | 92 | 91 |
| Units: Percent of participants | | | | |
| number (confidence interval 95%) | 31.9 (22.5 to 42.5) | 53.8 (43.1 to 64.4) | 66.3 (55.7 to 75.8) | 63.7 (53.0 to 73.6) |

Statistical analyses

No statistical analyses for this end point

Secondary: Vaccine sub-study. Percentage of participants achieving protective antibody titers to the seasonal influenza vaccine as measured by a hemagglutination inhibition (HI) assay titer of $\geq 1:40$ in ≥ 2 of 3 influenza antigens at vaccine sub-study visit 3 and 4

| | |
|-----------------|--|
| End point title | Vaccine sub-study. Percentage of participants achieving protective antibody titers to the seasonal influenza vaccine as measured by a hemagglutination inhibition (HI) assay titer of $\geq 1:40$ in ≥ 2 of 3 influenza antigens at vaccine sub-study visit 3 and 4 |
|-----------------|--|

End point description:

Number (%) of participants achieving protective antibody titers to the seasonal influenza vaccine as

measured by an HAI assay titer of $\geq 1:40$ in ≥ 2 of 3 influenza antigens measured at vaccine sub-study visits 3 and 4. The number of participants was the number with a determinate antibody titer to the given vaccine antigen within the population. 95% CI is based on Clopper-Pearson exact method for response rate.

Evaluable immunogenicity population.

| | |
|--|-----------|
| End point type | Secondary |
| End point timeframe: | |
| From vaccine sub-study visit 2 (baseline) to sub-study visit 4 | |

| End point values | Tofacitinib 10 mg BID Continuous Visit 3 | Tofacitinib 10 mg BID Interrupted Visit 3 | Tofacitinib 10 mg BID Continuous Visit 4 | Tofacitinib 10 mg BID Interrupted Visit 4 |
|----------------------------------|--|---|--|---|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 91 | 91 | 92 | 91 |
| Units: Percent of participants | | | | |
| number (confidence interval 95%) | 56.0 (45.2 to 66.4) | 69.2 (58.7 to 78.5) | 75.0 (64.9 to 83.4) | 82.4 (73.0 to 89.6) |

Statistical analyses

No statistical analyses for this end point

Secondary: Vaccine sub-study. Percentage of participants who respond to each of the 12 pneumococcal antigens as defined by ≥ 2 -fold increase in antibody concentrations from vaccine sub-study visit 2 (vaccination baseline) measured at vaccine sub-study visit 4

| | |
|-----------------|--|
| End point title | Vaccine sub-study. Percentage of participants who respond to each of the 12 pneumococcal antigens as defined by ≥ 2 -fold increase in antibody concentrations from vaccine sub-study visit 2 (vaccination baseline) measured at vaccine sub-study visit 4 |
|-----------------|--|

End point description:

Number (%) of participants achieving a satisfactory humoral response to the pneumococcal vaccine as defined by ≥ 2 -fold increase in antibody concentration from vaccine sub-study visit 2 (vaccination baseline) in ≥ 6 of 12 anti-pneumococcal antigens (serotypes 1, 3, 4, 5, 6B, 7F, 9V, 14, 18C, 19A, 19F, 23F) The number of participants was the number with a determinate antibody titer to the given vaccine antigen within the population. 95% CI is based on Clopper-Pearson exact method for response rate. Evaluable immunogenicity population.

| | |
|--|-----------|
| End point type | Secondary |
| End point timeframe: | |
| From vaccine sub-study visit 2 (baseline) to sub-study visit 4 | |

| End point values | Tofacitinib 10 mg BID Continuous | Tofacitinib 10 mg BID Interrupted | | |
|----------------------------------|----------------------------------|-----------------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 92 | 91 | | |
| Units: Percent of participants | | | | |
| number (confidence interval 95%) | | | | |
| Serotype 1 | 75 (64.9 to 83.4) | 82.4 (73.0 to 89.6) | | |
| Serotype 3 | 53.3 (42.6 to 63.7) | 71.4 (61.0 to 80.4) | | |
| Serotype 4 | 76.1 (66.1 to 84.4) | 76.9 (66.9 to 85.1) | | |
| Serotype 5 | 42.4 (32.1 to 53.1) | 49.5 (38.8 to 60.1) | | |
| Serotype 6B | 48.9 (38.3 to 59.6) | 56 (45.2 to 66.4) | | |
| Serotype 7F | 71.7 (61.4 to 80.6) | 78 (68.1 to 86.0) | | |
| Serotype 9V | 64.1 (53.5 to 73.9) | 78 (68.1 to 86.0) | | |
| Serotype 14 | 71.7 (61.4 to 80.6) | 75.8 (65.7 to 84.2) | | |
| Serotype 18C | 73.9 (63.7 to 82.5) | 83.5 (74.3 to 90.5) | | |
| Serotype 19A | 54.3 (43.6 to 64.8) | 56.0 (45.2 to 66.4) | | |
| Serotype 19F | 60.9 (50.1 to 70.9) | 71.4 (61.0 to 80.4) | | |
| Serotype 23F | 53.3 (42.6 to 63.7) | 70.3 (59.8 to 79.5) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Vaccine sub-study. Percentage of participants who respond to each of the 3 influenza antigens as defined by ≥ 4 -fold increase in antibody titers from vaccine sub-study visit 2 (vaccination baseline) measured at vaccine sub-study visit 4

| | |
|-----------------|--|
| End point title | Vaccine sub-study. Percentage of participants who respond to each of the 3 influenza antigens as defined by ≥ 4 -fold increase in antibody titers from vaccine sub-study visit 2 (vaccination baseline) measured at vaccine sub-study visit 4 |
|-----------------|--|

End point description:

Number (%) of participants achieving a satisfactory humoral response to the seasonal influenza vaccine defined as ≥ 4 -fold increase in antibody titers from visit 2 (vaccination baseline) in ≥ 2 of 3 influenza antigens (HAI B, HAI H1N1, and HAI H3N2). The number of participants was the number with a determinate antibody titer to the given vaccine antigen within the population. 95% CI is based on Clopper-Pearson exact method for response rate. Evaluable immunogenicity population.

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

End point timeframe:

From vaccine sub-study visit 2 (baseline) to sub-study visit 4

| End point values | Tofacitinib 10 mg BID Continuous Visit 4 | Tofacitinib 10 mg BID Interrupted Visit 4 | | |
|----------------------------------|--|---|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 92 | 91 | | |
| Units: Percent of participants | | | | |
| number (confidence interval 95%) | | | | |
| Antigen B | 45.7 (35.2 to 56.4) | 51.6 (40.9 to 62.3) | | |
| Antigen H1N1 | 71.7 (61.4 to 80.6) | 63.7 (53.0 to 73.6) | | |
| Antigen H3N2 | 66.3 (55.7 to 75.8) | 74.7 (64.5 to 83.3) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Vaccine sub-study. Fold increase of anti-pneumococcal antibody levels to each of the 12 pneumococcal antigens above vaccination baseline values (vaccine sub-study visit 2) at vaccine sub-study visit 4

| | |
|-----------------|--|
| End point title | Vaccine sub-study. Fold increase of anti-pneumococcal antibody levels to each of the 12 pneumococcal antigens above vaccination baseline values (vaccine sub-study visit 2) at vaccine sub-study visit 4 |
|-----------------|--|

End point description:

Geometric Mean Fold Increase From Baseline of Pneumococcal Antigens Measured at Visit 4. n was the number of participants with valid and determinate assay results for the specified serotype at the given visit. The stated number of participants analyzed was the total number of participants. The actual number of participants analyzed for some serotypes varied, and is provided where it differed from the total number of participants. Confidence Intervals (CIs) were back transformations of a CI based on the Student t distribution for the mean logarithm of the concentrations. Evaluable immunogenicity population.

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

End point timeframe:

From vaccine sub-study visit 2 (baseline) to sub-study visit 4

| End point values | Tofacitinib 10 mg BID Interrupted | Tofacitinib 10 mg Continuous | | |
|--|-----------------------------------|------------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 91 | 92 | | |
| Units: Antibody Level | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Serotype 1 (N=89,86) | 9.26 (6.89 to 12.44) | 5.87 (4.57 to 7.55) | | |

| | | | | |
|------------------------|---------------------|---------------------|--|--|
| Serotype 3 (N=91,89) | 4.20 (3.31 to 5.32) | 2.34 (1.97 to 2.79) | | |
| Serotype 4 (N=91,89) | 6.29 (4.65 to 8.51) | 5.32 (4.22 to 6.71) | | |
| Serotype 5 | 2.53 (2.12 to 3.02) | 2.02 (1.75 to 2.34) | | |
| Serotype 6B | 3.06 (2.53 to 3.69) | 2.32 (1.98 to 2.73) | | |
| Serotype 7F (N=92,89) | 6.41 (4.97 to 8.28) | 4.69 (3.73 to 5.90) | | |
| Serotype 9V (N=92,90) | 4.39 (3.62 to 5.34) | 3.17 (2.70 to 3.72) | | |
| Serotype 14 | 7.34 (5.50 to 9.79) | 5.23 (4.00 to 6.86) | | |
| Serotype 18C | 7.41 (5.77 to 9.53) | 3.97 (3.28 to 4.79) | | |
| Serotype 19A | 2.93 (2.46 to 3.50) | 2.33 (1.99 to 2.72) | | |
| Serotype 19F (N=90,90) | 4.60 (3.64 to 5.80) | 2.97 (2.44 to 3.62) | | |
| Serotype 23F (N=92,90) | 4.54 (3.58 to 5.75) | 2.74 (2.27 to 3.32) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Vaccine sub-study. Fold increase of anti-influenza antibody levels to each of the 3 influenza antigens above vaccination baseline values (vaccine sub-study visit 2) at vaccine sub-study visit 4

| | |
|-----------------|---|
| End point title | Vaccine sub-study. Fold increase of anti-influenza antibody levels to each of the 3 influenza antigens above vaccination baseline values (vaccine sub-study visit 2) at vaccine sub-study visit 4 |
|-----------------|---|

End point description:

Geometric Mean Fold Increase From Baseline of Influenza Antigens Measured at Visit 4. n was the number of participants with valid and determinate assay results for the specified HAI strain at the given visit. Confidence Intervals (CIs) were back transformations of a CI based on the Student t distribution for the mean logarithm of the titers.
Evaluable immunogenicity population.

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

End point timeframe:

From vaccine sub-study visit 2 (baseline) to sub-study visit 4

| End point values | Tofacitinib 10 mg BID Continuous | Tofacitinib 10 mg BID Interrupted | | |
|--|----------------------------------|-----------------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 92 | 91 | | |
| Units: Antibody titer | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Antigen B | 3.33 (2.57 to 4.32) | 4.17 (3.25 to 5.34) | | |

| | | | | |
|--------------|----------------------|----------------------|--|--|
| Antigen H1N1 | 7.94 (5.96 to 10.58) | 6.71 (4.94 to 9.12) | | |
| Antigen H3N2 | 7.80 (5.58 to 10.91) | 8.51 (6.45 to 11.21) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Vaccine sub-study. Concentrations of anti-pneumococcal antibodies at vaccine sub-study visit 3 and 4

| | |
|-----------------|--|
| End point title | Vaccine sub-study. Concentrations of anti-pneumococcal antibodies at vaccine sub-study visit 3 and 4 |
|-----------------|--|

End point description:

Mean pneumococcal concentrations (ug/mL) at vaccine baseline (visit 2) and post-vaccination visits (visits 3 and 4) by serotype. The stated number of participants analyzed was the total number of participants in each group. The actual number of participants analyzed for each serotype varied, and is provided for each individually. ug/mL=micrograms per milliliter
Evaluable immunogenicity population.

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

End point timeframe:

From vaccine sub-study visit 2 (baseline) to sub-study visit 4

| End point values | Tofacitinib 10 mg BID Interrupted Visit 3 | Tofacitinib 10 mg BID Continuous Visit 4 | Tofacitinib 10 mg BID Interrupted Visit 4 | Tofacitinib 10 mg BID Continuous Visit 2 |
|--|---|--|---|--|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 91 | 92 | 91 | 92 |
| Units: Concentration (ug/mL) | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Serotype 9V (N=92,90,91,91,92,91) | 2.26 (1.78 to 2.87) | 4.16 (3.29 to 5.27) | 4.80 (3.75 to 6.16) | 1.31 (1.08 to 1.60) |
| Serotype 14 (N=92,91,91,91,92,91) | 5.03 (3.77 to 6.71) | 12.09 (8.76 to 16.69) | 15.01 (10.80 to 20.88) | 2.31 (1.79 to 2.98) |
| Serotype 18C (N=92,91,91,91,92,91) | 2.41 (1.82 to 3.18) | 4.27 (3.34 to 5.47) | 6.61 (5.01 to 8.74) | 1.08 (0.86 to 1.36) |
| Serotype 19F (N=90,90,90,91,92,91) | 2.17 (1.61 to 2.91) | 3.52 (2.60 to 4.76) | 5.47 (3.98 to 7.52) | 1.17 (0.92 to 1.50) |
| Serotype 23F (92,90,90,91,92,91) | 2.24 (1.75 to 2.88) | 3.44 (2.66 to 4.44) | 5.27 (3.96 to 7.02) | 1.25 (1.01 to 1.56) |

| End point values | Tofacitinib 10 mg BID Interrupted Visit 2 | Tofacitinib 10 mg BID Continuous Visit 3 | | |
|------------------------------|---|--|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 91 | 92 | | |
| Units: Concentration (ug/mL) | | | | |

| | | | | |
|--|---------------------|---------------------|--|--|
| geometric mean (confidence interval 95%) | | | | |
| Serotype 9V (N=92,90,91,91,92,91) | 1.12 (0.89 to 1.42) | 2.00 (1.64 to 2.44) | | |
| Serotype 14 (N=92,91,91,91,92,91) | 2.05 (1.59 to 2.63) | 4.02 (3.04 to 5.32) | | |
| Serotype 18C (N=92,91,91,91,92,91) | 0.89 (0.70 to 1.14) | 1.81 (1.43 to 2.29) | | |
| Serotype 19F (N=90,90,90,91,92,91) | 1.18 (0.89 to 1.58) | 1.61 (1.25 to 2.08) | | |
| Serotype 23F (92,90,90,91,92,91) | 1.16 (0.93 to 1.44) | 1.80 (1.44 to 2.25) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Vaccine sub-study. Titers of anti-influenza antibodies at vaccine sub-study visit 3 and 4

| | |
|-----------------|---|
| End point title | Vaccine sub-study. Titers of anti-influenza antibodies at vaccine sub-study visit 3 and 4 |
|-----------------|---|

End point description:

Mean influenza antibody titers at visits 3 and 4.

Evaluable immunogenicity population.

| | |
|----------------|-----------|
| End point type | Secondary |
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End point timeframe:

From vaccine sub-study visit 2 (baseline) to sub-study visit 4

| End point values | Tofacitinib 10 mg BID Continuous Visit 3 | Tofacitinib 10 mg BID Interrupted Visit 3 | Tofacitinib 10 mg BID Continuous Visit 4 | Tofacitinib 10 mg BID Interrupted Visit 4 |
|--|--|---|--|---|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 91 | 91 | 92 | 91 |
| Units: Antibody Titer | | | | |
| geometric mean (confidence interval 95%) | | | | |
| HAI B | 23.29 (17.92 to 30.27) | 37.45 (28.17 to 49.78) | 38.06 (28.71 to 50.47) | 45.19 (35.01 to 58.34) |
| HAI H1N1 | 52.75 (37.97 to 73.28) | 105.2 (70.76 to 156.5) | 120.2 (89.83 to 160.8) | 136.0 (97.67 to 189.4) |
| HAI H3N2 | 55.07 (38.19 to 79.43) | 83.10 (57.38 to 120.4) | 141.8 (102.9 to 195.4) | 147.2 (107.8 to 201.0) |

| End point values | Tofacitinib 10 mg BID Continuous Visit 2 | Tofacitinib 10 mg BID Interrupted Visit 2 | | |
|-----------------------------|--|---|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 92 | 91 | | |

| | | | | |
|--|------------------------|------------------------|--|--|
| Units: Antibody Titer | | | | |
| geometric mean (confidence interval 95%) | | | | |
| HAI B | 11.43 (9.38 to 13.91) | 10.85 (8.90 to 13.22) | | |
| HAI H1N1 | 15.14 (11.67 to 19.64) | 20.26 (14.86 to 27.62) | | |
| HAI H3N2 | 18.18 (13.53 to 24.44) | 17.30 (12.98 to 23.07) | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

114 months for Initial Period; 13 months for Extension Period

Adverse event reporting additional description:

The same event may appear as both an AE and a SAE. However, what is presented are distinct events. An event may be categorized as serious in one subject and as non serious in another subject, or one subject may have experienced both a serious and non serious event during the study.

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

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
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|--------------------|------|
| Dictionary version | 19.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|---|
| Reporting group title | Tofa 5mg BID; ppts with avg total daily dose across study <15 |
|-----------------------|---|

Reporting group description:

Participants with non-zero average total daily dose across study <15 were assigned to 5 mg BID.
avg=average; BID=twice daily; mg=milligram; ppts=participants; tofa=tofacitinib

| | |
|-----------------------|--|
| Reporting group title | Tofa 10mg BID; ppts with avg total daily dose across study ≥15 |
|-----------------------|--|

Reporting group description:

Participants with non-zero average total daily dose across study ≥15 were assigned to 10 mg BID.
avg=average; BID=twice daily; mg=milligram; ppts=participants; tofa=tofacitinib

| | |
|-----------------------|-----------------|
| Reporting group title | All Tofacitinib |
|-----------------------|-----------------|

Reporting group description:

All participants treated with tofacitinib from 5 mg BID and 10 mg BID groups

| | |
|-----------------------|------------------------------------|
| Reporting group title | Extension Period: Tofacitinib 5 mg |
|-----------------------|------------------------------------|

Reporting group description:

Subjects who completed 2 years of lymphocyte assessment in Initial period and enrolled for extension period received Tofacitinib (CP-690,550) 5 mg orally, twice daily up to 12 months.

| Serious adverse events | Tofa 5mg BID; ppts with avg total daily dose across study <15 | Tofa 10mg BID; ppts with avg total daily dose across study ≥15 | All Tofacitinib |
|---|---|--|----------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 346 / 1123 (30.81%) | 997 / 3358 (29.69%) | 1343 / 4481 (29.97%) |
| number of deaths (all causes) | 39 | 46 | 85 |
| number of deaths resulting from adverse events | | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| 5q minus syndrome | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Acute promyelocytic leukaemia | | | |

| | | | |
|---|------------------|-------------------|-------------------|
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Adenocarcinoma of appendix | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Adenocarcinoma of colon | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Adenocarcinoma of the cervix | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Adrenal adenoma | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| B-cell lymphoma | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| B-cell small lymphocytic lymphoma | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Basal cell carcinoma | | | |
| subjects affected / exposed | 3 / 1123 (0.27%) | 12 / 3358 (0.36%) | 15 / 4481 (0.33%) |
| occurrences causally related to treatment / all | 1 / 3 | 6 / 12 | 7 / 15 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Benign salivary gland neoplasm | | | |

| | | | |
|---|------------------|-------------------|-------------------|
| subjects affected / exposed | 0 / 1123 (0.00%) | 2 / 3358 (0.06%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Benign tracheal neoplasm | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bladder cancer | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 2 / 3358 (0.06%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bladder neoplasm | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bladder transitional cell carcinoma | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| 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 cancer | | | |
| subjects affected / exposed | 4 / 1123 (0.36%) | 12 / 3358 (0.36%) | 16 / 4481 (0.36%) |
| occurrences causally related to treatment / all | 1 / 4 | 6 / 12 | 7 / 16 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Breast cancer metastatic | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| Bronchial carcinoma | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 3 / 3358 (0.09%) | 4 / 4481 (0.09%) |
| occurrences causally related to treatment / all | 0 / 1 | 2 / 3 | 2 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cervix carcinoma | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 1 / 1123 (0.09%) | 1 / 3358 (0.03%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 1 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cervix carcinoma stage 0 | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cholesteatoma | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Choroid plexus papilloma | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Colon adenoma | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 2 / 3358 (0.06%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Colon cancer | | | |
| subjects affected / exposed | 2 / 1123 (0.18%) | 1 / 3358 (0.03%) | 3 / 4481 (0.07%) |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 1 | 1 / 3 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| Colon cancer metastatic | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Colorectal adenocarcinoma | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 2 / 3358 (0.06%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diffuse large B-cell lymphoma | | | |

| | | | |
|--|------------------|------------------|------------------|
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Endometrial adenocarcinoma | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 2 / 3358 (0.06%) | 3 / 4481 (0.07%) |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 2 | 1 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Endometrial cancer | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 1 / 3358 (0.03%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 1 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Endometrial cancer stage I | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Extranodal marginal zone B-cell lymphoma (MALT type) | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Fibroadenoma of breast | | | |
| subjects affected / exposed | 2 / 1123 (0.18%) | 1 / 3358 (0.03%) | 3 / 4481 (0.07%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Fibroma | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gallbladder cancer | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 1 / 3358 (0.03%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| Gastric cancer | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Glioblastoma multiforme | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 2 / 3358 (0.06%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 2 | 2 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| Hepatic cancer | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 2 / 3358 (0.06%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| Hodgkin's disease | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Intraductal proliferative breast lesion | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 3 / 3358 (0.09%) | 3 / 4481 (0.07%) |
| occurrences causally related to treatment / all | 0 / 0 | 3 / 3 | 3 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Invasive ductal breast carcinoma | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 2 / 3358 (0.06%) | 3 / 4481 (0.07%) |
| occurrences causally related to treatment / all | 0 / 1 | 2 / 2 | 2 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Kaposi's sarcoma | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Laryngeal cancer | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Laryngeal squamous cell carcinoma | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 0 / 1123 (0.00%) | 2 / 3358 (0.06%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Leiomyosarcoma | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lipoma | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 2 / 3358 (0.06%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Liposarcoma | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lung adenocarcinoma | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 4 / 3358 (0.12%) | 4 / 4481 (0.09%) |
| occurrences causally related to treatment / all | 0 / 0 | 3 / 4 | 3 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| Lung adenocarcinoma metastatic | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 3 / 3358 (0.09%) | 3 / 4481 (0.07%) |
| occurrences causally related to treatment / all | 0 / 0 | 3 / 3 | 3 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 2 / 2 | 2 / 2 |
| Lung cancer metastatic | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 3 / 3358 (0.09%) | 3 / 4481 (0.07%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 3 | 1 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 2 / 3 | 2 / 3 |
| Lung neoplasm | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lung neoplasm malignant | | | |

| | | | |
|---|------------------|------------------|-------------------|
| subjects affected / exposed | 2 / 1123 (0.18%) | 3 / 3358 (0.09%) | 5 / 4481 (0.11%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 3 | 0 / 5 |
| deaths causally related to treatment / all | 0 / 2 | 1 / 3 | 1 / 5 |
| Lymphoma | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Malignant melanoma | | | |
| subjects affected / exposed | 3 / 1123 (0.27%) | 8 / 3358 (0.24%) | 11 / 4481 (0.25%) |
| occurrences causally related to treatment / all | 2 / 3 | 7 / 8 | 9 / 11 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Malignant melanoma in situ | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Malignant peritoneal neoplasm | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Mantle cell lymphoma | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Marginal zone lymphoma stage II | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Medullary thyroid cancer | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Meningioma | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 0 / 1123 (0.00%) | 2 / 3358 (0.06%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 2 | 2 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metastases to bone | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 1 |
| Metastases to liver | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 1 / 3358 (0.03%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 1 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| Metastases to lung | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 1 / 1 | 0 / 0 | 1 / 1 |
| Metastases to lymph nodes | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 2 / 3358 (0.06%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| Metastasis | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 1 / 3358 (0.03%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | 2 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metastatic malignant melanoma | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 2 / 3358 (0.06%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 2 | 2 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Mucoepidermoid carcinoma | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Neoplasm | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Neoplasm malignant | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nodular melanoma | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Non-Hodgkin's lymphoma | | | |
| subjects affected / exposed | 2 / 1123 (0.18%) | 2 / 3358 (0.06%) | 4 / 4481 (0.09%) |
| occurrences causally related to treatment / all | 0 / 2 | 1 / 2 | 1 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Non-small cell lung cancer | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 1 / 3358 (0.03%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| Non-small cell lung cancer metastatic | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 2 / 3358 (0.06%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| Oesophageal carcinoma | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ovarian adenoma | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 2 / 3358 (0.06%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ovarian cancer | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 1 / 1123 (0.09%) | 1 / 3358 (0.03%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ovarian cancer metastatic | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 2 / 3358 (0.06%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ovarian germ cell teratoma | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Papillary thyroid cancer | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 2 / 3358 (0.06%) | 3 / 4481 (0.07%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Parathyroid tumour | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Prostate cancer | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 7 / 3358 (0.21%) | 7 / 4481 (0.16%) |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 7 | 2 / 7 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Prostatic adenoma | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal cancer | | | |
| subjects affected / exposed | 2 / 1123 (0.18%) | 0 / 3358 (0.00%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | 1 / 2 |
| deaths causally related to treatment / all | 1 / 1 | 0 / 0 | 1 / 1 |
| Renal cell carcinoma | | | |

| | | | |
|---|------------------|-------------------|-------------------|
| subjects affected / exposed | 2 / 1123 (0.18%) | 1 / 3358 (0.03%) | 3 / 4481 (0.07%) |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 1 | 1 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Sebacous carcinoma | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Skin cancer | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Small cell lung cancer | | | |
| subjects affected / exposed | 2 / 1123 (0.18%) | 0 / 3358 (0.00%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 1 / 1 | 0 / 0 | 1 / 1 |
| Small cell lung cancer metastatic | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| Small intestine carcinoma | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Spindle cell sarcoma | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Squamous cell carcinoma | | | |
| subjects affected / exposed | 2 / 1123 (0.18%) | 10 / 3358 (0.30%) | 12 / 4481 (0.27%) |
| occurrences causally related to treatment / all | 1 / 2 | 6 / 10 | 7 / 12 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Squamous cell carcinoma of lung | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 2 / 1123 (0.18%) | 2 / 3358 (0.06%) | 4 / 4481 (0.09%) |
| occurrences causally related to treatment / all | 2 / 2 | 1 / 2 | 3 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| Squamous cell carcinoma of skin | | | |
| subjects affected / exposed | 3 / 1123 (0.27%) | 4 / 3358 (0.12%) | 7 / 4481 (0.16%) |
| occurrences causally related to treatment / all | 3 / 3 | 0 / 5 | 3 / 8 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Squamous cell carcinoma of the cervix | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Squamous cell carcinoma of the tongue | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Squamous cell carcinoma of the vulva | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 1 / 3358 (0.03%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Synovial sarcoma | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 1 / 1 | 0 / 0 | 1 / 1 |
| T-cell lymphoma | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Thyroid adenoma | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 2 / 3358 (0.06%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Thyroid cancer | | | |

| | | | |
|---|--------------------------------------|-------------------|-------------------|
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Thyroid neoplasm | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Tumour necrosis | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ureteral neoplasm | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Uterine leiomyoma | | | |
| subjects affected / exposed | 7 / 1123 (0.62%) | 14 / 3358 (0.42%) | 21 / 4481 (0.47%) |
| occurrences causally related to treatment / all | 0 / 7 | 1 / 14 | 1 / 21 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vulval cancer stage 0 | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Basal cell carcinoma 1 | Additional description: MedDRA v20.1 | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 0 / 3358 (0.00%) | 0 / 4481 (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 |
| Vascular disorders | | | |
| Accelerated hypertension | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Aortic aneurysm | | | |

| | | | |
|---|------------------|------------------|-------------------|
| subjects affected / exposed | 2 / 1123 (0.18%) | 3 / 3358 (0.09%) | 5 / 4481 (0.11%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 3 | 0 / 5 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Aortic dissection | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Aortic stenosis | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 1 / 3358 (0.03%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Arteriosclerosis | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 1 / 3358 (0.03%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| Circulatory collapse | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| Deep vein thrombosis | | | |
| subjects affected / exposed | 6 / 1123 (0.53%) | 9 / 3358 (0.27%) | 15 / 4481 (0.33%) |
| occurrences causally related to treatment / all | 3 / 7 | 3 / 10 | 6 / 17 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Extremity necrosis | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 1 / 3358 (0.03%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Haematoma | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypertension | | | |

| | | | |
|---|------------------|------------------|-------------------|
| subjects affected / exposed | 3 / 1123 (0.27%) | 7 / 3358 (0.21%) | 10 / 4481 (0.22%) |
| occurrences causally related to treatment / all | 0 / 4 | 2 / 8 | 2 / 12 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| Hypertensive crisis | | | |
| subjects affected / exposed | 3 / 1123 (0.27%) | 8 / 3358 (0.24%) | 11 / 4481 (0.25%) |
| occurrences causally related to treatment / all | 3 / 5 | 4 / 10 | 7 / 15 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypotension | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 2 / 3358 (0.06%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypovolaemic shock | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Peripheral artery occlusion | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Peripheral venous disease | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 2 / 3358 (0.06%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Shock | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| Thromboangiitis obliterans | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Thrombophlebitis | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 2 / 1123 (0.18%) | 1 / 3358 (0.03%) | 3 / 4481 (0.07%) |
| occurrences causally related to treatment / all | 0 / 2 | 1 / 1 | 1 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Varicose vein | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 5 / 3358 (0.15%) | 5 / 4481 (0.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 6 | 0 / 6 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Venous thrombosis limb | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Surgical and medical procedures | | | |
| Arthrodesis | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hip arthroplasty | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Knee arthroplasty | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pregnancy, puerperium and perinatal conditions | | | |
| Abortion spontaneous | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 2 / 3358 (0.06%) | 3 / 4481 (0.07%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 2 | 1 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Foetal death | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|--|------------------|-------------------|-------------------|
| Pregnancy | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Unintended pregnancy | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General disorders and administration site conditions | | | |
| Abscess sterile | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Asthenia | | | |
| subjects affected / exposed | 2 / 1123 (0.18%) | 1 / 3358 (0.03%) | 3 / 4481 (0.07%) |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 1 | 1 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Chest discomfort | | | |
| subjects affected / exposed | 2 / 1123 (0.18%) | 1 / 3358 (0.03%) | 3 / 4481 (0.07%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Chest pain | | | |
| subjects affected / exposed | 5 / 1123 (0.45%) | 12 / 3358 (0.36%) | 17 / 4481 (0.38%) |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 12 | 0 / 17 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Death | | | |
| subjects affected / exposed | 3 / 1123 (0.27%) | 1 / 3358 (0.03%) | 4 / 4481 (0.09%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 1 | 0 / 4 |
| deaths causally related to treatment / all | 3 / 3 | 1 / 1 | 4 / 4 |
| Drug ineffective | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|------------------|------------------|------------------|
| Fatigue | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Fibrosis | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gait disturbance | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hernia | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Multiple organ dysfunction syndrome | | | |
| subjects affected / exposed | 2 / 1123 (0.18%) | 2 / 3358 (0.06%) | 4 / 4481 (0.09%) |
| occurrences causally related to treatment / all | 1 / 2 | 1 / 2 | 2 / 4 |
| deaths causally related to treatment / all | 1 / 2 | 2 / 2 | 3 / 4 |
| Non-cardiac chest pain | | | |
| subjects affected / exposed | 2 / 1123 (0.18%) | 1 / 3358 (0.03%) | 3 / 4481 (0.07%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Oedema | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Oedema peripheral | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Peripheral swelling | | | |

| | | | |
|---|------------------|------------------|-------------------|
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pyrexia | | | |
| subjects affected / exposed | 5 / 1123 (0.45%) | 5 / 3358 (0.15%) | 10 / 4481 (0.22%) |
| occurrences causally related to treatment / all | 3 / 5 | 2 / 5 | 5 / 10 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Sudden death | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| Systemic inflammatory response syndrome | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Immune system disorders | | | |
| Allergy to arthropod bite | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Allergy to arthropod sting | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Anaphylactic reaction | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Anaphylactic shock | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Social circumstances | | | |

| | | | |
|--|------------------|------------------|------------------|
| Activities of daily living impaired subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Physical abuse subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Reproductive system and breast disorders | | | |
| Adenomyosis subjects affected / exposed | 0 / 1123 (0.00%) | 2 / 3358 (0.06%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Benign prostatic hyperplasia subjects affected / exposed | 0 / 1123 (0.00%) | 4 / 3358 (0.12%) | 4 / 4481 (0.09%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 4 | 0 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Breast enlargement subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Breast hyperplasia subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Breast mass subjects affected / exposed | 1 / 1123 (0.09%) | 1 / 3358 (0.03%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cervical dysplasia subjects affected / exposed | 0 / 1123 (0.00%) | 3 / 3358 (0.09%) | 3 / 4481 (0.07%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 3 | 1 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

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| Cystocele | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 1 / 3358 (0.03%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dysfunctional uterine bleeding | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Endometrial dysplasia | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Fallopian tube cyst | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Haemorrhagic ovarian cyst | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Menometrorrhagia | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metrorrhagia | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 2 / 3358 (0.06%) | 3 / 4481 (0.07%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ovarian cyst | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 8 / 3358 (0.24%) | 9 / 4481 (0.20%) |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 8 | 1 / 9 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Postmenopausal haemorrhage | | | |

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|---|------------------|------------------|------------------|
| subjects affected / exposed | 1 / 1123 (0.09%) | 2 / 3358 (0.06%) | 3 / 4481 (0.07%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Prostatomegaly | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Rectocele | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Uterine polyp | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 1 / 3358 (0.03%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Uterine prolapse | | | |
| subjects affected / exposed | 3 / 1123 (0.27%) | 1 / 3358 (0.03%) | 4 / 4481 (0.09%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 1 | 0 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Uterovaginal prolapse | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 2 / 3358 (0.06%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vaginal prolapse | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Acute interstitial pneumonitis | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Acute pulmonary oedema | | | |

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|---|------------------|------------------|------------------|
| subjects affected / exposed | 1 / 1123 (0.09%) | 1 / 3358 (0.03%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Acute respiratory distress syndrome | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 3 / 3358 (0.09%) | 4 / 4481 (0.09%) |
| occurrences causally related to treatment / all | 1 / 1 | 3 / 3 | 4 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 2 / 2 | 2 / 2 |
| Acute respiratory failure | | | |
| subjects affected / exposed | 2 / 1123 (0.18%) | 2 / 3358 (0.06%) | 4 / 4481 (0.09%) |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 2 | 1 / 4 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| Adenoidal hypertrophy | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Alveolitis allergic | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Asthma | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bronchiectasis | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 3 / 3358 (0.09%) | 3 / 4481 (0.07%) |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 3 | 2 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bronchospasm | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Chronic obstructive pulmonary disease | | | |

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|---|------------------|------------------|-------------------|
| subjects affected / exposed | 5 / 1123 (0.45%) | 6 / 3358 (0.18%) | 11 / 4481 (0.25%) |
| occurrences causally related to treatment / all | 0 / 5 | 2 / 6 | 2 / 11 |
| deaths causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 2 |
| Cough | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dyspnoea | | | |
| subjects affected / exposed | 2 / 1123 (0.18%) | 4 / 3358 (0.12%) | 6 / 4481 (0.13%) |
| occurrences causally related to treatment / all | 1 / 2 | 1 / 4 | 2 / 6 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Haemoptysis | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 1 / 3358 (0.03%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hydrothorax | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Interstitial lung disease | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 3 / 3358 (0.09%) | 4 / 4481 (0.09%) |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 3 | 1 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Laryngeal oedema | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lower respiratory tract inflammation | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lung disorder | | | |

| | | | |
|---|------------------|-------------------|-------------------|
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lung infiltration | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 2 / 3358 (0.06%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Organising pneumonia | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pleural effusion | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 3 / 3358 (0.09%) | 3 / 4481 (0.07%) |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 3 | 2 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonitis | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 2 / 3358 (0.06%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 2 | 2 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumothorax | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 3 / 3358 (0.09%) | 3 / 4481 (0.07%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary embolism | | | |
| subjects affected / exposed | 3 / 1123 (0.27%) | 16 / 3358 (0.48%) | 19 / 4481 (0.42%) |
| occurrences causally related to treatment / all | 0 / 4 | 4 / 16 | 4 / 20 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| Pulmonary fibrosis | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 1 / 3358 (0.03%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary hypertension | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary mass | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiration abnormal | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory acidosis | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 1 / 1 | 0 / 0 | 1 / 1 |
| Respiratory distress | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory failure | | | |
| subjects affected / exposed | 5 / 1123 (0.45%) | 3 / 3358 (0.09%) | 8 / 4481 (0.18%) |
| occurrences causally related to treatment / all | 2 / 5 | 1 / 3 | 3 / 8 |
| deaths causally related to treatment / all | 1 / 3 | 0 / 1 | 1 / 4 |
| Rhinitis allergic | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Sleep apnoea syndrome | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 2 / 3358 (0.06%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Psychiatric disorders | | | |
| Affective disorder | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Alcoholism | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Anxiety | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Anxiety disorder | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Completed suicide | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 1 / 3358 (0.03%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 2 |
| Confusional state | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 1 / 3358 (0.03%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Depression | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 3 / 3358 (0.09%) | 3 / 4481 (0.07%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Drug abuse | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Post-traumatic stress disorder | | | |

| | | | |
|---|--------------------------------------|------------------|------------------|
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Psychotic disorder due to a general medical condition | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Restlessness | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Stress | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Suicidal ideation | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Depression 1 | Additional description: MedDRA v20.1 | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 0 / 3358 (0.00%) | 0 / 4481 (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 |
| Product issues | | | |
| Device dislocation | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 2 / 3358 (0.06%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Device electrical impedance issue | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Device loosening | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 0 / 1123 (0.00%) | 2 / 3358 (0.06%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatobiliary disorders | | | |
| Bile duct stone | | | |
| subjects affected / exposed | 2 / 1123 (0.18%) | 2 / 3358 (0.06%) | 4 / 4481 (0.09%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | 0 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Biliary colic | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cholangitis acute | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| Cholangitis chronic | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cholecystitis | | | |
| subjects affected / exposed | 2 / 1123 (0.18%) | 1 / 3358 (0.03%) | 3 / 4481 (0.07%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cholecystitis acute | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 4 / 3358 (0.12%) | 5 / 4481 (0.11%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 4 | 0 / 5 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cholecystitis chronic | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 3 / 3358 (0.09%) | 4 / 4481 (0.09%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 3 | 0 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cholelithiasis | | | |

| | | | |
|---|-------------------|-------------------|-------------------|
| subjects affected / exposed | 10 / 1123 (0.89%) | 13 / 3358 (0.39%) | 23 / 4481 (0.51%) |
| occurrences causally related to treatment / all | 1 / 10 | 1 / 14 | 2 / 24 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Drug-induced liver injury | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gallbladder disorder | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gallbladder non-functioning | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatic cirrhosis | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatic congestion | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatic failure | | | |
| subjects affected / exposed | 2 / 1123 (0.18%) | 0 / 3358 (0.00%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| Hepatic steatosis | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatitis | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatotoxicity | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 1 / 3358 (0.03%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 1 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypertransaminasaemia | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Sphincter of Oddi dysfunction | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Investigations | | | |
| Airway peak pressure increased | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| B-lymphocyte count increased | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood creatine phosphokinase increased | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 2 / 3358 (0.06%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| C-reactive protein increased | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac murmur | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Electrocardiogram T wave abnormal | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Electrocardiogram T wave inversion | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Electrocardiogram abnormal | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Haematocrit decreased | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Haemoglobin decreased | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatic enzyme increased | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 4 / 3358 (0.12%) | 4 / 4481 (0.09%) |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 4 | 2 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Human papilloma virus test positive | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Liver function test increased | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metamyelocyte count increased | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Myelocyte count increased | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Red blood cell sedimentation rate increased | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Transaminases increased | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 2 / 3358 (0.06%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Troponin I increased | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Weight decreased | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 2 / 3358 (0.06%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Weight increased | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 2 / 3358 (0.06%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Injury, poisoning and procedural complications | | | |

| | | | |
|---|------------------|------------------|------------------|
| Accidental overdose | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Acetabulum fracture | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 3 / 3358 (0.09%) | 3 / 4481 (0.07%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Anastomotic ulcer | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ankle fracture | | | |
| subjects affected / exposed | 2 / 1123 (0.18%) | 7 / 3358 (0.21%) | 9 / 4481 (0.20%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 7 | 0 / 9 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Burns second degree | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cervical vertebral fracture | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Clavicle fracture | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Concussion | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Contusion | | | |

| | | | |
|---|------------------|-------------------|-------------------|
| subjects affected / exposed | 0 / 1123 (0.00%) | 2 / 3358 (0.06%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dislocation of vertebra | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Exposure via father | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Fall | | | |
| subjects affected / exposed | 7 / 1123 (0.62%) | 9 / 3358 (0.27%) | 16 / 4481 (0.36%) |
| occurrences causally related to treatment / all | 0 / 7 | 0 / 9 | 0 / 16 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Femoral neck fracture | | | |
| subjects affected / exposed | 4 / 1123 (0.36%) | 3 / 3358 (0.09%) | 7 / 4481 (0.16%) |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 4 | 0 / 9 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Femur fracture | | | |
| subjects affected / exposed | 2 / 1123 (0.18%) | 12 / 3358 (0.36%) | 14 / 4481 (0.31%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 12 | 0 / 14 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Fibula fracture | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Foetal exposure during pregnancy | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 2 / 3358 (0.06%) | 3 / 4481 (0.07%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Foot fracture | | | |

| | | | |
|---|------------------|-------------------|-------------------|
| subjects affected / exposed | 1 / 1123 (0.09%) | 4 / 3358 (0.12%) | 5 / 4481 (0.11%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 4 | 0 / 5 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Forearm fracture | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 2 / 3358 (0.06%) | 3 / 4481 (0.07%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Fracture | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Fractured ischium | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 1 / 3358 (0.03%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gun shot wound | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hip fracture | | | |
| subjects affected / exposed | 6 / 1123 (0.53%) | 2 / 3358 (0.06%) | 8 / 4481 (0.18%) |
| occurrences causally related to treatment / all | 0 / 6 | 0 / 2 | 0 / 8 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Humerus fracture | | | |
| subjects affected / exposed | 2 / 1123 (0.18%) | 11 / 3358 (0.33%) | 13 / 4481 (0.29%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 12 | 0 / 14 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Incisional hernia | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 2 / 3358 (0.06%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Incorrect dose administered | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Injury | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Joint dislocation | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 4 / 3358 (0.12%) | 5 / 4481 (0.11%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 4 | 0 / 5 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Joint dislocation postoperative | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Joint injury | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Laceration | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 3 / 3358 (0.09%) | 4 / 4481 (0.09%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 3 | 0 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ligament rupture | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 1 / 3358 (0.03%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 1 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lower limb fracture | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 3 / 3358 (0.09%) | 4 / 4481 (0.09%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 3 | 0 / 4 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| Lumbar vertebral fracture | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 2 / 1123 (0.18%) | 1 / 3358 (0.03%) | 3 / 4481 (0.07%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Maternal exposure timing unspecified | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 2 / 3358 (0.06%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Meniscus injury | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 3 / 3358 (0.09%) | 4 / 4481 (0.09%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 3 | 0 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Muscle injury | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 2 / 3358 (0.06%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Patella fracture | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pelvic fracture | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 2 / 3358 (0.06%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Periprosthetic fracture | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Perirenal haematoma | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Post procedural haemorrhage | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 0 / 1123 (0.00%) | 3 / 3358 (0.09%) | 3 / 4481 (0.07%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Post procedural oedema | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Postoperative hernia | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Postoperative ileus | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Procedural pain | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Radius fracture | | | |
| subjects affected / exposed | 4 / 1123 (0.36%) | 3 / 3358 (0.09%) | 7 / 4481 (0.16%) |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 3 | 0 / 7 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Rib fracture | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 5 / 3358 (0.15%) | 5 / 4481 (0.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 5 | 0 / 5 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Road traffic accident | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 5 / 3358 (0.15%) | 5 / 4481 (0.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 5 | 0 / 5 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| Scapula fracture | | | |

| | | | |
|---|------------------|-------------------|-------------------|
| subjects affected / exposed | 1 / 1123 (0.09%) | 1 / 3358 (0.03%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Skull fracture | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Soft tissue injury | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Spinal column injury | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Spinal compression fracture | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 4 / 3358 (0.12%) | 4 / 4481 (0.09%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 4 | 0 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Sternal fracture | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Subdural haematoma | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Tendon rupture | | | |
| subjects affected / exposed | 2 / 1123 (0.18%) | 10 / 3358 (0.30%) | 12 / 4481 (0.27%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 10 | 0 / 12 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Thermal burn | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Thoracic vertebral fracture | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Tibia fracture | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 7 / 3358 (0.21%) | 7 / 4481 (0.16%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 8 | 0 / 8 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Traumatic liver injury | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Twiddler's syndrome | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ulna fracture | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 3 / 3358 (0.09%) | 4 / 4481 (0.09%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 4 | 0 / 5 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Upper limb fracture | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 4 / 3358 (0.12%) | 5 / 4481 (0.11%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 4 | 0 / 5 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Wound | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 2 / 3358 (0.06%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Wound dehiscence | | | |

| | | | |
|---|--------------------------------------|------------------|------------------|
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Wrist fracture | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 2 / 3358 (0.06%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Humerus fracture 1 | Additional description: MedDRA v20.1 | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 0 / 3358 (0.00%) | 0 / 4481 (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 |
| Congenital, familial and genetic disorders | | | |
| Atrial septal defect | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Developmental hip dysplasia | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hydrocele | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Tourette's disorder | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac disorders | | | |
| Acute myocardial infarction | | | |
| subjects affected / exposed | 4 / 1123 (0.36%) | 4 / 3358 (0.12%) | 8 / 4481 (0.18%) |
| occurrences causally related to treatment / all | 0 / 4 | 1 / 4 | 1 / 8 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |

| | | | |
|---|------------------|-------------------|-------------------|
| Angina pectoris | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Angina unstable | | | |
| subjects affected / exposed | 3 / 1123 (0.27%) | 5 / 3358 (0.15%) | 8 / 4481 (0.18%) |
| occurrences causally related to treatment / all | 1 / 3 | 1 / 5 | 2 / 8 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Aortic valve incompetence | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Aortic valve stenosis | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Arrhythmia | | | |
| subjects affected / exposed | 2 / 1123 (0.18%) | 1 / 3358 (0.03%) | 3 / 4481 (0.07%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 2 |
| Arteriosclerosis coronary artery | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Atrial fibrillation | | | |
| subjects affected / exposed | 6 / 1123 (0.53%) | 14 / 3358 (0.42%) | 20 / 4481 (0.45%) |
| occurrences causally related to treatment / all | 0 / 6 | 4 / 15 | 4 / 21 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Atrial flutter | | | |
| subjects affected / exposed | 2 / 1123 (0.18%) | 1 / 3358 (0.03%) | 3 / 4481 (0.07%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | 0 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Atrioventricular block complete | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 1 / 1123 (0.09%) | 1 / 3358 (0.03%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 1 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Atrioventricular block second degree | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bradycardia | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 1 / 3358 (0.03%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bundle branch block right | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac arrest | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 1 / 3358 (0.03%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 2 |
| Cardiac failure | | | |
| subjects affected / exposed | 3 / 1123 (0.27%) | 5 / 3358 (0.15%) | 8 / 4481 (0.18%) |
| occurrences causally related to treatment / all | 0 / 4 | 1 / 5 | 1 / 9 |
| deaths causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| Cardiac failure congestive | | | |
| subjects affected / exposed | 4 / 1123 (0.36%) | 3 / 3358 (0.09%) | 7 / 4481 (0.16%) |
| occurrences causally related to treatment / all | 0 / 6 | 0 / 3 | 0 / 9 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac tamponade | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardio-respiratory arrest | | | |

| | | | |
|---|------------------|-------------------|-------------------|
| subjects affected / exposed | 3 / 1123 (0.27%) | 1 / 3358 (0.03%) | 4 / 4481 (0.09%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 1 | 0 / 4 |
| deaths causally related to treatment / all | 0 / 2 | 0 / 1 | 0 / 3 |
| Cardiogenic shock | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| Cardiopulmonary failure | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| Cardiovascular insufficiency | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Coronary artery disease | | | |
| subjects affected / exposed | 4 / 1123 (0.36%) | 11 / 3358 (0.33%) | 15 / 4481 (0.33%) |
| occurrences causally related to treatment / all | 1 / 4 | 0 / 11 | 1 / 15 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Coronary artery stenosis | | | |
| subjects affected / exposed | 2 / 1123 (0.18%) | 0 / 3358 (0.00%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Coronary artery thrombosis | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypertensive heart disease | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| Long QT syndrome | | | |

| | | | |
|---|------------------|-------------------|-------------------|
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Mitral valve incompetence | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Mitral valve stenosis | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Myocardial infarction | | | |
| subjects affected / exposed | 8 / 1123 (0.71%) | 13 / 3358 (0.39%) | 21 / 4481 (0.47%) |
| occurrences causally related to treatment / all | 1 / 8 | 3 / 13 | 4 / 21 |
| deaths causally related to treatment / all | 0 / 2 | 0 / 1 | 0 / 3 |
| Myocardial ischaemia | | | |
| subjects affected / exposed | 4 / 1123 (0.36%) | 3 / 3358 (0.09%) | 7 / 4481 (0.16%) |
| occurrences causally related to treatment / all | 1 / 4 | 1 / 3 | 2 / 7 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Palpitations | | | |
| subjects affected / exposed | 2 / 1123 (0.18%) | 1 / 3358 (0.03%) | 3 / 4481 (0.07%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pericardial effusion | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 1 / 3358 (0.03%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 1 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Sinus node dysfunction | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Sinus tachycardia | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Stress cardiomyopathy | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Supraventricular tachycardia | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 2 / 3358 (0.06%) | 3 / 4481 (0.07%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Tachycardia | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 2 / 3358 (0.06%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Tricuspid valve incompetence | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ventricular arrhythmia | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ventricular tachycardia | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Wolff-Parkinson-White syndrome | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| Aphasia | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Brain injury | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| Brain stem infarction | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| Carotid artery aneurysm | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Carotid artery stenosis | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 2 / 3358 (0.06%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Carpal tunnel syndrome | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Central nervous system lesion | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cerebellar ataxia | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 2 / 3358 (0.06%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 2 | 2 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cerebral arteriosclerosis | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 0 / 1123 (0.00%) | 2 / 3358 (0.06%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cerebral haematoma | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cerebral haemorrhage | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 4 / 3358 (0.12%) | 5 / 4481 (0.11%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 4 | 0 / 5 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 2 |
| Cerebral infarction | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 2 / 3358 (0.06%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| Cerebrovascular accident | | | |
| subjects affected / exposed | 2 / 1123 (0.18%) | 6 / 3358 (0.18%) | 8 / 4481 (0.18%) |
| occurrences causally related to treatment / all | 0 / 2 | 1 / 6 | 1 / 8 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| Cervical cord compression | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 2 / 3358 (0.06%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cervical myelopathy | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cervical radiculopathy | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dizziness | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 1 / 1123 (0.09%) | 2 / 3358 (0.06%) | 3 / 4481 (0.07%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 2 | 1 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Facial nerve disorder | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Facial paralysis | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 2 / 3358 (0.06%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Haemorrhagic stroke | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 2 / 3358 (0.06%) | 3 / 4481 (0.07%) |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 2 | 1 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| Headache | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 2 / 3358 (0.06%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hemianopia | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hemiparesis | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Intensive care unit acquired weakness | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Intracranial aneurysm | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Intraventricular haemorrhage | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ischaemic stroke | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 3 / 3358 (0.09%) | 3 / 4481 (0.07%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 3 | 1 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Loss of consciousness | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lumbar radiculopathy | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 1 / 3358 (0.03%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lumbosacral radiculopathy | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolic encephalopathy | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 2 / 3358 (0.06%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Migraine | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Monoplegia | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Multiple sclerosis | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Myasthenia gravis | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Myelopathy | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nerve root compression | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 2 / 3358 (0.06%) | 3 / 4481 (0.07%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Neuritis | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pachymeningitis | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Parkinson's disease | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 2 / 3358 (0.06%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Post herpetic neuralgia | | | |

| | | | |
|---|------------------|------------------|-------------------|
| subjects affected / exposed | 0 / 1123 (0.00%) | 2 / 3358 (0.06%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Posterior reversible encephalopathy syndrome | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Presyncope | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 1 / 3358 (0.03%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Quadriparesis | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Radicular syndrome | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Radiculopathy | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ruptured cerebral aneurysm | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| Sciatica | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 9 / 3358 (0.27%) | 10 / 4481 (0.22%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 9 | 0 / 10 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Seizure | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Sensory loss | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Serotonin syndrome | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Small fibre neuropathy | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Spinal claudication | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 2 / 3358 (0.06%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Spinal subdural haematoma | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Spondylitic myelopathy | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Syncope | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 5 / 3358 (0.15%) | 6 / 4481 (0.13%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 5 | 0 / 6 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Tension headache | | | |

| | | | |
|---|------------------|-------------------|-------------------|
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Transient ischaemic attack | | | |
| subjects affected / exposed | 2 / 1123 (0.18%) | 11 / 3358 (0.33%) | 13 / 4481 (0.29%) |
| occurrences causally related to treatment / all | 0 / 2 | 3 / 12 | 3 / 14 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vasculitis cerebral | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 4 / 1123 (0.36%) | 10 / 3358 (0.30%) | 14 / 4481 (0.31%) |
| occurrences causally related to treatment / all | 1 / 4 | 4 / 10 | 5 / 14 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Haemorrhagic anaemia | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 2 / 3358 (0.06%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Iron deficiency anaemia | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 2 / 3358 (0.06%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Leukocytosis | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Leukopenia | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 3 / 3358 (0.09%) | 4 / 4481 (0.09%) |
| occurrences causally related to treatment / all | 1 / 1 | 2 / 3 | 3 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Mastocytosis | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pancytopenia | | | |
| subjects affected / exposed | 2 / 1123 (0.18%) | 0 / 3358 (0.00%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Paratracheal lymphadenopathy | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Splenic infarction | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Thrombocytopenia | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ear and labyrinth disorders | | | |
| Acute vestibular syndrome | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vertigo | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 1 / 3358 (0.03%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 1 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vertigo positional | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 3 / 3358 (0.09%) | 4 / 4481 (0.09%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 3 | 0 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vestibular disorder | | | |

| | | | |
|---|------------------|------------------|-------------------|
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Eye disorders | | | |
| Cataract | | | |
| subjects affected / exposed | 2 / 1123 (0.18%) | 8 / 3358 (0.24%) | 10 / 4481 (0.22%) |
| occurrences causally related to treatment / all | 0 / 3 | 1 / 8 | 1 / 11 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Glaucoma | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 2 / 3358 (0.06%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Keratitis interstitial | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Necrotising retinitis | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Optic disc drusen | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Retinal artery occlusion | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 2 / 3358 (0.06%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Retinal detachment | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ulcerative keratitis | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 1 / 1123 (0.09%) | 1 / 3358 (0.03%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 1 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Uveitis | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 2 / 3358 (0.06%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Visual acuity reduced | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| Abdominal hernia | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Abdominal incarcerated hernia | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 3 / 3358 (0.09%) | 3 / 4481 (0.07%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 3 | 1 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Abdominal pain lower | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Abdominal pain upper | | | |
| subjects affected / exposed | 2 / 1123 (0.18%) | 0 / 3358 (0.00%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ascites | | | |

| | | | |
|---|------------------|------------------|-------------------|
| subjects affected / exposed | 1 / 1123 (0.09%) | 1 / 3358 (0.03%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 1 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Chronic gastritis | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 1 / 3358 (0.03%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 1 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Colitis | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 5 / 3358 (0.15%) | 6 / 4481 (0.13%) |
| occurrences causally related to treatment / all | 0 / 1 | 3 / 5 | 3 / 6 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Colitis ischaemic | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Colitis ulcerative | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 1 / 3358 (0.03%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Crohn's disease | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diarrhoea | | | |
| subjects affected / exposed | 2 / 1123 (0.18%) | 8 / 3358 (0.24%) | 10 / 4481 (0.22%) |
| occurrences causally related to treatment / all | 1 / 2 | 2 / 8 | 3 / 10 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diverticular perforation | | | |
| subjects affected / exposed | 3 / 1123 (0.27%) | 5 / 3358 (0.15%) | 8 / 4481 (0.18%) |
| occurrences causally related to treatment / all | 1 / 3 | 3 / 5 | 4 / 8 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diverticulum | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 2 / 1123 (0.18%) | 0 / 3358 (0.00%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Duodenal polyp | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Duodenal ulcer haemorrhage | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dyspepsia | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Enterocoele | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Enterocolitis | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 2 / 3358 (0.06%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Faecaloma | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 2 / 3358 (0.06%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Fistula of small intestine | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Food poisoning | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastric disorder | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastric perforation | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastric polyps | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastric ulcer | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 1 / 3358 (0.03%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 1 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastric ulcer haemorrhage | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastritis | | | |
| subjects affected / exposed | 3 / 1123 (0.27%) | 4 / 3358 (0.12%) | 7 / 4481 (0.16%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 4 | 0 / 7 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastritis erosive | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorder | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 2 / 1123 (0.18%) | 0 / 3358 (0.00%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal inflammation | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal perforation | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrooesophageal reflux disease | | | |
| subjects affected / exposed | 2 / 1123 (0.18%) | 0 / 3358 (0.00%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Haematemesis | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| Haematochezia | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Haemorrhagic erosive gastritis | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Haemorrhoidal haemorrhage | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 0 / 1123 (0.00%) | 2 / 3358 (0.06%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Haemorrhoids | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hiatus hernia | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ileus | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ileus paralytic | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Inguinal hernia | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 2 / 3358 (0.06%) | 3 / 4481 (0.07%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 3 | 0 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Intestinal ischaemia | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 2 / 3358 (0.06%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| Intestinal obstruction | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Large intestinal stenosis | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Large intestine perforation | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Large intestine polyp | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 2 / 3358 (0.06%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lower gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Melaena | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Mesenteric vein thrombosis | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nausea | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Oesophageal spasm | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pancreatitis | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 1 / 1123 (0.09%) | 4 / 3358 (0.12%) | 5 / 4481 (0.11%) |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 5 | 2 / 6 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pancreatitis acute | | | |
| subjects affected / exposed | 4 / 1123 (0.36%) | 4 / 3358 (0.12%) | 8 / 4481 (0.18%) |
| occurrences causally related to treatment / all | 1 / 4 | 1 / 4 | 2 / 8 |
| deaths causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 2 |
| Peptic ulcer haemorrhage | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Rectal haemorrhage | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 1 / 3358 (0.03%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Rectal prolapse | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Retroperitoneal haematoma | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Small intestinal obstruction | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 3 / 3358 (0.09%) | 3 / 4481 (0.07%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 5 | 0 / 5 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Tooth disorder | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Tooth impacted | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Umbilical hernia | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 3 / 3358 (0.09%) | 4 / 4481 (0.09%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 3 | 0 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Upper gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vomiting | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 1 / 3358 (0.03%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Skin and subcutaneous tissue disorders | | | |
| Actinic keratosis | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 1 / 3358 (0.03%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 1 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Decubitus ulcer | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Drug reaction with eosinophilia and systemic symptoms | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Panniculitis | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Rash | | | |

| | | | |
|---|------------------|------------------|-------------------|
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Rash maculo-papular | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Scar pain | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Skin lesion | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Skin ulcer | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urticaria | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal and urinary disorders | | | |
| Acute kidney injury | | | |
| subjects affected / exposed | 6 / 1123 (0.53%) | 6 / 3358 (0.18%) | 12 / 4481 (0.27%) |
| occurrences causally related to treatment / all | 1 / 6 | 0 / 6 | 1 / 12 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| Anuria | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Calculus bladder | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Calculus urinary | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Chronic kidney disease | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Haematuria | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 2 / 3358 (0.06%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hydronephrosis | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Mixed incontinence | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nephrolithiasis | | | |
| subjects affected / exposed | 2 / 1123 (0.18%) | 5 / 3358 (0.15%) | 7 / 4481 (0.16%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 5 | 0 / 7 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Obstructive uropathy | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 2 / 3358 (0.06%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Proteinuria | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pyelocaliectasis | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal colic | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 3 / 3358 (0.09%) | 4 / 4481 (0.09%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 3 | 0 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal failure | | | |
| subjects affected / exposed | 3 / 1123 (0.27%) | 1 / 3358 (0.03%) | 4 / 4481 (0.09%) |
| occurrences causally related to treatment / all | 0 / 3 | 1 / 1 | 1 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| Renal impairment | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ureteral necrosis | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ureteric stenosis | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ureterolithiasis | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 4 / 3358 (0.12%) | 4 / 4481 (0.09%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 4 | 0 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urethral meatus stenosis | | | |

| | | | |
|---|------------------|------------------|-------------------|
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urinary incontinence | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 2 / 3358 (0.06%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urinary retention | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 2 / 3358 (0.06%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Endocrine disorders | | | |
| Adrenal insufficiency | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Goitre | | | |
| subjects affected / exposed | 3 / 1123 (0.27%) | 7 / 3358 (0.21%) | 10 / 4481 (0.22%) |
| occurrences causally related to treatment / all | 0 / 3 | 1 / 7 | 1 / 10 |
| deaths causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| Hyperparathyroidism primary | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hyperthyroidism | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 4 / 3358 (0.12%) | 4 / 4481 (0.09%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 4 | 0 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Acquired claw toe | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 2 / 3358 (0.06%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|------------------|-------------------|-------------------|
| Arthralgia | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 8 / 3358 (0.24%) | 9 / 4481 (0.20%) |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 8 | 1 / 9 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Arthritis | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 4 / 3358 (0.12%) | 5 / 4481 (0.11%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 5 | 0 / 6 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Arthropathy | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 4 / 3358 (0.12%) | 4 / 4481 (0.09%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 5 | 0 / 5 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Atlantoaxial instability | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Back pain | | | |
| subjects affected / exposed | 4 / 1123 (0.36%) | 13 / 3358 (0.39%) | 17 / 4481 (0.38%) |
| occurrences causally related to treatment / all | 0 / 6 | 0 / 14 | 0 / 20 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bone disorder | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bursitis | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 1 / 3358 (0.03%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cervical spinal stenosis | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dupuytren's contracture | | | |

| | | | |
|---|------------------|-------------------|-------------------|
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Exostosis | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 1 / 3358 (0.03%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Extraskkeletal ossification | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Finger deformity | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Foot deformity | | | |
| subjects affected / exposed | 5 / 1123 (0.45%) | 12 / 3358 (0.36%) | 17 / 4481 (0.38%) |
| occurrences causally related to treatment / all | 0 / 6 | 0 / 12 | 0 / 18 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gouty arthritis | | | |
| subjects affected / exposed | 2 / 1123 (0.18%) | 0 / 3358 (0.00%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Groin pain | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Haemarthrosis | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 1 / 3358 (0.03%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | 2 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hand deformity | | | |

| | | | |
|---|------------------|-------------------|-------------------|
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Intervertebral disc disorder | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 4 / 3358 (0.12%) | 4 / 4481 (0.09%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 4 | 0 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Intervertebral disc protrusion | | | |
| subjects affected / exposed | 3 / 1123 (0.27%) | 11 / 3358 (0.33%) | 14 / 4481 (0.31%) |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 11 | 0 / 15 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Joint contracture | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 2 / 3358 (0.06%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Joint destruction | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Joint range of motion decreased | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 2 / 3358 (0.06%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Joint swelling | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 2 / 3358 (0.06%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Kyphosis | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ligament disorder | | | |

| | | | |
|---|-------------------|-------------------|-------------------|
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lumbar spinal stenosis | | | |
| subjects affected / exposed | 5 / 1123 (0.45%) | 4 / 3358 (0.12%) | 9 / 4481 (0.20%) |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 4 | 0 / 9 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Meniscal degeneration | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metatarsalgia | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal chest pain | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 3 / 3358 (0.09%) | 3 / 4481 (0.07%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Myopathy | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Osteoarthritis | | | |
| subjects affected / exposed | 21 / 1123 (1.87%) | 63 / 3358 (1.88%) | 84 / 4481 (1.87%) |
| occurrences causally related to treatment / all | 0 / 25 | 2 / 67 | 2 / 92 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Osteonecrosis | | | |
| subjects affected / exposed | 2 / 1123 (0.18%) | 5 / 3358 (0.15%) | 7 / 4481 (0.16%) |
| occurrences causally related to treatment / all | 0 / 2 | 1 / 5 | 1 / 7 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pain in extremity | | | |

| | | | |
|---|-------------------|-------------------|-------------------|
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pathological fracture | | | |
| subjects affected / exposed | 2 / 1123 (0.18%) | 1 / 3358 (0.03%) | 3 / 4481 (0.07%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Polyarthritis | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Rhabdomyolysis | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Rheumatic disorder | | | |
| subjects affected / exposed | 2 / 1123 (0.18%) | 1 / 3358 (0.03%) | 3 / 4481 (0.07%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Rheumatoid arthritis | | | |
| subjects affected / exposed | 11 / 1123 (0.98%) | 23 / 3358 (0.68%) | 34 / 4481 (0.76%) |
| occurrences causally related to treatment / all | 0 / 12 | 2 / 24 | 2 / 36 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Rheumatoid nodule | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Rotator cuff syndrome | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 7 / 3358 (0.21%) | 7 / 4481 (0.16%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 7 | 0 / 7 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Spinal column stenosis | | | |

| | | | |
|---|------------------|------------------|-------------------|
| subjects affected / exposed | 1 / 1123 (0.09%) | 8 / 3358 (0.24%) | 9 / 4481 (0.20%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 9 | 0 / 10 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Spinal osteoarthritis | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Spinal pain | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 2 / 3358 (0.06%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Spondylitis | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 1 / 3358 (0.03%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Spondylolisthesis | | | |
| subjects affected / exposed | 2 / 1123 (0.18%) | 8 / 3358 (0.24%) | 10 / 4481 (0.22%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 8 | 0 / 10 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Synovial disorder | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Synovitis | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 2 / 3358 (0.06%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Tendon calcification | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Tenosynovitis | | | |

| | | | |
|---|------------------|-------------------|-------------------|
| subjects affected / exposed | 0 / 1123 (0.00%) | 2 / 3358 (0.06%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Abdominal abscess | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Abdominal wall abscess | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Abscess | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Abscess limb | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 3 / 3358 (0.09%) | 4 / 4481 (0.09%) |
| occurrences causally related to treatment / all | 1 / 1 | 2 / 3 | 3 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Abscess neck | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Anal abscess | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Appendicitis | | | |
| subjects affected / exposed | 6 / 1123 (0.53%) | 11 / 3358 (0.33%) | 17 / 4481 (0.38%) |
| occurrences causally related to treatment / all | 2 / 6 | 2 / 11 | 4 / 17 |
| deaths causally related to treatment / all | 1 / 1 | 0 / 0 | 1 / 1 |
| Appendicitis perforated | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 0 / 1123 (0.00%) | 3 / 3358 (0.09%) | 3 / 4481 (0.07%) |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 3 | 2 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Arthritis bacterial | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 4 / 3358 (0.12%) | 5 / 4481 (0.11%) |
| occurrences causally related to treatment / all | 0 / 2 | 3 / 4 | 3 / 6 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| Arthritis infective | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Atypical pneumonia | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 3 / 3358 (0.09%) | 3 / 4481 (0.07%) |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 3 | 2 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bacteraemia | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 2 / 3358 (0.06%) | 3 / 4481 (0.07%) |
| occurrences causally related to treatment / all | 0 / 1 | 2 / 2 | 2 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bacterial pyelonephritis | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bartholin's abscess | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bone tuberculosis | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 1 / 3358 (0.03%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | 2 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bronchiolitis | | | |

| | | | |
|---|------------------|-------------------|-------------------|
| subjects affected / exposed | 1 / 1123 (0.09%) | 1 / 3358 (0.03%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 1 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bronchitis | | | |
| subjects affected / exposed | 3 / 1123 (0.27%) | 5 / 3358 (0.15%) | 8 / 4481 (0.18%) |
| occurrences causally related to treatment / all | 2 / 3 | 3 / 5 | 5 / 8 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bronchopulmonary aspergillosis | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| Bursitis infective | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 2 / 3358 (0.06%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Campylobacter gastroenteritis | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cellulitis | | | |
| subjects affected / exposed | 2 / 1123 (0.18%) | 14 / 3358 (0.42%) | 16 / 4481 (0.36%) |
| occurrences causally related to treatment / all | 0 / 2 | 7 / 14 | 7 / 16 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cellulitis gangrenous | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Chronic sinusitis | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 2 / 3358 (0.06%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Chronic tonsillitis | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 1 / 1123 (0.09%) | 1 / 3358 (0.03%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Clostridial infection | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Clostridium difficile colitis | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 2 / 3358 (0.06%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| Clostridium difficile infection | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Colonic abscess | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 2 / 3358 (0.06%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 2 | 2 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cytomegalovirus chorioretinitis | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cytomegalovirus hepatitis | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dengue fever | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 3 / 3358 (0.09%) | 3 / 4481 (0.07%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Device related infection | | | |

| | | | |
|---|------------------|-------------------|-------------------|
| subjects affected / exposed | 1 / 1123 (0.09%) | 3 / 3358 (0.09%) | 4 / 4481 (0.09%) |
| occurrences causally related to treatment / all | 0 / 1 | 2 / 3 | 2 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| Diabetic gangrene | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diarrhoea infectious | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Disseminated tuberculosis | | | |
| subjects affected / exposed | 3 / 1123 (0.27%) | 4 / 3358 (0.12%) | 7 / 4481 (0.16%) |
| occurrences causally related to treatment / all | 3 / 3 | 4 / 4 | 7 / 7 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diverticulitis | | | |
| subjects affected / exposed | 5 / 1123 (0.45%) | 12 / 3358 (0.36%) | 17 / 4481 (0.38%) |
| occurrences causally related to treatment / all | 4 / 5 | 8 / 12 | 12 / 17 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Encephalitis | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 1 / 3358 (0.03%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | 2 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| Epstein-Barr virus infection | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Erysipelas | | | |
| subjects affected / exposed | 2 / 1123 (0.18%) | 2 / 3358 (0.06%) | 4 / 4481 (0.09%) |
| occurrences causally related to treatment / all | 1 / 2 | 2 / 2 | 3 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Escherichia bacteraemia | | | |

| | | | |
|---|------------------|-------------------|-------------------|
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Escherichia sepsis | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Extradural abscess | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 2 / 3358 (0.06%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 2 | 2 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Eye infection fungal | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastroenteritis | | | |
| subjects affected / exposed | 2 / 1123 (0.18%) | 13 / 3358 (0.39%) | 15 / 4481 (0.33%) |
| occurrences causally related to treatment / all | 0 / 2 | 4 / 13 | 4 / 15 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastroenteritis viral | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 4 / 3358 (0.12%) | 4 / 4481 (0.09%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 4 | 0 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal viral infection | | | |
| subjects affected / exposed | 2 / 1123 (0.18%) | 0 / 3358 (0.00%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Groin abscess | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| H1N1 influenza | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 0 / 1123 (0.00%) | 2 / 3358 (0.06%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 2 | 2 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| HIV infection | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatitis A | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatitis B | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 2 / 3358 (0.06%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatitis C | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatitis E | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Herpes dermatitis | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Herpes simplex | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Herpes virus infection | | | |

| | | | |
|---|------------------|-------------------|-------------------|
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Herpes zoster | | | |
| subjects affected / exposed | 2 / 1123 (0.18%) | 16 / 3358 (0.48%) | 18 / 4481 (0.40%) |
| occurrences causally related to treatment / all | 2 / 2 | 16 / 16 | 18 / 18 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Herpes zoster cutaneous disseminated | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Herpes zoster disseminated | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 5 / 3358 (0.15%) | 5 / 4481 (0.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 5 / 5 | 5 / 5 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Herpes zoster oticus | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Incision site infection | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infected seroma | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infected skin ulcer | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infectious colitis | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infectious mononucleosis | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infective exacerbation of bronchiectasis | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infective exacerbation of chronic obstructive airways disease | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infective spondylitis | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Influenza | | | |
| subjects affected / exposed | 3 / 1123 (0.27%) | 0 / 3358 (0.00%) | 3 / 4481 (0.07%) |
| occurrences causally related to treatment / all | 1 / 3 | 0 / 0 | 1 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Joint abscess | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Joint tuberculosis | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lower respiratory tract infection | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 1 / 1123 (0.09%) | 1 / 3358 (0.03%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 1 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lower respiratory tract infection bacterial | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lung infection | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lyme disease | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lymph node tuberculosis | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 3 / 3358 (0.09%) | 3 / 4481 (0.07%) |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 3 | 2 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Meningitis | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Meningitis bacterial | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Meningitis cryptococcal | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Meningococcal bacteraemia | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Meningoencephalitis bacterial | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nasopharyngitis | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Necrotising fasciitis | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 1 / 3358 (0.03%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | 2 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Oesophageal candidiasis | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 1 / 3358 (0.03%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 1 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ophthalmic herpes simplex | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 2 / 3358 (0.06%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 2 | 2 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ophthalmic herpes zoster | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Osteomyelitis | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 4 / 3358 (0.12%) | 4 / 4481 (0.09%) |
| occurrences causally related to treatment / all | 0 / 0 | 5 / 5 | 5 / 5 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Otitis media | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pelvic inflammatory disease | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Periorbital cellulitis | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Perirectal abscess | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Peritoneal tuberculosis | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Peritonitis | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 3 / 3358 (0.09%) | 4 / 4481 (0.09%) |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 3 | 1 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Peritonsillar abscess | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pertussis | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pharyngeal abscess | | | |

| | | | |
|---|-------------------|-------------------|-------------------|
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia | | | |
| subjects affected / exposed | 21 / 1123 (1.87%) | 70 / 3358 (2.08%) | 91 / 4481 (2.03%) |
| occurrences causally related to treatment / all | 10 / 21 | 53 / 71 | 63 / 92 |
| deaths causally related to treatment / all | 2 / 4 | 3 / 4 | 5 / 8 |
| Pneumonia bacterial | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 2 / 3358 (0.06%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 2 | 2 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| Pneumonia cryptococcal | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 2 / 3358 (0.06%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 2 | 2 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia cytomegaloviral | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia legionella | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 2 / 3358 (0.06%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 2 | 2 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia necrotising | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 2 / 3358 (0.06%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 2 | 2 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| Pneumonia pneumococcal | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 1 / 3358 (0.03%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 1 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia streptococcal | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Post procedural infection | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Postoperative abscess | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 2 / 3358 (0.06%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Postoperative wound infection | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 5 / 3358 (0.15%) | 5 / 4481 (0.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 4 / 5 | 4 / 5 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Primary syphilis | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Psoas abscess | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary sepsis | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary tuberculosis | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 7 / 3358 (0.21%) | 8 / 4481 (0.18%) |
| occurrences causally related to treatment / all | 1 / 1 | 7 / 7 | 8 / 8 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulpitis dental | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pyelonephritis | | | |
| subjects affected / exposed | 3 / 1123 (0.27%) | 2 / 3358 (0.06%) | 5 / 4481 (0.11%) |
| occurrences causally related to treatment / all | 3 / 3 | 2 / 2 | 5 / 5 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pyelonephritis acute | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 5 / 3358 (0.15%) | 6 / 4481 (0.13%) |
| occurrences causally related to treatment / all | 0 / 1 | 2 / 5 | 2 / 6 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pyoderma streptococcal | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pyometra | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Rectal abscess | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal abscess | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal cyst infection | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory tract infection | | | |

| | | | |
|---|------------------|------------------|-------------------|
| subjects affected / exposed | 0 / 1123 (0.00%) | 5 / 3358 (0.15%) | 5 / 4481 (0.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 4 / 5 | 4 / 5 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Retinitis | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Salpingo-oophoritis | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Secondary syphilis | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Sepsis | | | |
| subjects affected / exposed | 5 / 1123 (0.45%) | 8 / 3358 (0.24%) | 13 / 4481 (0.29%) |
| occurrences causally related to treatment / all | 1 / 5 | 5 / 8 | 6 / 13 |
| deaths causally related to treatment / all | 1 / 3 | 2 / 2 | 3 / 5 |
| Sepsis syndrome | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Septic shock | | | |
| subjects affected / exposed | 3 / 1123 (0.27%) | 4 / 3358 (0.12%) | 7 / 4481 (0.16%) |
| occurrences causally related to treatment / all | 3 / 3 | 2 / 4 | 5 / 7 |
| deaths causally related to treatment / all | 1 / 1 | 1 / 2 | 2 / 3 |
| Sinusitis | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 4 / 3358 (0.12%) | 4 / 4481 (0.09%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 4 | 1 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Sinusitis aspergillus | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Sinusitis fungal | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Skin infection | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 2 / 3358 (0.06%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 2 | 2 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Splenic abscess | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Staphylococcal bacteraemia | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 3 / 3358 (0.09%) | 3 / 4481 (0.07%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 3 | 1 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Staphylococcal infection | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 1 / 3358 (0.03%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| Staphylococcal sepsis | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Streptococcal infection | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Subcutaneous abscess | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Superinfection | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Tonsillitis | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 2 / 3358 (0.06%) | 3 / 4481 (0.07%) |
| occurrences causally related to treatment / all | 0 / 1 | 2 / 2 | 2 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Tooth abscess | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Toxic shock syndrome | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| Tuberculosis | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 1 / 3358 (0.03%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 1 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Tuberculosis of central nervous system | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Tubo-ovarian abscess | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Upper respiratory tract infection | | | |

| | | | |
|---|------------------|-------------------|-------------------|
| subjects affected / exposed | 0 / 1123 (0.00%) | 2 / 3358 (0.06%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Upper respiratory tract infection bacterial | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urinary tract infection | | | |
| subjects affected / exposed | 8 / 1123 (0.71%) | 14 / 3358 (0.42%) | 22 / 4481 (0.49%) |
| occurrences causally related to treatment / all | 6 / 10 | 9 / 14 | 15 / 24 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| Urinary tract infection bacterial | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urosepsis | | | |
| subjects affected / exposed | 2 / 1123 (0.18%) | 0 / 3358 (0.00%) | 2 / 4481 (0.04%) |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Varicella zoster virus infection | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vestibular neuronitis | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Viral infection | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Wound infection | | | |

| | | | |
|---|--------------------------------------|------------------|------------------|
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Wound infection bacterial | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Wound infection staphylococcal | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Herpes zoster 1 | Additional description: MedDRA v20.1 | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 0 / 3358 (0.00%) | 0 / 4481 (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 1 | Additional description: MedDRA v20.1 | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 0 / 3358 (0.00%) | 0 / 4481 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolism and nutrition disorders | | | |
| Dehydration | | | |
| subjects affected / exposed | 3 / 1123 (0.27%) | 6 / 3358 (0.18%) | 9 / 4481 (0.20%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 6 | 0 / 9 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diabetes mellitus | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 3 / 3358 (0.09%) | 4 / 4481 (0.09%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 3 | 0 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diabetic ketoacidosis | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hyperglycaemia | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypoglycaemia unawareness | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 1 / 3358 (0.03%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypokalaemia | | | |
| subjects affected / exposed | 3 / 1123 (0.27%) | 1 / 3358 (0.03%) | 4 / 4481 (0.09%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 1 | 0 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypovolaemia | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolic syndrome | | | |
| subjects affected / exposed | 1 / 1123 (0.09%) | 0 / 3358 (0.00%) | 1 / 4481 (0.02%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Obesity | | | |
| subjects affected / exposed | 0 / 1123 (0.00%) | 3 / 3358 (0.09%) | 3 / 4481 (0.07%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| Serious adverse events | Extension Period: Tofacitinib 5 mg | | |
|---|---------------------------------------|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 5 / 48 (10.42%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| 5q minus syndrome | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | | |
|--|----------------|--|--|--|
| Acute promyelocytic leukaemia subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Adenocarcinoma of appendix subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Adenocarcinoma of colon subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Adenocarcinoma of the cervix subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Adrenal adenoma subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| B-cell lymphoma subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| B-cell small lymphocytic lymphoma subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Basal cell carcinoma subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Benign salivary gland neoplasm | | | | |

| | | | | |
|---|----------------|--|--|--|
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Benign tracheal neoplasm | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Bladder cancer | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Bladder neoplasm | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Bladder transitional cell carcinoma | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Breast cancer | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Breast cancer metastatic | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Bronchial carcinoma | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Cervix carcinoma | | | | |

| | | | | |
|---|----------------|--|--|--|
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Cervix carcinoma stage 0 | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Cholesteatoma | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Choroid plexus papilloma | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Colon adenoma | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Colon cancer | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Colon cancer metastatic | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Colorectal adenocarcinoma | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Diffuse large B-cell lymphoma | | | | |

| | | | | |
|--|----------------|--|--|--|
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Endometrial adenocarcinoma | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Endometrial cancer | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Endometrial cancer stage I | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Extranodal marginal zone B-cell lymphoma (MALT type) | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Fibroadenoma of breast | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Fibroma | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Gallbladder cancer | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Gastric cancer | | | | |

| | | | | |
|---|----------------|--|--|--|
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Glioblastoma multiforme | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Hepatic cancer | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Hodgkin's disease | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Intraductal proliferative breast lesion | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Invasive ductal breast carcinoma | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Kaposi's sarcoma | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Laryngeal cancer | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Laryngeal squamous cell carcinoma | | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Leiomyosarcoma | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Lipoma | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Liposarcoma | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Lung adenocarcinoma | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Lung adenocarcinoma metastatic | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Lung cancer metastatic | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Lung neoplasm | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Lung neoplasm malignant | | | |

| | | | | |
|---|----------------|--|--|--|
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Lymphoma | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Malignant melanoma | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Malignant melanoma in situ | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Malignant peritoneal neoplasm | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Mantle cell lymphoma | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Marginal zone lymphoma stage II | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Medullary thyroid cancer | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Meningioma | | | | |

| | | | | |
|---|----------------|--|--|--|
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Metastases to bone | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Metastases to liver | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Metastases to lung | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Metastases to lymph nodes | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Metastasis | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Metastatic malignant melanoma | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Mucoepidermoid carcinoma | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Neoplasm | | | | |

| | | | | |
|---|----------------|--|--|--|
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Neoplasm malignant | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Nodular melanoma | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Non-Hodgkin's lymphoma | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Non-small cell lung cancer | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Non-small cell lung cancer metastatic | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Oesophageal carcinoma | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Ovarian adenoma | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Ovarian cancer | | | | |

| | | | | |
|---|----------------|--|--|--|
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Ovarian cancer metastatic | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Ovarian germ cell teratoma | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Papillary thyroid cancer | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Parathyroid tumour | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Prostate cancer | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Prostatic adenoma | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Renal cancer | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Renal cell carcinoma | | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Sebacaceous carcinoma | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Skin cancer | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Small cell lung cancer | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Small cell lung cancer metastatic | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Small intestine carcinoma | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Spindle cell sarcoma | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Squamous cell carcinoma | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Squamous cell carcinoma of lung | | | |

| | | | | |
|---|----------------|--|--|--|
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Squamous cell carcinoma of skin | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Squamous cell carcinoma of the cervix | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Squamous cell carcinoma of the tongue | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Squamous cell carcinoma of the vulva | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Synovial sarcoma | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| T-cell lymphoma | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Thyroid adenoma | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Thyroid cancer | | | | |

| | | | |
|---|--------------------------------------|--|--|
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Thyroid neoplasm | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Tumour necrosis | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Ureteral neoplasm | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Uterine leiomyoma | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Vulval cancer stage 0 | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Basal cell carcinoma 1 | Additional description: MedDRA v20.1 | | |
| subjects affected / exposed | 1 / 48 (2.08%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Vascular disorders | | | |
| Accelerated hypertension | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Aortic aneurysm | | | |

| | | | | |
|---|----------------|--|--|--|
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Aortic dissection | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Aortic stenosis | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Arteriosclerosis | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Circulatory collapse | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Deep vein thrombosis | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Extremity necrosis | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Haematoma | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Hypertension | | | | |

| | | | | |
|---|----------------|--|--|--|
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Hypertensive crisis | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Hypotension | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Hypovolaemic shock | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Peripheral artery occlusion | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Peripheral venous disease | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Shock | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Thromboangiitis obliterans | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Thrombophlebitis | | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Varicose vein | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Venous thrombosis limb | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Surgical and medical procedures | | | |
| Arthrodesis | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hip arthroplasty | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Knee arthroplasty | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pregnancy, puerperium and perinatal conditions | | | |
| Abortion spontaneous | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Foetal death | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | |
|--|----------------|--|--|
| Pregnancy | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Unintended pregnancy | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| General disorders and administration site conditions | | | |
| Abscess sterile | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Asthenia | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Chest discomfort | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Chest pain | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Death | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Drug ineffective | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | | |
|---|----------------|--|--|--|
| Fatigue | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Fibrosis | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Gait disturbance | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Hernia | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Multiple organ dysfunction syndrome | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Non-cardiac chest pain | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Oedema | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Oedema peripheral | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Peripheral swelling | | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pyrexia | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Sudden death | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Systemic inflammatory response syndrome | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Immune system disorders | | | |
| Allergy to arthropod bite | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Allergy to arthropod sting | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Anaphylactic reaction | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Anaphylactic shock | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Social circumstances | | | |

| | | | |
|--|----------------|--|--|
| Activities of daily living impaired subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Physical abuse subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Reproductive system and breast disorders | | | |
| Adenomyosis subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Benign prostatic hyperplasia subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Breast enlargement subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Breast hyperplasia subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Breast mass subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cervical dysplasia subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | | |
|---|----------------|--|--|--|
| Cystocele | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Dysfunctional uterine bleeding | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Endometrial dysplasia | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Fallopian tube cyst | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Haemorrhagic ovarian cyst | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Menometrorrhagia | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Metrorrhagia | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Ovarian cyst | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Postmenopausal haemorrhage | | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Prostatomegaly | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Rectocele | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Uterine polyp | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Uterine prolapse | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Uterovaginal prolapse | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Vaginal prolapse | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Acute interstitial pneumonitis | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Acute pulmonary oedema | | | |

| | | | | |
|---|----------------|--|--|--|
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Acute respiratory distress syndrome | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Acute respiratory failure | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Adenoidal hypertrophy | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Alveolitis allergic | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Asthma | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Bronchiectasis | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Bronchospasm | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Chronic obstructive pulmonary disease | | | | |

| | | | | |
|---|----------------|--|--|--|
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Cough | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Dyspnoea | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Haemoptysis | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Hydrothorax | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Interstitial lung disease | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Laryngeal oedema | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Lower respiratory tract inflammation | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Lung disorder | | | | |

| | | | | |
|---|----------------|--|--|--|
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Lung infiltration | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Organising pneumonia | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pleural effusion | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pneumonitis | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pneumothorax | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pulmonary embolism | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pulmonary fibrosis | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pulmonary hypertension | | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pulmonary mass | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiration abnormal | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory acidosis | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory distress | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory failure | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Rhinitis allergic | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Sleep apnoea syndrome | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Psychiatric disorders | | | |
| Affective disorder | | | |

| | | | | |
|---|----------------|--|--|--|
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Alcoholism | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Anxiety | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Anxiety disorder | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Completed suicide | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Confusional state | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Depression | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Drug abuse | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Post-traumatic stress disorder | | | | |

| | | | |
|---|--------------------------------------|--|--|
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Psychotic disorder due to a general medical condition | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Restlessness | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Stress | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Suicidal ideation | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Depression 1 | Additional description: MedDRA v20.1 | | |
| subjects affected / exposed | 1 / 48 (2.08%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Product issues | | | |
| Device dislocation | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Device electrical impedance issue | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Device loosening | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hepatobiliary disorders | | | |
| Bile duct stone | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Biliary colic | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cholangitis acute | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cholangitis chronic | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cholecystitis | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cholecystitis acute | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cholecystitis chronic | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cholelithiasis | | | |

| | | | | |
|---|----------------|--|--|--|
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Drug-induced liver injury | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Gallbladder disorder | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Gallbladder non-functioning | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Hepatic cirrhosis | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Hepatic congestion | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Hepatic failure | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Hepatic steatosis | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Hepatitis | | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hepatotoxicity | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hypertransaminasaemia | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Sphincter of Oddi dysfunction | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Investigations | | | |
| Airway peak pressure increased | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| B-lymphocyte count increased | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Blood creatine phosphokinase increased | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| C-reactive protein increased | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cardiac murmur | | | |

| | | | | |
|---|----------------|--|--|--|
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Electrocardiogram T wave abnormal | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Electrocardiogram T wave inversion | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Electrocardiogram abnormal | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Haematocrit decreased | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Haemoglobin decreased | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Hepatic enzyme increased | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Human papilloma virus test positive | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Liver function test increased | | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Metamyelocyte count increased | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Myelocyte count increased | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Red blood cell sedimentation rate increased | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Transaminases increased | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Troponin I increased | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Weight decreased | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Weight increased | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Injury, poisoning and procedural complications | | | |

| | | | | |
|---|----------------|--|--|--|
| Accidental overdose | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Acetabulum fracture | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Anastomotic ulcer | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Ankle fracture | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Burns second degree | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Cervical vertebral fracture | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Clavicle fracture | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Concussion | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Contusion | | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Dislocation of vertebra | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Exposure via father | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Fall | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Femoral neck fracture | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Femur fracture | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Fibula fracture | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Foetal exposure during pregnancy | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Foot fracture | | | |

| | | | | |
|---|----------------|--|--|--|
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Forearm fracture | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Fracture | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Fractured ischium | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Gun shot wound | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Hip fracture | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Humerus fracture | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Incisional hernia | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Incorrect dose administered | | | | |

| | | | | |
|---|----------------|--|--|--|
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Injury | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Joint dislocation | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Joint dislocation postoperative | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Joint injury | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Laceration | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Ligament rupture | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Lower limb fracture | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Lumbar vertebral fracture | | | | |

| | | | | |
|---|----------------|--|--|--|
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Maternal exposure timing unspecified | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Meniscus injury | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Muscle injury | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Patella fracture | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pelvic fracture | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Periprosthetic fracture | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Perirenal haematoma | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Post procedural haemorrhage | | | | |

| | | | | |
|---|----------------|--|--|--|
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Post procedural oedema | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Postoperative hernia | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Postoperative ileus | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Procedural pain | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Radius fracture | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Rib fracture | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Road traffic accident | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Scapula fracture | | | | |

| | | | | |
|---|----------------|--|--|--|
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Skull fracture | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Soft tissue injury | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Spinal column injury | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Spinal compression fracture | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Sternal fracture | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Subdural haematoma | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Tendon rupture | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Thermal burn | | | | |

| | | | | |
|---|----------------|--|--|--|
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Thoracic vertebral fracture | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Tibia fracture | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Traumatic liver injury | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Twiddler's syndrome | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Ulna fracture | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Upper limb fracture | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Wound | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Wound dehiscence | | | | |

| | | | |
|---|--------------------------------------|--|--|
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Wrist fracture | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Humerus fracture 1 | Additional description: MedDRA v20.1 | | |
| subjects affected / exposed | 1 / 48 (2.08%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Congenital, familial and genetic disorders | | | |
| Atrial septal defect | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Developmental hip dysplasia | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hydrocele | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Tourette's disorder | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cardiac disorders | | | |
| Acute myocardial infarction | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | | |
|---|----------------|--|--|--|
| Angina pectoris | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Angina unstable | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Aortic valve incompetence | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Aortic valve stenosis | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Arrhythmia | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Arteriosclerosis coronary artery | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Atrial fibrillation | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Atrial flutter | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Atrioventricular block complete | | | | |

| | | | | |
|---|----------------|--|--|--|
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Atrioventricular block second degree | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Bradycardia | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Bundle branch block right | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Cardiac arrest | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Cardiac failure | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Cardiac failure congestive | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Cardiac tamponade | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Cardio-respiratory arrest | | | | |

| | | | | |
|---|----------------|--|--|--|
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Cardiogenic shock | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Cardiopulmonary failure | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Cardiovascular insufficiency | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Coronary artery disease | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Coronary artery stenosis | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Coronary artery thrombosis | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Hypertensive heart disease | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Long QT syndrome | | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Mitral valve incompetence | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Mitral valve stenosis | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Myocardial infarction | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Myocardial ischaemia | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Palpitations | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pericardial effusion | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Sinus node dysfunction | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Sinus tachycardia | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Stress cardiomyopathy | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Supraventricular tachycardia | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Tachycardia | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Tricuspid valve incompetence | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Ventricular arrhythmia | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Ventricular tachycardia | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Wolff-Parkinson-White syndrome | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Nervous system disorders | | | |
| Aphasia | | | |

| | | | | |
|---|----------------|--|--|--|
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Brain injury | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Brain stem infarction | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Carotid artery aneurysm | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Carotid artery stenosis | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Carpal tunnel syndrome | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Central nervous system lesion | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Cerebellar ataxia | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Cerebral arteriosclerosis | | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cerebral haematoma | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cerebral haemorrhage | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cerebral infarction | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cerebrovascular accident | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cervical cord compression | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cervical myelopathy | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cervical radiculopathy | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Dizziness | | | |

| | | | | |
|---|----------------|--|--|--|
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Facial nerve disorder | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Facial paralysis | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Haemorrhagic stroke | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Headache | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Hemianopia | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Hemiparesis | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Intensive care unit acquired weakness | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Intracranial aneurysm | | | | |

| | | | | |
|---|----------------|--|--|--|
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Intraventricular haemorrhage | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Ischaemic stroke | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Loss of consciousness | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Lumbar radiculopathy | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Lumbosacral radiculopathy | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Metabolic encephalopathy | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Migraine | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Monoplegia | | | | |

| | | | | |
|---|----------------|--|--|--|
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Multiple sclerosis | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Myasthenia gravis | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Myelopathy | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Nerve root compression | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Neuritis | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pachymeningitis | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Parkinson's disease | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Post herpetic neuralgia | | | | |

| | | | | |
|---|----------------|--|--|--|
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Posterior reversible encephalopathy syndrome | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Presyncope | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Quadriparesis | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Radicular syndrome | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Radiculopathy | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Ruptured cerebral aneurysm | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Sciatica | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Seizure | | | | |

| | | | | |
|---|----------------|--|--|--|
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Sensory loss | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Serotonin syndrome | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Small fibre neuropathy | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Spinal claudication | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Spinal subdural haematoma | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Spondylitic myelopathy | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Syncope | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Tension headache | | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Transient ischaemic attack | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Vasculitis cerebral | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Haemorrhagic anaemia | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Iron deficiency anaemia | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Leukocytosis | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Leukopenia | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Mastocytosis | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pancytopenia | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Paratracheal lymphadenopathy | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Splenic infarction | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Thrombocytopenia | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Ear and labyrinth disorders | | | |
| Acute vestibular syndrome | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Vertigo | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Vertigo positional | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Vestibular disorder | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Eye disorders | | | |
| Cataract | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Glaucoma | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Keratitis interstitial | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Necrotising retinitis | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Optic disc drusen | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Retinal artery occlusion | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Retinal detachment | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Ulcerative keratitis | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Uveitis | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Visual acuity reduced | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrointestinal disorders | | | |
| Abdominal hernia | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Abdominal incarcerated hernia | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Abdominal pain lower | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Abdominal pain upper | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Ascites | | | |

| | | | | |
|---|----------------|--|--|--|
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Chronic gastritis | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Colitis | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Colitis ischaemic | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Colitis ulcerative | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Crohn's disease | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Diarrhoea | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Diverticular perforation | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Diverticulum | | | | |

| | | | | |
|---|----------------|--|--|--|
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Duodenal polyp | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Duodenal ulcer haemorrhage | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Dyspepsia | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Enterocoele | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Enterocolitis | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Faecaloma | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Fistula of small intestine | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Food poisoning | | | | |

| | | | | |
|---|----------------|--|--|--|
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Gastric disorder | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Gastric perforation | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Gastric polyps | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Gastric ulcer | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Gastric ulcer haemorrhage | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Gastritis | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Gastritis erosive | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Gastrointestinal disorder | | | | |

| | | | | |
|---|----------------|--|--|--|
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Gastrointestinal haemorrhage | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Gastrointestinal inflammation | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Gastrointestinal perforation | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Gastrooesophageal reflux disease | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Haematemesis | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Haematochezia | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Haemorrhagic erosive gastritis | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Haemorrhoidal haemorrhage | | | | |

| | | | | |
|---|----------------|--|--|--|
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Haemorrhoids | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Hiatus hernia | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Ileus | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Ileus paralytic | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Inguinal hernia | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Intestinal ischaemia | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Intestinal obstruction | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Large intestinal stenosis | | | | |

| | | | | |
|---|----------------|--|--|--|
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Large intestine perforation | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Large intestine polyp | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Lower gastrointestinal haemorrhage | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Melaena | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Mesenteric vein thrombosis | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Nausea | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Oesophageal spasm | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pancreatitis | | | | |

| | | | | |
|---|----------------|--|--|--|
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pancreatitis acute | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Peptic ulcer haemorrhage | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Rectal haemorrhage | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Rectal prolapse | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Retroperitoneal haematoma | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Small intestinal obstruction | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Tooth disorder | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Tooth impacted | | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Umbilical hernia | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Upper gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Vomiting | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Skin and subcutaneous tissue disorders | | | |
| Actinic keratosis | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Decubitus ulcer | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Drug reaction with eosinophilia and systemic symptoms | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Panniculitis | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Rash | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Rash maculo-papular | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Scar pain | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Skin lesion | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Skin ulcer | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Urticaria | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Renal and urinary disorders | | | |
| Acute kidney injury | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Anuria | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Calculus bladder | | | |

| | | | | |
|---|----------------|--|--|--|
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Calculus urinary | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Chronic kidney disease | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Haematuria | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Hydronephrosis | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Mixed incontinence | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Nephrolithiasis | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Obstructive uropathy | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Proteinuria | | | | |

| | | | | |
|---|----------------|--|--|--|
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pyelocaliectasis | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Renal colic | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Renal failure | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Renal impairment | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Ureteral necrosis | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Ureteric stenosis | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Ureterolithiasis | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Urethral meatus stenosis | | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Urinary incontinence | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Urinary retention | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Endocrine disorders | | | |
| Adrenal insufficiency | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Goitre | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hyperparathyroidism primary | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hyperthyroidism | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Musculoskeletal and connective tissue disorders | | | |
| Acquired claw toe | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | | |
|---|----------------|--|--|--|
| Arthralgia | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Arthritis | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Arthropathy | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Atlantoaxial instability | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Back pain | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Bone disorder | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Bursitis | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Cervical spinal stenosis | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Dupuytren's contracture | | | | |

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|---|----------------|--|--|--|
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Exostosis | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Extraskkeletal ossification | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Finger deformity | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Foot deformity | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Gouty arthritis | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Groin pain | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Haemarthrosis | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Hand deformity | | | | |

| | | | | |
|---|----------------|--|--|--|
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Intervertebral disc disorder | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Intervertebral disc protrusion | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Joint contracture | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Joint destruction | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Joint range of motion decreased | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Joint swelling | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Kyphosis | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Ligament disorder | | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Lumbar spinal stenosis | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Meniscal degeneration | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Metatarsalgia | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Musculoskeletal chest pain | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Myopathy | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Osteoarthritis | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Osteonecrosis | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pain in extremity | | | |

| | | | | |
|---|----------------|--|--|--|
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pathological fracture | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Polyarthritis | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Rhabdomyolysis | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Rheumatic disorder | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Rheumatoid arthritis | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Rheumatoid nodule | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Rotator cuff syndrome | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Spinal column stenosis | | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Spinal osteoarthritis | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Spinal pain | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Spondylitis | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Spondylolisthesis | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Synovial disorder | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Synovitis | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Tendon calcification | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Tenosynovitis | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infections and infestations | | | |
| Abdominal abscess | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Abdominal wall abscess | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Abscess | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Abscess limb | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Abscess neck | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Anal abscess | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Appendicitis | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Appendicitis perforated | | | |

| | | | | |
|---|----------------|--|--|--|
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Arthritis bacterial | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Arthritis infective | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Atypical pneumonia | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Bacteraemia | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Bacterial pyelonephritis | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Bartholin's abscess | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Bone tuberculosis | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Bronchiolitis | | | | |

| | | | | |
|---|----------------|--|--|--|
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Bronchitis | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Bronchopulmonary aspergillosis | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Bursitis infective | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Campylobacter gastroenteritis | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Cellulitis | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Cellulitis gangrenous | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Chronic sinusitis | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Chronic tonsillitis | | | | |

| | | | | |
|---|----------------|--|--|--|
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Clostridial infection | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Clostridium difficile colitis | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Clostridium difficile infection | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Colonic abscess | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Cytomegalovirus chorioretinitis | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Cytomegalovirus hepatitis | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Dengue fever | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Device related infection | | | | |

| | | | | |
|---|----------------|--|--|--|
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Diabetic gangrene | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Diarrhoea infectious | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Disseminated tuberculosis | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Diverticulitis | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Encephalitis | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Epstein-Barr virus infection | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Erysipelas | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Escherichia bacteraemia | | | | |

| | | | | |
|---|----------------|--|--|--|
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Escherichia sepsis | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Extradural abscess | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Eye infection fungal | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Gastroenteritis | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Gastroenteritis viral | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Gastrointestinal viral infection | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Groin abscess | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| H1N1 influenza | | | | |

| | | | | |
|---|----------------|--|--|--|
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| HIV infection | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Hepatitis A | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Hepatitis B | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Hepatitis C | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Hepatitis E | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Herpes dermatitis | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Herpes simplex | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Herpes virus infection | | | | |

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|---|----------------|--|--|--|
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Herpes zoster | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Herpes zoster cutaneous disseminated | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Herpes zoster disseminated | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Herpes zoster oticus | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Incision site infection | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Infected seroma | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Infected skin ulcer | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Infectious colitis | | | | |

| | | | | |
|---|----------------|--|--|--|
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Infectious mononucleosis | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Infective exacerbation of bronchiectasis | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Infective exacerbation of chronic obstructive airways disease | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Infective spondylitis | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Influenza | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Joint abscess | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Joint tuberculosis | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Lower respiratory tract infection | | | | |

| | | | | |
|---|----------------|--|--|--|
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Lower respiratory tract infection bacterial | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Lung infection | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Lyme disease | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Lymph node tuberculosis | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Meningitis | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Meningitis bacterial | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Meningitis cryptococcal | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Meningococcal bacteraemia | | | | |

| | | | | |
|---|----------------|--|--|--|
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Meningoencephalitis bacterial | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Nasopharyngitis | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Necrotising fasciitis | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Oesophageal candidiasis | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Ophthalmic herpes simplex | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Ophthalmic herpes zoster | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Osteomyelitis | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Otitis media | | | | |

| | | | | |
|---|----------------|--|--|--|
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pelvic inflammatory disease | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Periorbital cellulitis | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Perirectal abscess | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Peritoneal tuberculosis | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Peritonitis | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Peritonsillar abscess | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pertussis | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pharyngeal abscess | | | | |

| | | | | |
|---|----------------|--|--|--|
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pneumonia | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pneumonia bacterial | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pneumonia cryptococcal | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pneumonia cytomegaloviral | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pneumonia legionella | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pneumonia necrotising | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pneumonia pneumococcal | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pneumonia streptococcal | | | | |

| | | | | |
|---|----------------|--|--|--|
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Post procedural infection | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Postoperative abscess | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Postoperative wound infection | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Primary syphilis | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Psoas abscess | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pulmonary sepsis | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pulmonary tuberculosis | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pulpitis dental | | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pyelonephritis | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pyelonephritis acute | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pyoderma streptococcal | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pyometra | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Rectal abscess | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Renal abscess | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Renal cyst infection | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory tract infection | | | |

| | | | | |
|---|----------------|--|--|--|
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Retinitis | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Salpingo-oophoritis | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Secondary syphilis | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Sepsis | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Sepsis syndrome | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Septic shock | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Sinusitis | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Sinusitis aspergillus | | | | |

| | | | | |
|---|----------------|--|--|--|
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Sinusitis fungal | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Skin infection | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Splenic abscess | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Staphylococcal bacteraemia | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Staphylococcal infection | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Staphylococcal sepsis | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Streptococcal infection | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Subcutaneous abscess | | | | |

| | | | | |
|---|----------------|--|--|--|
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Superinfection | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Tonsillitis | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Tooth abscess | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Toxic shock syndrome | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Tuberculosis | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Tuberculosis of central nervous system | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Tubo-ovarian abscess | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Upper respiratory tract infection | | | | |

| | | | | |
|---|----------------|--|--|--|
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Upper respiratory tract infection bacterial | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Urinary tract infection | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Urinary tract infection bacterial | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Urosepsis | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Varicella zoster virus infection | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Vestibular neuronitis | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Viral infection | | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Wound infection | | | | |

| | | | |
|---|--------------------------------------|--|--|
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Wound infection bacterial | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Wound infection staphylococcal | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Herpes zoster 1 | Additional description: MedDRA v20.1 | | |
| subjects affected / exposed | 1 / 48 (2.08%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pneumonia 1 | Additional description: MedDRA v20.1 | | |
| subjects affected / exposed | 1 / 48 (2.08%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Metabolism and nutrition disorders | | | |
| Dehydration | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Diabetes mellitus | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Diabetic ketoacidosis | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hyperglycaemia | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hypoglycaemia unawareness | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hypokalaemia | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hypovolaemia | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Metabolic syndrome | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Obesity | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

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

| Non-serious adverse events | Tofa 5mg BID; ppts with avg total daily dose across study <15 | Tofa 10mg BID; ppts with avg total daily dose across study ≥15 | All Tofacitinib |
|---|---|--|----------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 807 / 1123 (71.86%) | 2422 / 3358 (72.13%) | 3229 / 4481 (72.06%) |
| Investigations | | | |
| Alanine aminotransferase increased | | | |

| | | | |
|---|---------------------|--------------------|---------------------|
| subjects affected / exposed | 63 / 1123 (5.61%) | 122 / 3358 (3.63%) | 185 / 4481 (4.13%) |
| occurrences (all) | 79 | 155 | 234 |
| Blood creatine phosphokinase increased | | | |
| subjects affected / exposed | 91 / 1123 (8.10%) | 247 / 3358 (7.36%) | 338 / 4481 (7.54%) |
| occurrences (all) | 127 | 316 | 443 |
| Blood creatinine increased | | | |
| subjects affected / exposed | 60 / 1123 (5.34%) | 116 / 3358 (3.45%) | 176 / 4481 (3.93%) |
| occurrences (all) | 66 | 123 | 189 |
| Injury, poisoning and procedural complications | | | |
| Fall | | | |
| subjects affected / exposed | 64 / 1123 (5.70%) | 209 / 3358 (6.22%) | 273 / 4481 (6.09%) |
| occurrences (all) | 74 | 247 | 321 |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 139 / 1123 (12.38%) | 311 / 3358 (9.26%) | 450 / 4481 (10.04%) |
| occurrences (all) | 160 | 352 | 512 |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 67 / 1123 (5.97%) | 201 / 3358 (5.99%) | 268 / 4481 (5.98%) |
| occurrences (all) | 79 | 239 | 318 |
| Blood and lymphatic system disorders | | | |
| Anemia | | | |
| subjects affected / exposed | 64 / 1123 (5.70%) | 176 / 3358 (5.24%) | 240 / 4481 (5.36%) |
| occurrences (all) | 75 | 202 | 277 |
| Gastrointestinal disorders | | | |
| Diarrhoea | | | |
| subjects affected / exposed | 72 / 1123 (6.41%) | 213 / 3358 (6.34%) | 285 / 4481 (6.36%) |
| occurrences (all) | 86 | 252 | 338 |
| Nausea | | | |
| subjects affected / exposed | 56 / 1123 (4.99%) | 175 / 3358 (5.21%) | 231 / 4481 (5.16%) |
| occurrences (all) | 60 | 196 | 256 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |
| subjects affected / exposed | 65 / 1123 (5.79%) | 202 / 3358 (6.02%) | 267 / 4481 (5.96%) |
| occurrences (all) | 75 | 229 | 304 |
| Musculoskeletal and connective tissue | | | |

| | | | |
|-----------------------------------|---------------------|---------------------|---------------------|
| disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 87 / 1123 (7.75%) | 265 / 3358 (7.89%) | 352 / 4481 (7.86%) |
| occurrences (all) | 119 | 341 | 460 |
| Back pain | | | |
| subjects affected / exposed | 106 / 1123 (9.44%) | 291 / 3358 (8.67%) | 397 / 4481 (8.86%) |
| occurrences (all) | 141 | 330 | 471 |
| Rheumatoid arthritis | | | |
| subjects affected / exposed | 103 / 1123 (9.17%) | 293 / 3358 (8.73%) | 396 / 4481 (8.84%) |
| occurrences (all) | 141 | 386 | 527 |
| Infections and infestations | | | |
| Bronchitis | | | |
| subjects affected / exposed | 141 / 1123 (12.56%) | 430 / 3358 (12.81%) | 571 / 4481 (12.74%) |
| occurrences (all) | 226 | 625 | 851 |
| Herpes zoster | | | |
| subjects affected / exposed | 117 / 1123 (10.42%) | 373 / 3358 (11.11%) | 490 / 4481 (10.94%) |
| occurrences (all) | 123 | 402 | 525 |
| Influenza | | | |
| subjects affected / exposed | 78 / 1123 (6.95%) | 199 / 3358 (5.93%) | 277 / 4481 (6.18%) |
| occurrences (all) | 96 | 249 | 345 |
| Nasopharyngitis | | | |
| subjects affected / exposed | 138 / 1123 (12.29%) | 517 / 3358 (15.40%) | 655 / 4481 (14.62%) |
| occurrences (all) | 220 | 812 | 1032 |
| Pharyngitis | | | |
| subjects affected / exposed | 58 / 1123 (5.16%) | 148 / 3358 (4.41%) | 206 / 4481 (4.60%) |
| occurrences (all) | 61 | 180 | 241 |
| Sinusitis | | | |
| subjects affected / exposed | 70 / 1123 (6.23%) | 239 / 3358 (7.12%) | 309 / 4481 (6.90%) |
| occurrences (all) | 117 | 358 | 475 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 228 / 1123 (20.30%) | 613 / 3358 (18.25%) | 841 / 4481 (18.77%) |
| occurrences (all) | 439 | 1083 | 1522 |
| Urinary tract infection | | | |
| subjects affected / exposed | 161 / 1123 (14.34%) | 447 / 3358 (13.31%) | 608 / 4481 (13.57%) |
| occurrences (all) | 283 | 739 | 1022 |

| | | | |
|---|-------------------------------------|---------------------------|---------------------------|
| Bronchitis 1 subjects affected / exposed occurrences (all) | Additional description: MedDRA 20.1 | | |
| | 0 / 1123 (0.00%) 0 | 0 / 3358 (0.00%) 0 | 0 / 4481 (0.00%) 0 |
| Metabolism and nutrition disorders Hypercholesterolaemia subjects affected / exposed occurrences (all) | 62 / 1123 (5.52%) 67 | 153 / 3358 (4.56%) 170 | 215 / 4481 (4.80%) 237 |

| | | | |
|--|---------------------------------------|--|--|
| Non-serious adverse events | Extension Period: Tofacitinib 5 mg | | |
| Total subjects affected by non-serious adverse events subjects affected / exposed | 3 / 48 (6.25%) | | |
| Investigations Alanine aminotransferase increased subjects affected / exposed occurrences (all) | 0 / 48 (0.00%) 0 | | |
| Blood creatine phosphokinase increased subjects affected / exposed occurrences (all) | 0 / 48 (0.00%) 0 | | |
| Blood creatinine increased subjects affected / exposed occurrences (all) | 0 / 48 (0.00%) 0 | | |
| Injury, poisoning and procedural complications Fall subjects affected / exposed occurrences (all) | 0 / 48 (0.00%) 0 | | |
| Vascular disorders Hypertension subjects affected / exposed occurrences (all) | 0 / 48 (0.00%) 0 | | |
| Nervous system disorders Headache subjects affected / exposed occurrences (all) | 0 / 48 (0.00%) 0 | | |
| Blood and lymphatic system disorders Anemia subjects affected / exposed occurrences (all) | 0 / 48 (0.00%) 0 | | |

| | | | |
|---|--|--|--|
| Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all) | 0 / 48 (0.00%) 0 0 / 48 (0.00%) 0 | | |
| Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) | 0 / 48 (0.00%) 0 | | |
| Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) Back pain subjects affected / exposed occurrences (all) Rheumatoid arthritis subjects affected / exposed occurrences (all) | 0 / 48 (0.00%) 0 0 / 48 (0.00%) 0 0 / 48 (0.00%) 0 | | |
| Infections and infestations Bronchitis subjects affected / exposed occurrences (all) Herpes zoster subjects affected / exposed occurrences (all) Influenza subjects affected / exposed occurrences (all) Nasopharyngitis subjects affected / exposed occurrences (all) Pharyngitis | 0 / 48 (0.00%) 0 0 / 48 (0.00%) 0 0 / 48 (0.00%) 0 0 / 48 (0.00%) 0 | | |

| | | | |
|------------------------------------|-------------------------------------|--|--|
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences (all) | 0 | | |
| Sinusitis | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences (all) | 0 | | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences (all) | 0 | | |
| Urinary tract infection | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences (all) | 0 | | |
| Bronchitis 1 | Additional description: MedDRA 20.1 | | |
| subjects affected / exposed | 3 / 48 (6.25%) | | |
| occurrences (all) | 3 | | |
| Metabolism and nutrition disorders | | | |
| Hypercholesterolaemia | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences (all) | 0 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|------------------|--|
| 08 February 2007 | The amendment was based on recommendations from the USA Food and Drug Administration about safety monitoring parameters for this protocol including some recommendations on specific cut-off values for certain parameters e.g., requiring some to be stricter than suggested by the Sponsor. For example, the (confirmed) hemoglobin level requiring discontinuation was raised from 7.5 to 8.0 g/dL. In addition, monitoring guidelines were added for subjects with serum creatinine levels >10% from baseline at the time of discontinuation. |
| 25 July 2007 | Updated exclusion criteria with the following modification for exclusion criteria number 11, 15 and 16, respectively: Included history of recurrent or disseminated herpes zoster or as otherwise judged by the Investigator; if an intra-articular injection was performed in the course of a qualifying study <4 weeks before the baseline visit of this study, the injected joint was to be considered to have its pre-injection status from the index study for the full length of this protocol; bariatric procedures, such as gastric banding, that simply divide the stomach into separate chambers were not exclusionary. Updated with rescue therapy for subjects who were not on stable, background opioid therapy. Measurement of the ESR was added to several visits, in order to facilitate determination of the DAS 28-4 (ESR) response. In addition, ACR responses were determined at every 3 months throughout the study instead of only during the first year of participation. Updated with intake of dietary supplements allowed during the study. Updated with prohibition of vaccination with live components during the study and for 8 weeks after last dose of study drug. |
| 21 January 2009 | The primary justification for this amendment was to provide for dosing of subjects at 10 mg BID and provide for long-term follow-up testing (e.g., radiographs of hands and feet, lipid profiles) consistent with tofacitinib Phase 3 protocols. |
| 18 February 2009 | Updated assessment of cardiovascular (CV) risk as every 6 months through Month 24 and then yearly after Month 24 throughout the document. Updated dose of tofacitinib as 5 mg BID and 10 mg BID in secondary objectives. Specified ESR and CRP for laboratory testing and SF-36 Health Survey in Section 6.1.3. Added DAS 2/8 assessment in Section 6.2.3 and height in Section 6.2.5. |
| 30 June 2009 | The purpose of this amendment was to align with Phase 3 protocols, to decrease the withdrawal period required for adalimumab (Humira®), and extend the supply of tofacitinib to at least 2 years after first global marketing approval. |
| 26 February 2010 | Removed the option for subjects to enroll in non-drug extension Study A3921029 after 26 February 2010. Removed text in inclusion criteria regarding subjects who discontinued their qualifying index study due to lack of efficacy. The criteria required 24 weeks of participation in the index study in order to be eligible to enroll in Study A3921024. This text was removed to accommodate differing timeframe requirements in the index study protocols. Updated monitoring and discontinuation guidelines surrounding serum creatinine elevations to allow for adjustments in concomitant medications and study drug dosing. |
| 24 December 2010 | Schedule of Activities: plasma samples for the analysis of tofacitinib concentrations were to be collected to explore relationships with long-term efficacy and safety outcomes. Included exploratory objective of establishing the PK of tofacitinib. Moved HAQ-DI to the second secondary objective. Clarified monitoring guideline for serum creatinine. Removed wording to allow intra-articular hyaluronate sodium injections prior to the Month 6 visit if appropriate and clarified frequency. Added guideline on use of opioid agent hydrocodone. |

| | |
|------------------|---|
| 30 August 2012 | Added an exclusion criterion for lymphocytopenia, monitoring and discontinuation criteria with regard to lymphocyte counts <500/mm ³ . Removed active tuberculosis (TB) infection to clarify that any subject with active TB infection was not allowed to receive the study drug. Added description of the relationship between treated and serious infections and lymphocyte counts <500/mm ³ in the RA tofacitinib program. Added to the list of contraceptive methods that were considered highly effective. Added the requirement for written dosing instructions. Added language for drug storage temperature monitoring. Added language: "Topical administration, eg, cutaneous, ophthalmic, or intravaginal, of medications that are prohibited if administered systemically, are allowed in the study". Modified CV risk factor assessment requirements after screening. Decreased frequency for radiographs of hands and feet after Month 12. Added language allowing for additional safety endpoint adjudication. Clarified requirement for the average weekly alcohol consumption to be updated at visits every 6 months through Month 24 and then annually thereafter for all subjects. |
| 11 March 2013 | Additional hepatitis B tests added. Medical history and vaccination of zoster added. Washout period for CYP3A inhibitors and/or CYP3A inducers added. Clarified the allowed non-steroidal anti-inflammatory drugs/cyclooxygenase-2 inhibitors/oral corticosteroids during the study. |
| 05 February 2014 | Added a follow-up visit (at least 28 days after the last dose of study drug). Removed the tests of apolipoprotein A and B. Decreased the frequency of ECG testing during the study. Removed work limitation questionnaire. Reduced the frequency of questionnaires (SF-36 Health Survey, FACIT Fatigue, EuroQol EQ-5D, RA-HCRU) to be performed annually. Specified the collections of radiographs of hands/feet procedures up to Month 36 only and at EOT visit. Added lymphocyte substudy. Extended the study duration to November 2019 or up to the marketing approval of tofacitinib in certain countries. Allowed subjects to reduce the study dose to 5 mg BID from 10 mg BID at the discretion of the Investigators. Allowed subjects who were enrolled to receive either 5 or 10 mg BID dose at the discretion of the Investigators. Added the discussions of potential reproductive risk and contraceptive use. Added and removed some prohibited concomitant drugs and clarified that study drug was to be interrupted if a CYP3A inhibitor was administered concomitantly. Applied the existing discontinuation criterion of opportunistic infection to all subjects. |
| 15 January 2015 | Added TB screening annually for subjects in the high-risk countries. Removed height measurements during the study and weight measurements at some timepoints during the study. Removed temperature, rheumatoid factor, anti-cyclic citrullinated peptide, ECG, urinalysis, and radiographs of hands and feet. Removed SF-36, FACIT Fatigue, EQ-5D, RA Healthcare questionnaires. Reduced the study duration to April 2016 for subjects who were not participating in the lymphocyte substudy and clarified the study durations for subjects who were participating in the lymphocyte substudy. Added more definitions/clarifications of medication errors. Clarified wording to continue a subject with latent TB infection during the study. Added Cohort 3 to enroll subjects from Study A3921237 in the lymphocyte substudy. |

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.

All information is based on protocol Amendment 25 with a database release date of 02 March 2017. One serious adverse event in the Tofacitinib 5mg BID group could not be coded ("septic shock and pneumonia") and has not been included.

Notes: