

**Clinical trial results:**

An open-label, prospective, non-randomized, multicenter study to evaluate clear skin effect on health-related quality of life outcomes at 16 and 52 weeks in patients with moderate to severe plaque psoriasis treated with secukinumab 300 mg s.c. with or without previous exposure to systemic therapy

Summary

| | |
|--------------------------|-------------------------------------|
| EudraCT number | 2015-003701-42 |
| Trial protocol | ES DE GB BE LV PT SK LT PL GR RO IT |
| Global end of trial date | 28 March 2018 |

Results information

| | |
|--------------------------------|---------------|
| Result version number | v1 (current) |
| This version publication date | 06 April 2019 |
| First version publication date | 06 April 2019 |

Trial information**Trial identification**

| | |
|-----------------------|--------------|
| Sponsor protocol code | CAIN457A3401 |
|-----------------------|--------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02752776 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | Novartis Pharma, AG |
| Sponsor organisation address | CH-4002, Basel, Switzerland, |
| Public contact | Clinical Disclosure Manager, Novartis Pharma, AG, +41 613241111, novartis.email@novartis.com |
| Scientific contact | Clinical Disclosure Manager, Novartis Pharma, AG, +41 613241111, novartis.email@novartis.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 | 28 March 2018 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 28 March 2018 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study was to assess the proportion of patients achieving a Dermatology Life Quality Index (DLQI) 0/1 response at Week 16 in 3 pre-defined subpopulations and in the overall study population.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines. All the local regulatory requirements pertinent to safety of trial subjects were also followed during the conduct of the trial.

Background therapy: -

Evidence for comparator: -

| | |
|---|---------------|
| Actual start date of recruitment | 17 March 2016 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|---------------------|
| Country: Number of subjects enrolled | Belgium: 20 |
| Country: Number of subjects enrolled | Bulgaria: 25 |
| Country: Number of subjects enrolled | Czech Republic: 33 |
| Country: Number of subjects enrolled | Estonia: 46 |
| Country: Number of subjects enrolled | France: 297 |
| Country: Number of subjects enrolled | Germany: 506 |
| Country: Number of subjects enrolled | United Kingdom: 108 |
| Country: Number of subjects enrolled | Greece: 16 |
| Country: Number of subjects enrolled | Israel: 30 |
| Country: Number of subjects enrolled | Italy: 40 |
| Country: Number of subjects enrolled | Latvia: 34 |
| Country: Number of subjects enrolled | Lithuania: 32 |
| Country: Number of subjects enrolled | Poland: 148 |
| Country: Number of subjects enrolled | Portugal: 34 |
| Country: Number of subjects enrolled | Romania: 21 |
| Country: Number of subjects enrolled | Slovakia: 31 |
| Country: Number of subjects enrolled | Spain: 239 |
| Worldwide total number of subjects | 1660 |
| EEA total number of subjects | 1630 |

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) | 1524 |
| From 65 to 84 years | 134 |
| 85 years and over | 2 |

Subject disposition

Recruitment

Recruitment details:

A total of 1660 participants were treated and included in the Safety set.

Pre-assignment

Screening details:

A total of 1858 patients were screened in this study.

Period 1

| | |
|------------------------------|--------------------------------|
| Period 1 title | Overall Study (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Not applicable |
| Blinding used | Not blinded |

Arms

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

| | |
|------------------|-------------------------|
| Arm title | Subpopulation A (naive) |
|------------------|-------------------------|

Arm description:

Subjects who were naïve to any systemic treatment, e.g. participants failing or intolerant to previous topical treatment, including narrow band UVB, but never exposed to any systemic treatment, with or without contraindications to the use of conventional systemic treatment and in a need of a first systemic treatment.

| | |
|--|------------------|
| Arm type | Experimental |
| Investigational medicinal product name | secukinumab |
| Investigational medicinal product code | AIN457 |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

secukinumab/AIN457 300 mg s.c. as per EU SmPC. Secukinumab 300 mg (2 × PFS of the 150 mg dose) was self-administered by the patient (or caregiver).

| | |
|------------------|--------------------------------|
| Arm title | Subpopulation B (non-biologic) |
|------------------|--------------------------------|

Arm description:

Subjects who have been previously exposed to at least one conventional systemic therapy; either because of failure or intolerance to their previous conventional systemic treatment, they were in a need of a first biologic systemic treatment.

| | |
|--|------------------|
| Arm type | Experimental |
| Investigational medicinal product name | secukinumab |
| Investigational medicinal product code | AIN457 |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

secukinumab/AIN457 300 mg s.c. as per EU SmPC. Secukinumab 300 mg (2 × PFS of the 150 mg dose) was self-administered by the patient (or caregiver).

| | |
|------------------|----------------------------|
| Arm title | Subpopulation C (biologic) |
|------------------|----------------------------|

Arm description:

Subjects who have been previously exposed to at least one biologic systemic therapy; either because of failure or intolerance to their previous biologic systemic treatment, they were in a need of a different biologic systemic treatment.

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

| | |
|--|------------------|
| Investigational medicinal product name | secukinumab |
| Investigational medicinal product code | AIN457 |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

secukinumab/AIN457 300 mg s.c. as per EU SmPC. Secukinumab 300 mg (2 × PFS of the 150 mg dose) was self-administered by the patient (or caregiver).

| Number of subjects in period 1 | Subpopulation A (naive) | Subpopulation B (non-biologic) | Subpopulation C (biologic) |
|---------------------------------------|----------------------------|-----------------------------------|-------------------------------|
| Started | 663 | 673 | 324 |
| Full Analysis Set | 662 | 673 | 324 |
| Completed | 611 | 597 | 276 |
| Not completed | 52 | 76 | 48 |
| Adverse event, serious fatal | - | - | 1 |
| Physician decision | 2 | 6 | 2 |
| Consent withdrawn by subject | 3 | 4 | 2 |
| Adverse event, non-fatal | 15 | 23 | 11 |
| Non-compliance with study treatment | - | - | 1 |
| Pregnancy | 1 | 6 | 3 |
| Lost to follow-up | 11 | 12 | 4 |
| Subject/guardian decision | 8 | 6 | 4 |
| Lack of efficacy | 2 | 6 | 14 |
| Protocol deviation | 10 | 13 | 6 |

Baseline characteristics

Reporting groups

| | |
|--|--------------------------------|
| Reporting group title | Subpopulation A (naïve) |
| Reporting group description: Subjects who were naïve to any systemic treatment, e.g. participants failing or intolerant to previous topical treatment, including narrow band UVB, but never exposed to any systemic treatment, with or without contraindications to the use of conventional systemic treatment and in a need of a first systemic treatment. | |
| Reporting group title | Subpopulation B (non-biologic) |
| Reporting group description: Subjects who have been previously exposed to at least one conventional systemic therapy; either because of failure or intolerance to their previous conventional systemic treatment, they were in a need of a first biologic systemic treatment. | |
| Reporting group title | Subpopulation C (biologic) |
| Reporting group description: Subjects who have been previously exposed to at least one biologic systemic therapy; either because of failure or intolerance to their previous biologic systemic treatment, they were in a need of a different biologic systemic treatment. | |

| Reporting group values | Subpopulation A (naïve) | Subpopulation B (non-biologic) | Subpopulation C (biologic) |
|---|-------------------------|--------------------------------|----------------------------|
| Number of subjects | 663 | 673 | 324 |
| Age categorical Units: Subjects | | | |
| Adults (18-64 years) | 617 | 617 | 290 |
| From 65-84 years | 44 | 56 | 34 |
| 85 years and over | 2 | 0 | 0 |
| Age Continuous Units: years | | | |
| arithmetic mean | 43.2 | 44.4 | 47.4 |
| standard deviation | ± 14.03 | ± 13.67 | ± 12.89 |
| Sex: Female, Male Units: Subjects | | | |
| Female | 224 | 222 | 107 |
| Male | 439 | 451 | 217 |
| Race/Ethnicity, Customized Units: Subjects | | | |
| Caucasian | 626 | 642 | 307 |
| Black | 3 | 2 | 0 |
| Asian | 12 | 6 | 2 |
| Other | 22 | 23 | 15 |

| Reporting group values | Total | | |
|------------------------------------|-------|--|--|
| Number of subjects | 1660 | | |
| Age categorical Units: Subjects | | | |
| Adults (18-64 years) | 1524 | | |
| From 65-84 years | 134 | | |
| 85 years and over | 2 | | |

| | | | |
|---|------|--|--|
| Age Continuous Units: years arithmetic mean standard deviation | - | | |
| Sex: Female, Male Units: Subjects | | | |
| Female | 553 | | |
| Male | 1107 | | |
| Race/Ethnicity, Customized Units: Subjects | | | |
| Caucasian | 1575 | | |
| Black | 5 | | |
| Asian | 20 | | |
| Other | 60 | | |

End points

End points reporting groups

| | |
|--|----------------------------------|
| Reporting group title | Subpopulation A (naive) |
| Reporting group description: Subjects who were naïve to any systemic treatment, e.g. participants failing or intolerant to previous topical treatment, including narrow band UVB, but never exposed to any systemic treatment, with or without contraindications to the use of conventional systemic treatment and in a need of a first systemic treatment. | |
| Reporting group title | Subpopulation B (non-biologic) |
| Reporting group description: Subjects who have been previously exposed to at least one conventional systemic therapy; either because of failure or intolerance to their previous conventional systemic treatment, they were in a need of a first biologic systemic treatment. | |
| Reporting group title | Subpopulation C (biologic) |
| Reporting group description: Subjects who have been previously exposed to at least one biologic systemic therapy; either because of failure or intolerance to their previous biologic systemic treatment, they were in a need of a different biologic systemic treatment. | |
| Subject analysis set title | All Subjects - Full Analysis Set |
| Subject analysis set type | Full analysis |
| Subject analysis set description: Subjects from all 3 subpopulations: Subpopulation A B & C combined | |

Primary: Percentage of participants with a Dermatology life quality index 0/1 (DLQI 0/1) response at Week 16

| | |
|---|--|
| End point title | Percentage of participants with a Dermatology life quality index 0/1 (DLQI 0/1) response at Week 16 ^[1] |
| End point description: Assessed the percentage of participants who achieved a Dermatology life quality index 0/1 (DLQI 0/1) response at Week 16 in 3 pre-defined subpopulations and in the overall study population. | |
| End point type | Primary |
| End point timeframe: 16 weeks | |

Notes:

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

Justification: No statistical analysis was planned for this endpoint

| End point values | Subpopulation A (naive) | Subpopulation B (non-biologic) | Subpopulation C (biologic) | All Subjects - Full Analysis Set |
|-----------------------------------|-------------------------|--------------------------------|----------------------------|----------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 662 | 673 | 324 | 1659 |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | 74.7 (71.2 to 78.0) | 71.3 (67.7 to 74.7) | 61.7 (56.1 to 67.0) | 70.8 (68.5 to 73.0) |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with a Dermatology life quality index 0/1 (DLQI 0/1) response at Week 52

| | |
|-----------------|---|
| End point title | Percentage of participants with a Dermatology life quality index 0/1 (DLQI 0/1) response at Week 52 |
|-----------------|---|

End point description:

Assessed the percentage of participants who achieved a Dermatology life quality index 0/1 (DLQI 0/1) response at Week 52 in 3 pre-defined subpopulations and in the overall study population.

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

End point timeframe:

52 weeks

| End point values | Subpopulation A (naive) | Subpopulation B (non-biologic) | Subpopulation C (biologic) | All Subjects - Full Analysis Set |
|-----------------------------------|-------------------------|--------------------------------|----------------------------|----------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 662 | 673 | 324 | 1659 |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | 75.3 (71.7 to 78.5) | 73.3 (69.8 to 76.6) | 62.0 (56.5 to 67.3) | 71.9 (69.6 to 74.0) |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants in each DLQI score category at Week 16 and Week 52

| | |
|-----------------|---|
| End point title | Percentage of participants in each DLQI score category at Week 16 and Week 52 |
|-----------------|---|

End point description:

Assessed the percentage of participants with Dermatology life quality index scores at Week 16 & 52 in 3 pre-defined subpopulations and in the overall study population.

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

End point timeframe:

52 weeks

| End point values | Subpopulation A (naive) | Subpopulation B (non-biologic) | Subpopulation C (biologic) | All Subjects - Full Analysis Set |
|---|-------------------------|--------------------------------|----------------------------|----------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 662 | 673 | 324 | 1659 |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | | | | |
| Wk 16: DLQI cat. score: 2-5 (n=649,666,321,1636) | 18.3 (15.5 to 21.6) | 19.1 (16.2 to 22.3) | 21.2 (16.9 to 26.2) | 19.2 (17.3 to 21.2) |
| Wk 16: DLQI cat. score: 6-10 (n=649,666,321,1636) | 5.7 (4.1 to 7.8) | 6.3 (4.6 to 8.5) | 9.3 (6.5 to 13.2) | 6.7 (5.5 to 8.0) |

| | | | | |
|---|---------------------|---------------------|---------------------|---------------------|
| Wk 16: DLQI cat. score: 11-20 (n=649,666,321,1636) | 1.2 (0.6 to 2.5) | 2.9 (1.8 to 4.5) | 5.3 (3.2 to 8.5) | 2.7 (2.0 to 3.6) |
| Wk 16: DLQI cat. score: 21-30 (n=649,666,321,1636) | 0.0 (0.0 to 0.7) | 0.5 (0.1 to 1.4) | 2.5 (1.2 to 5.0) | 0.7 (0.4 to 1.2) |
| Wk 52: DLQI cat. score: 2-5 (n=655,671,324,1650) | 17.9 (15.0 to 21.1) | 14.0 (11.5 to 16.9) | 18.2 (14.2 to 23.0) | 16.4 (14.6 to 18.3) |
| Wk 52: DLQI cat. score: 6-10 (n=655,671,324,1650) | 4.7 (3.3 to 6.7) | 7.2 (5.4 to 9.4) | 9.6 (6.7 to 13.4) | 6.7 (5.5 to 8.0) |
| Wk 52: DLQI cat. score: 11-20 (n=655,671,324,1650) | 1.8 (1.0 to 3.3) | 4.0 (2.7 to 5.9) | 8.3 (5.7 to 12.0) | 4.0 (3.1 to 5.1) |
| Wk 52: DLQI cat. score: 21-30 (n=655,671,324,1650) | 0.3 (0.1 to 1.2) | 1.5 (0.8 to 2.8) | 1.9 (0.8 to 4.2) | 1.1 (0.7 to 1.8) |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with PASI 50, PASI 75, PASI 90, PASI 100 or IGA mod 2011 0/1 response at Week 16 and 52

| | |
|--|--|
| End point title | Percentage of participants with PASI 50, PASI 75, PASI 90, PASI 100 or IGA mod 2011 0/1 response at Week 16 and 52 |
| End point description: | |
| Assessed the percentage of participants who achieved PASI 50, PASI 75, PASI 90, PASI 100 and investigator's global assessment (IGA) mod 2011 0/1 responses at Week 16 and Week 52 in 3 pre-defined subpopulations and in the overall study population. | |
| End point type | Secondary |
| End point timeframe: | |
| Week 16, Week 52 | |

| End point values | Subpopulation A (naive) | Subpopulation B (non-biologic) | Subpopulation C (biologic) | All Subjects - Full Analysis Set |
|---|-------------------------|--------------------------------|----------------------------|----------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 662 | 673 | 324 | 1659 |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | | | | |
| Wk 16: PASI 50 (n = 658, 670, 323, 1651) | 97.7 (96.2 to 98.7) | 97.5 (95.9 to 98.5) | 95.0 (91.9 to 97.2) | 97.1 (96.1 to 97.8) |
| Wk 16: PASI 75 (n = 658, 670, 323, 1651) | 94.4 (92.3 to 96.0) | 92.8 (90.5 to 94.7) | 85.4 (81.0 to 89.1) | 92.0 (90.6 to 93.3) |
| Wk 16: PASI 90 (n = 658, 670, 323, 1651) | 82.4 (79.2 to 85.2) | 78.8 (75.5 to 81.8) | 69.0 (63.6 to 74.0) | 78.3 (76.2 to 80.3) |
| Wk 16: PASI 100 (n = 658, 670, 323, 1651) | 47.3 (43.4 to 51.2) | 38.8 (35.1 to 42.6) | 33.4 (28.4 to 38.9) | 41.1 (38.7 to 43.6) |
| Wk 16: IGA 01 (n = 658, 671, 323, 1651) | 87.4 (84.5 to 89.8) | 84.9 (82.0 to 87.5) | 76.2 (71.1 to 80.7) | 84.2 (82.3 to 85.9) |
| Wk 52: PASI 50 | 97.9 (96.4 to 98.9) | 96.3 (94.5 to 97.6) | 92.9 (89.4 to 95.5) | 96.3 (95.2 to 97.1) |
| Wk 52: PASI 75 | 94.4 (92.3 to 96.0) | 89.7 (87.1 to 91.9) | 83.3 (78.7 to 87.2) | 90.4 (88.8 to 91.7) |
| Wk 52: PASI 90 | 80.8 (77.6 to 83.7) | 75.5 (72.0 to 78.7) | 63.9 (58.4 to 69.1) | 75.3 (73.2 to 77.4) |

| | | | | |
|-----------------|---------------------|---------------------|---------------------|---------------------|
| Wk 52: PASI 100 | 56.9 (53.1 to 60.8) | 45.5 (41.7 to 49.3) | 37.0 (31.8 to 42.6) | 48.4 (46.0 to 50.8) |
| Wk 52: IGA 0/1 | 86.4 (83.5 to 88.9) | 79.9 (76.7 to 82.9) | 71.3 (66.0 to 76.1) | 80.8 (78.8 to 82.7) |

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute change from baseline in EQ-5D-5L crosswalk index at Week 16 and Week 52

| | |
|-----------------|--|
| End point title | Absolute change from baseline in EQ-5D-5L crosswalk index at Week 16 and Week 52 |
|-----------------|--|

End point description:

Assessed the effects of treatment with secukinumab 300 mg with respect to changes in EuroQOL 5-Dimension Health Questionnaire (EQ-5D®) response over time up to Week 16 and Week 52 compared to Baseline in 3 pre-defined subpopulations and in the overall study population.

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

End point timeframe:

Week 16, Week 52

| End point values | Subpopulation A (naive) | Subpopulation B (non-biologic) | Subpopulation C (biologic) | All Subjects - Full Analysis Set |
|--------------------------------------|-------------------------|--------------------------------|----------------------------|----------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 662 | 673 | 324 | 1659 |
| Units: scores on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 16 (n = 643, 656, 314, 1613) | 0.217 (± 0.2294) | 0.201 (± 0.2277) | 0.235 (± 0.2602) | 0.214 (± 0.2352) |
| Week 52 (n = 647, 659, 317, 1623) | 0.221 (± 0.2353) | 0.193 (± 0.2360) | 0.226 (± 0.2596) | 0.211 (± 0.2408) |

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute change from baseline in EQ-5D-5L visual analogue scale (VAS) at Week 16 and Week 52

| | |
|-----------------|--|
| End point title | Absolute change from baseline in EQ-5D-5L visual analogue scale (VAS) at Week 16 and Week 52 |
|-----------------|--|

End point description:

Assessed the effects of treatment with secukinumab 300 mg with respect to changes in EuroQOL 5-Dimension Health Questionnaire (EQ-5D®) response over time up to Week 16 and Week 52 compared to Baseline in 3 pre-defined subpopulations and in the overall study population.

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

End point timeframe:

Week 16, Week 52

| End point values | Subpopulation A (naive) | Subpopulation B (non-biologic) | Subpopulation C (biologic) | All Subjects - Full Analysis Set |
|--------------------------------------|-------------------------|--------------------------------|----------------------------|----------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 662 | 673 | 324 | 1659 |
| Units: scores on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 16 (n = 644, 656, 314, 1614) | 19.7 (± 24.36) | 21.4 (± 25.66) | 18.7 (± 26.66) | 20.2 (± 25.36) |
| Week 52 (n = 647, 659, 317, 1623) | 21.7 (± 24.11) | 22.6 (± 25.47) | 19.5 (± 25.14) | 21.7 (± 24.88) |

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute change from baseline in HAQ-DI at Week 16 and Week 52

| | |
|--|--|
| End point title | Absolute change from baseline in HAQ-DI at Week 16 and Week 52 |
| End point description: | |
| Assessed the effects of treatment with secukinumab 300 mg with respect to changes in Health assessment questionnaire disability index (HAQ©-DI) response over time up to Week 16 and Week 52 compared to Baseline in 3 pre-defined subpopulations and in the overall study population. | |
| End point type | Secondary |
| End point timeframe: | |
| Week 16 and Week 52 | |

| End point values | Subpopulation A (naive) | Subpopulation B (non-biologic) | Subpopulation C (biologic) | All Subjects - Full Analysis Set |
|--------------------------------------|-------------------------|--------------------------------|----------------------------|----------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 44 | 117 | 90 | 251 |
| Units: scores on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 16 (n = 43, 109, 87, 239) | -0.7 (± 0.97) | -0.5 (± 0.83) | -0.3 (± 0.85) | -0.5 (± 0.87) |
| Week 52 (n = 44, 110, 88, 242) | -0.7 (± 0.90) | -0.5 (± 0.90) | -0.4 (± 0.85) | -0.5 (± 0.88) |

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute change from baseline in Numeric rating scale (NRS) at Week 16 and Week 52

| | |
|-----------------|--|
| End point title | Absolute change from baseline in Numeric rating scale (NRS) at Week 16 and Week 52 |
|-----------------|--|

End point description:

Assessed the effects of treatment with secukinumab 300 mg with respect to changes in Numeric rating scale: patient's assessment of pain, itching and scaling response over time up to Week 16 and Week 52 compared to Baseline in 3 pre-defined subpopulations and in the overall study population.

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

End point timeframe:

16 and 52 weeks

| End point values | Subpopulation A (naïve) | Subpopulation B (non-biologic) | Subpopulation C (biologic) | All Subjects - Full Analysis Set |
|--|-------------------------|--------------------------------|----------------------------|----------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 662 | 673 | 324 | 1659 |
| Units: scores on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Pain: Wk 16 (n = 640, 649, 310, 1599) | -3.0 (± 2.87) | -3.3 (± 3.11) | -3.3 (± 3.30) | -3.2 (± 3.06) |
| Pain: Wk 52 (n = 645, 657, 316, 1618) | -3.1 (± 2.95) | -3.2 (± 3.22) | -3.3 (± 3.36) | -3.2 (± 3.14) |
| Itching: Wk 16 (n = 640, 649, 311, 1600) | -4.9 (± 2.96) | -4.9 (± 3.06) | -4.8 (± 3.31) | -4.9 (± 3.07) |
| Itching: Wk 52 (n = 646, 656, 317, 1619) | -5.0 (± 2.92) | -5.0 (± 3.10) | -4.6 (± 3.28) | -4.9 (± 3.07) |
| Scaling: Wk 16 (n = 640, 650, 312, 1602) | -5.5 (± 2.68) | -5.5 (± 2.71) | -5.2 (± 3.26) | -5.4 (± 2.81) |
| Scaling: Wk 52 (n = 646, 657, 317, 1620) | -5.4 (± 2.72) | -5.3 (± 2.87) | -4.9 (± 3.27) | -5.3 (± 2.90) |

Statistical analyses

No statistical analyses for this end point

Secondary: Treatment Satisfaction Questionnaire for Medication (TSQM) scale scores at Week 16 and Week 52

| | |
|-----------------|--|
| End point title | Treatment Satisfaction Questionnaire for Medication (TSQM) scale scores at Week 16 and Week 52 |
|-----------------|--|

End point description:

Assessed the effects of treatment with secukinumab 300 mg with respect to changes in TSQM scale scores (Effectiveness, Convenience, Global satisfaction scores) over time up to Week 16 and Week 52 compared to Baseline in 3 pre-defined subpopulations and in the overall study population.

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

End point timeframe:

16 and 52 weeks

| End point values | Subpopulation A (naive) | Subpopulation B (non-biologic) | Subpopulation C (biologic) | All Subjects - Full Analysis Set |
|---|-------------------------|--------------------------------|----------------------------|----------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 662 | 673 | 324 | 1659 |
| Units: scores on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Effectiveness: Wk 16 (n = 650, 668, 318, 1636) | 81.5 (± 24.02) | 80.9 (± 25.13) | 75.0 (± 23.43) | 80.8 (± 24.48) |
| Effectiveness: Wk 52 (n = 655, 671, 322, 1648) | 85.1 (± 20.64) | 82.0 (± 25.05) | 74.9 (± 24.24) | 81.9 (± 23.50) |
| Convenience: Wk 16 (n = 650, 668, 319, 1637) | 79.2 (± 15.50) | 80.8 (± 15.83) | 75.9 (± 15.20) | 79.2 (± 15.67) |
| Convenience: Wk 52 (n = 655, 671, 323, 1649) | 82.8 (± 15.67) | 83.9 (± 15.42) | 78.9 (± 15.14) | 82.5 (± 15.57) |
| Global satisfaction: Wk 16 (n=650,668,319,1637) | 83.8 (± 14.71) | 83.3 (± 16.68) | 75.1 (± 20.07) | 81.9 (± 16.99) |
| Global satisfaction: Wk 52 (n=655,671,322,1648) | 83.9 (± 17.23) | 81.9 (± 20.38) | 73.5 (± 23.10) | 81.1 (± 20.14) |

Statistical analyses

No statistical analyses for this end point

Secondary: Patient benefit index (PBI) at Week 16 and Week 52

| | |
|------------------------|---|
| End point title | Patient benefit index (PBI) at Week 16 and Week 52 |
| End point description: | Assessed the effects of treatment with secukinumab 300 mg with respect to changes in Patient benefit index (PBI) response over time up to Week 16 and Week 52 compared to Baseline in 3 pre-defined subpopulations and in the overall study population. |
| End point type | Secondary |
| End point timeframe: | Week 16 and Week 52 |

| End point values | Subpopulation A (naive) | Subpopulation B (non-biologic) | Subpopulation C (biologic) | All Subjects - Full Analysis Set |
|--------------------------------------|-------------------------|--------------------------------|----------------------------|----------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 662 | 673 | 324 | 1659 |
| Units: scores on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 16 (n = 439, 472, 226, 1137) | 3.5 (± 0.61) | 3.4 (± 0.69) | 3.2 (± 0.85) | 3.4 (± 0.70) |
| Week 52 (n= 509, 532, 253, 1294) | 3.5 (± 0.70) | 3.4 (± 0.80) | 3.2 (± 0.96) | 3.4 (± 0.80) |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse Events are collected from First Patient First Visit (FPFV) until Last Patient Last Visit (LPLV). All Adverse Events reported in this record are from date of First Patient First Treatment until Last Patient Last Visit.

Adverse event reporting additional description:

Consistent with EudraCT disclosure specifications, Novartis has reported under the Serious adverse events field "number of deaths resulting from adverse events" all those deaths, resulting from serious adverse events that are deemed to be causally related to treatment by the investigator.

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 20.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|-------------------------|
| Reporting group title | Subpopulation A (naïve) |
|-----------------------|-------------------------|

Reporting group description:

Subjects who were naïve to any systemic treatment, e.g. subjects failing or intolerant to previous topical treatment, including narrow band UVB, but never exposed to any systemic treatment, with or without contraindications to the use of conventional systemic treatment and in a need of a first systemic treatment.

| | |
|-----------------------|--------------------------------|
| Reporting group title | Subpopulation B (non-biologic) |
|-----------------------|--------------------------------|

Reporting group description:

Subjects who have been previously exposed to at least one conventional systemic therapy; either because of failure or intolerance to their previous conventional systemic treatment, they were in a need of a first biologic systemic treatment.

| | |
|-----------------------|----------------------------|
| Reporting group title | Subpopulation C (biologic) |
|-----------------------|----------------------------|

Reporting group description:

Subjects who have been previously exposed to at least one biologic systemic therapy; either because of failure or intolerance to their previous biologic systemic treatment, they were in a need of a different biologic systemic treatment.

| | |
|-----------------------|--------------|
| Reporting group title | All Subjects |
|-----------------------|--------------|

Reporting group description:

Subjects from all 3 subpopulations: Subpopulation A B & C combined.

| Serious adverse events | Subpopulation A (naïve) | Subpopulation B (non-biologic) | Subpopulation C (biologic) |
|---|-------------------------|--------------------------------|----------------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 43 / 663 (6.49%) | 44 / 673 (6.54%) | 32 / 324 (9.88%) |
| number of deaths (all causes) | 0 | 0 | 1 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Adenocarcinoma of colon | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 663 (0.00%) | 1 / 673 (0.15%) | 0 / 324 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Basal cell carcinoma | | | |
| subjects affected / exposed | 0 / 663 (0.00%) | 1 / 673 (0.15%) | 1 / 324 (0.31%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bladder transitional cell carcinoma | | | |
| subjects affected / exposed | 1 / 663 (0.15%) | 1 / 673 (0.15%) | 0 / 324 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bronchial carcinoma | | | |
| subjects affected / exposed | 0 / 663 (0.00%) | 1 / 673 (0.15%) | 0 / 324 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal tract adenoma | | | |
| subjects affected / exposed | 0 / 663 (0.00%) | 1 / 673 (0.15%) | 0 / 324 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Malignant melanoma | | | |
| subjects affected / exposed | 0 / 663 (0.00%) | 1 / 673 (0.15%) | 0 / 324 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Myelodysplastic syndrome | | | |
| subjects affected / exposed | 0 / 663 (0.00%) | 1 / 673 (0.15%) | 0 / 324 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pituitary tumour benign | | | |
| subjects affected / exposed | 1 / 663 (0.15%) | 0 / 673 (0.00%) | 0 / 324 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Seborrhoeic keratosis | | | |

| | | | |
|--|-----------------|-----------------|-----------------|
| subjects affected / exposed | 1 / 663 (0.15%) | 0 / 673 (0.00%) | 0 / 324 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Squamous cell carcinoma | | | |
| subjects affected / exposed | 0 / 663 (0.00%) | 1 / 673 (0.15%) | 0 / 324 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Thyroid cancer | | | |
| subjects affected / exposed | 0 / 663 (0.00%) | 1 / 673 (0.15%) | 0 / 324 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 2 / 663 (0.30%) | 0 / 673 (0.00%) | 0 / 324 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypovolaemic shock | | | |
| subjects affected / exposed | 0 / 663 (0.00%) | 0 / 673 (0.00%) | 1 / 324 (0.31%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Varicose vein | | | |
| subjects affected / exposed | 0 / 663 (0.00%) | 0 / 673 (0.00%) | 1 / 324 (0.31%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pregnancy, puerperium and perinatal conditions | | | |
| Abortion spontaneous | | | |
| subjects affected / exposed | 0 / 663 (0.00%) | 1 / 673 (0.15%) | 1 / 324 (0.31%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General disorders and administration site conditions | | | |
| Chest pain | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 1 / 663 (0.15%) | 0 / 673 (0.00%) | 0 / 324 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Non-cardiac chest pain | | | |
| subjects affected / exposed | 1 / 663 (0.15%) | 0 / 673 (0.00%) | 1 / 324 (0.31%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Sudden death | | | |
| subjects affected / exposed | 0 / 663 (0.00%) | 0 / 673 (0.00%) | 1 / 324 (0.31%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Immune system disorders | | | |
| Anaphylactic reaction | | | |
| subjects affected / exposed | 0 / 663 (0.00%) | 0 / 673 (0.00%) | 1 / 324 (0.31%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Reproductive system and breast disorders | | | |
| Cervical dysplasia | | | |
| subjects affected / exposed | 1 / 663 (0.15%) | 0 / 673 (0.00%) | 0 / 324 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Erectile dysfunction | | | |
| subjects affected / exposed | 0 / 663 (0.00%) | 0 / 673 (0.00%) | 1 / 324 (0.31%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Prostatitis | | | |
| subjects affected / exposed | 0 / 663 (0.00%) | 0 / 673 (0.00%) | 1 / 324 (0.31%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Asthma | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 1 / 663 (0.15%) | 0 / 673 (0.00%) | 0 / 324 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Chronic obstructive pulmonary disease | | | |
| subjects affected / exposed | 0 / 663 (0.00%) | 1 / 673 (0.15%) | 0 / 324 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dyspnoea | | | |
| subjects affected / exposed | 1 / 663 (0.15%) | 1 / 673 (0.15%) | 0 / 324 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pharyngeal cyst | | | |
| subjects affected / exposed | 1 / 663 (0.15%) | 0 / 673 (0.00%) | 0 / 324 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vocal cord leukoplakia | | | |
| subjects affected / exposed | 0 / 663 (0.00%) | 1 / 673 (0.15%) | 0 / 324 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Psychiatric disorders | | | |
| Alcohol abuse | | | |
| subjects affected / exposed | 1 / 663 (0.15%) | 0 / 673 (0.00%) | 0 / 324 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Alcohol withdrawal syndrome | | | |
| subjects affected / exposed | 0 / 663 (0.00%) | 1 / 673 (0.15%) | 0 / 324 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Suicidal ideation | | | |
| subjects affected / exposed | 0 / 663 (0.00%) | 1 / 673 (0.15%) | 0 / 324 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Suicide attempt | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 663 (0.00%) | 1 / 673 (0.15%) | 0 / 324 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Injury, poisoning and procedural complications | | | |
| Alcohol poisoning | | | |
| subjects affected / exposed | 1 / 663 (0.15%) | 1 / 673 (0.15%) | 0 / 324 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Concussion | | | |
| subjects affected / exposed | 1 / 663 (0.15%) | 0 / 673 (0.00%) | 0 / 324 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Fall | | | |
| subjects affected / exposed | 0 / 663 (0.00%) | 0 / 673 (0.00%) | 1 / 324 (0.31%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Femoral neck fracture | | | |
| subjects affected / exposed | 1 / 663 (0.15%) | 0 / 673 (0.00%) | 0 / 324 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Head injury | | | |
| subjects affected / exposed | 0 / 663 (0.00%) | 1 / 673 (0.15%) | 0 / 324 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Humerus fracture | | | |
| subjects affected / exposed | 0 / 663 (0.00%) | 1 / 673 (0.15%) | 0 / 324 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lower limb fracture | | | |
| subjects affected / exposed | 1 / 663 (0.15%) | 1 / 673 (0.15%) | 0 / 324 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lumbar vertebral fracture | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 663 (0.00%) | 0 / 673 (0.00%) | 1 / 324 (0.31%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pelvic fracture | | | |
| subjects affected / exposed | 0 / 663 (0.00%) | 0 / 673 (0.00%) | 2 / 324 (0.62%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Procedural dizziness | | | |
| subjects affected / exposed | 1 / 663 (0.15%) | 0 / 673 (0.00%) | 0 / 324 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Radius fracture | | | |
| subjects affected / exposed | 0 / 663 (0.00%) | 1 / 673 (0.15%) | 0 / 324 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Skin abrasion | | | |
| subjects affected / exposed | 0 / 663 (0.00%) | 0 / 673 (0.00%) | 1 / 324 (0.31%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Subdural haematoma | | | |
| subjects affected / exposed | 0 / 663 (0.00%) | 1 / 673 (0.15%) | 0 / 324 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Tendon rupture | | | |
| subjects affected / exposed | 0 / 663 (0.00%) | 1 / 673 (0.15%) | 0 / 324 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Upper limb fracture | | | |
| subjects affected / exposed | 0 / 663 (0.00%) | 2 / 673 (0.30%) | 1 / 324 (0.31%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac disorders | | | |
| Acute myocardial infarction | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 663 (0.00%) | 1 / 673 (0.15%) | 0 / 324 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Angina pectoris | | | |
| subjects affected / exposed | 1 / 663 (0.15%) | 0 / 673 (0.00%) | 1 / 324 (0.31%) |
| 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 | 1 / 663 (0.15%) | 1 / 673 (0.15%) | 0 / 324 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Atrial flutter | | | |
| subjects affected / exposed | 0 / 663 (0.00%) | 1 / 673 (0.15%) | 0 / 324 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac failure | | | |
| subjects affected / exposed | 0 / 663 (0.00%) | 0 / 673 (0.00%) | 1 / 324 (0.31%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiomyopathy | | | |
| subjects affected / exposed | 1 / 663 (0.15%) | 0 / 673 (0.00%) | 0 / 324 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Coronary artery disease | | | |
| subjects affected / exposed | 0 / 663 (0.00%) | 1 / 673 (0.15%) | 0 / 324 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Left ventricular failure | | | |
| subjects affected / exposed | 1 / 663 (0.15%) | 0 / 673 (0.00%) | 0 / 324 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Myocardial infarction | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 2 / 663 (0.30%) | 2 / 673 (0.30%) | 0 / 324 (0.00%) |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Palpitations | | | |
| subjects affected / exposed | 1 / 663 (0.15%) | 0 / 673 (0.00%) | 0 / 324 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ventricular fibrillation | | | |
| subjects affected / exposed | 0 / 663 (0.00%) | 1 / 673 (0.15%) | 0 / 324 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| Carotid arteriosclerosis | | | |
| subjects affected / exposed | 1 / 663 (0.15%) | 0 / 673 (0.00%) | 0 / 324 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cerebral infarction | | | |
| subjects affected / exposed | 0 / 663 (0.00%) | 1 / 673 (0.15%) | 0 / 324 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diabetic hyperglycaemic coma | | | |
| subjects affected / exposed | 0 / 663 (0.00%) | 0 / 673 (0.00%) | 1 / 324 (0.31%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diabetic neuropathy | | | |
| subjects affected / exposed | 0 / 663 (0.00%) | 0 / 673 (0.00%) | 1 / 324 (0.31%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dizziness | | | |
| subjects affected / exposed | 0 / 663 (0.00%) | 1 / 673 (0.15%) | 0 / 324 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dysaesthesia | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 663 (0.00%) | 1 / 673 (0.15%) | 0 / 324 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Facial paralysis | | | |
| subjects affected / exposed | 0 / 663 (0.00%) | 0 / 673 (0.00%) | 1 / 324 (0.31%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Generalised tonic-clonic seizure | | | |
| subjects affected / exposed | 0 / 663 (0.00%) | 0 / 673 (0.00%) | 1 / 324 (0.31%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Headache | | | |
| subjects affected / exposed | 1 / 663 (0.15%) | 0 / 673 (0.00%) | 0 / 324 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Intracranial aneurysm | | | |
| subjects affected / exposed | 0 / 663 (0.00%) | 1 / 673 (0.15%) | 0 / 324 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ischaemic stroke | | | |
| subjects affected / exposed | 0 / 663 (0.00%) | 0 / 673 (0.00%) | 3 / 324 (0.93%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Migraine | | | |
| subjects affected / exposed | 0 / 663 (0.00%) | 1 / 673 (0.15%) | 0 / 324 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Radiculopathy | | | |
| subjects affected / exposed | 1 / 663 (0.15%) | 0 / 673 (0.00%) | 0 / 324 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Transient ischaemic attack | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 663 (0.00%) | 0 / 673 (0.00%) | 1 / 324 (0.31%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ear and labyrinth disorders | | | |
| Vertigo | | | |
| subjects affected / exposed | 0 / 663 (0.00%) | 0 / 673 (0.00%) | 1 / 324 (0.31%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Eye disorders | | | |
| Pupils unequal | | | |
| subjects affected / exposed | 0 / 663 (0.00%) | 0 / 673 (0.00%) | 1 / 324 (0.31%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vitreous haemorrhage | | | |
| subjects affected / exposed | 1 / 663 (0.15%) | 0 / 673 (0.00%) | 0 / 324 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 1 / 663 (0.15%) | 0 / 673 (0.00%) | 0 / 324 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Abdominal pain upper | | | |
| subjects affected / exposed | 0 / 663 (0.00%) | 1 / 673 (0.15%) | 0 / 324 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Colitis ulcerative | | | |
| subjects affected / exposed | 2 / 663 (0.30%) | 0 / 673 (0.00%) | 0 / 324 (0.00%) |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Constipation | | | |
| subjects affected / exposed | 0 / 663 (0.00%) | 1 / 673 (0.15%) | 0 / 324 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|-----------------|-----------------|-----------------|
| Crohn's disease | | | |
| subjects affected / exposed | 1 / 663 (0.15%) | 3 / 673 (0.45%) | 0 / 324 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 4 / 4 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Food poisoning | | | |
| subjects affected / exposed | 1 / 663 (0.15%) | 0 / 673 (0.00%) | 0 / 324 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Functional gastrointestinal disorder | | | |
| subjects affected / exposed | 1 / 663 (0.15%) | 0 / 673 (0.00%) | 0 / 324 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Haemorrhoids | | | |
| subjects affected / exposed | 0 / 663 (0.00%) | 1 / 673 (0.15%) | 0 / 324 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ileus paralytic | | | |
| subjects affected / exposed | 0 / 663 (0.00%) | 0 / 673 (0.00%) | 1 / 324 (0.31%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Inguinal hernia | | | |
| subjects affected / exposed | 0 / 663 (0.00%) | 1 / 673 (0.15%) | 0 / 324 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Oedematous pancreatitis | | | |
| subjects affected / exposed | 0 / 663 (0.00%) | 0 / 673 (0.00%) | 1 / 324 (0.31%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatobiliary disorders | | | |
| Cholelithiasis | | | |
| subjects affected / exposed | 0 / 663 (0.00%) | 1 / 673 (0.15%) | 0 / 324 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatic cirrhosis | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 1 / 663 (0.15%) | 0 / 673 (0.00%) | 0 / 324 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Skin and subcutaneous tissue disorders | | | |
| Angioedema | | | |
| subjects affected / exposed | 0 / 663 (0.00%) | 1 / 673 (0.15%) | 1 / 324 (0.31%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Drug eruption | | | |
| subjects affected / exposed | 0 / 663 (0.00%) | 1 / 673 (0.15%) | 0 / 324 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Erythema multiforme | | | |
| subjects affected / exposed | 0 / 663 (0.00%) | 1 / 673 (0.15%) | 0 / 324 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pruritus | | | |
| subjects affected / exposed | 0 / 663 (0.00%) | 1 / 673 (0.15%) | 0 / 324 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Psoriasis | | | |
| subjects affected / exposed | 1 / 663 (0.15%) | 2 / 673 (0.30%) | 2 / 324 (0.62%) |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 2 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal and urinary disorders | | | |
| Acute kidney injury | | | |
| subjects affected / exposed | 0 / 663 (0.00%) | 0 / 673 (0.00%) | 1 / 324 (0.31%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hydronephrosis | | | |
| subjects affected / exposed | 0 / 663 (0.00%) | 0 / 673 (0.00%) | 1 / 324 (0.31%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nephrolithiasis | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 663 (0.00%) | 1 / 673 (0.15%) | 2 / 324 (0.62%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal failure | | | |
| subjects affected / exposed | 1 / 663 (0.15%) | 0 / 673 (0.00%) | 0 / 324 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urinary retention | | | |
| subjects affected / exposed | 1 / 663 (0.15%) | 0 / 673 (0.00%) | 0 / 324 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Endocrine disorders | | | |
| Thyroid mass | | | |
| subjects affected / exposed | 0 / 663 (0.00%) | 1 / 673 (0.15%) | 0 / 324 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 0 / 663 (0.00%) | 0 / 673 (0.00%) | 1 / 324 (0.31%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bursitis | | | |
| subjects affected / exposed | 0 / 663 (0.00%) | 0 / 673 (0.00%) | 1 / 324 (0.31%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Intervertebral disc protrusion | | | |
| subjects affected / exposed | 1 / 663 (0.15%) | 2 / 673 (0.30%) | 0 / 324 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Muscular weakness | | | |
| subjects affected / exposed | 1 / 663 (0.15%) | 0 / 673 (0.00%) | 0 / 324 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|-----------------|-----------------|-----------------|
| Musculoskeletal pain | | | |
| subjects affected / exposed | 1 / 663 (0.15%) | 0 / 673 (0.00%) | 0 / 324 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Osteitis | | | |
| subjects affected / exposed | 1 / 663 (0.15%) | 0 / 673 (0.00%) | 0 / 324 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Osteoarthritis | | | |
| subjects affected / exposed | 0 / 663 (0.00%) | 0 / 673 (0.00%) | 1 / 324 (0.31%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Osteonecrosis | | | |
| subjects affected / exposed | 0 / 663 (0.00%) | 0 / 673 (0.00%) | 1 / 324 (0.31%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Rotator cuff syndrome | | | |
| subjects affected / exposed | 1 / 663 (0.15%) | 1 / 673 (0.15%) | 0 / 324 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Appendicitis | | | |
| subjects affected / exposed | 0 / 663 (0.00%) | 1 / 673 (0.15%) | 0 / 324 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cellulitis | | | |
| subjects affected / exposed | 1 / 663 (0.15%) | 1 / 673 (0.15%) | 1 / 324 (0.31%) |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Clostridium difficile colitis | | | |
| subjects affected / exposed | 0 / 663 (0.00%) | 0 / 673 (0.00%) | 1 / 324 (0.31%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dermo-hypodermatitis | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 663 (0.00%) | 0 / 673 (0.00%) | 1 / 324 (0.31%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diverticulitis | | | |
| subjects affected / exposed | 1 / 663 (0.15%) | 0 / 673 (0.00%) | 0 / 324 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Erysipelas | | | |
| subjects affected / exposed | 4 / 663 (0.60%) | 2 / 673 (0.30%) | 0 / 324 (0.00%) |
| occurrences causally related to treatment / all | 1 / 4 | 3 / 3 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Febrile infection | | | |
| subjects affected / exposed | 0 / 663 (0.00%) | 1 / 673 (0.15%) | 0 / 324 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastroenteritis | | | |
| subjects affected / exposed | 0 / 663 (0.00%) | 0 / 673 (0.00%) | 1 / 324 (0.31%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Herpes virus infection | | | |
| subjects affected / exposed | 0 / 663 (0.00%) | 0 / 673 (0.00%) | 1 / 324 (0.31%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 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 / 663 (0.00%) | 0 / 673 (0.00%) | 1 / 324 (0.31%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 2 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Necrotising fasciitis | | | |
| subjects affected / exposed | 1 / 663 (0.15%) | 0 / 673 (0.00%) | 0 / 324 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Oral candidiasis | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 1 / 663 (0.15%) | 0 / 673 (0.00%) | 0 / 324 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Otitis media chronic | | | |
| subjects affected / exposed | 1 / 663 (0.15%) | 0 / 673 (0.00%) | 0 / 324 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia | | | |
| subjects affected / exposed | 1 / 663 (0.15%) | 0 / 673 (0.00%) | 1 / 324 (0.31%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Post procedural infection | | | |
| subjects affected / exposed | 1 / 663 (0.15%) | 0 / 673 (0.00%) | 0 / 324 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary sepsis | | | |
| subjects affected / exposed | 0 / 663 (0.00%) | 0 / 673 (0.00%) | 1 / 324 (0.31%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Purulent discharge | | | |
| subjects affected / exposed | 0 / 663 (0.00%) | 1 / 673 (0.15%) | 0 / 324 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pyelonephritis | | | |
| subjects affected / exposed | 1 / 663 (0.15%) | 1 / 673 (0.15%) | 0 / 324 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory tract infection viral | | | |
| subjects affected / exposed | 1 / 663 (0.15%) | 0 / 673 (0.00%) | 0 / 324 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Septic shock | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 663 (0.00%) | 0 / 673 (0.00%) | 1 / 324 (0.31%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Tinea pedis | | | |
| subjects affected / exposed | 0 / 663 (0.00%) | 0 / 673 (0.00%) | 1 / 324 (0.31%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Tonsillitis | | | |
| subjects affected / exposed | 0 / 663 (0.00%) | 2 / 673 (0.30%) | 0 / 324 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urinary tract infection | | | |
| subjects affected / exposed | 1 / 663 (0.15%) | 0 / 673 (0.00%) | 0 / 324 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |
| subjects affected / exposed | 0 / 663 (0.00%) | 1 / 673 (0.15%) | 0 / 324 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diabetic ketoacidosis | | | |
| subjects affected / exposed | 0 / 663 (0.00%) | 0 / 673 (0.00%) | 1 / 324 (0.31%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Type 3 diabetes mellitus | | | |
| subjects affected / exposed | 0 / 663 (0.00%) | 0 / 673 (0.00%) | 1 / 324 (0.31%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|--------------------|--|--|
| Serious adverse events | All Subjects | | |
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 119 / 1660 (7.17%) | | |
| number of deaths (all causes) | 1 | | |
| number of deaths resulting from adverse events | 0 | | |

| | | | |
|---|------------------|--|--|
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Adenocarcinoma of colon | | | |
| subjects affected / exposed | 1 / 1660 (0.06%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Basal cell carcinoma | | | |
| subjects affected / exposed | 2 / 1660 (0.12%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Bladder transitional cell carcinoma | | | |
| subjects affected / exposed | 2 / 1660 (0.12%) | | |
| occurrences causally related to treatment / all | 1 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Bronchial carcinoma | | | |
| subjects affected / exposed | 1 / 1660 (0.06%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrointestinal tract adenoma | | | |
| subjects affected / exposed | 1 / 1660 (0.06%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Malignant melanoma | | | |
| subjects affected / exposed | 1 / 1660 (0.06%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Myelodysplastic syndrome | | | |
| subjects affected / exposed | 1 / 1660 (0.06%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pituitary tumour benign | | | |
| subjects affected / exposed | 1 / 1660 (0.06%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | |
|--|------------------|--|--|
| Seborrhoeic keratosis | | | |
| subjects affected / exposed | 1 / 1660 (0.06%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Squamous cell carcinoma | | | |
| subjects affected / exposed | 1 / 1660 (0.06%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Thyroid cancer | | | |
| subjects affected / exposed | 1 / 1660 (0.06%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 2 / 1660 (0.12%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hypovolaemic shock | | | |
| subjects affected / exposed | 1 / 1660 (0.06%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Varicose vein | | | |
| subjects affected / exposed | 1 / 1660 (0.06%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pregnancy, puerperium and perinatal conditions | | | |
| Abortion spontaneous | | | |
| subjects affected / exposed | 2 / 1660 (0.12%) | | |
| occurrences causally related to treatment / all | 1 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| General disorders and administration site conditions | | | |
| Chest pain | | | |

| | | | |
|---|------------------|--|--|
| subjects affected / exposed | 1 / 1660 (0.06%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Non-cardiac chest pain | | | |
| subjects affected / exposed | 2 / 1660 (0.12%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Sudden death | | | |
| subjects affected / exposed | 1 / 1660 (0.06%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| Immune system disorders | | | |
| Anaphylactic reaction | | | |
| subjects affected / exposed | 1 / 1660 (0.06%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Reproductive system and breast disorders | | | |
| Cervical dysplasia | | | |
| subjects affected / exposed | 1 / 1660 (0.06%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Erectile dysfunction | | | |
| subjects affected / exposed | 1 / 1660 (0.06%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Prostatitis | | | |
| subjects affected / exposed | 1 / 1660 (0.06%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Asthma | | | |

| | | | |
|---|------------------|--|--|
| subjects affected / exposed | 1 / 1660 (0.06%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Chronic obstructive pulmonary disease | | | |
| subjects affected / exposed | 1 / 1660 (0.06%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Dyspnoea | | | |
| subjects affected / exposed | 2 / 1660 (0.12%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pharyngeal cyst | | | |
| subjects affected / exposed | 1 / 1660 (0.06%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Vocal cord leukoplakia | | | |
| subjects affected / exposed | 1 / 1660 (0.06%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Psychiatric disorders | | | |
| Alcohol abuse | | | |
| subjects affected / exposed | 1 / 1660 (0.06%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Alcohol withdrawal syndrome | | | |
| subjects affected / exposed | 1 / 1660 (0.06%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Suicidal ideation | | | |
| subjects affected / exposed | 1 / 1660 (0.06%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Suicide attempt | | | |

| | | | |
|---|------------------|--|--|
| subjects affected / exposed | 1 / 1660 (0.06%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Injury, poisoning and procedural complications | | | |
| Alcohol poisoning | | | |
| subjects affected / exposed | 2 / 1660 (0.12%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Concussion | | | |
| subjects affected / exposed | 1 / 1660 (0.06%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Fall | | | |
| subjects affected / exposed | 1 / 1660 (0.06%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Femoral neck fracture | | | |
| subjects affected / exposed | 1 / 1660 (0.06%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Head injury | | | |
| subjects affected / exposed | 1 / 1660 (0.06%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Humerus fracture | | | |
| subjects affected / exposed | 1 / 1660 (0.06%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Lower limb fracture | | | |
| subjects affected / exposed | 2 / 1660 (0.12%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Lumbar vertebral fracture | | | |

| | | | |
|---|------------------|--|--|
| subjects affected / exposed | 1 / 1660 (0.06%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pelvic fracture | | | |
| subjects affected / exposed | 2 / 1660 (0.12%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Procedural dizziness | | | |
| subjects affected / exposed | 1 / 1660 (0.06%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Radius fracture | | | |
| subjects affected / exposed | 1 / 1660 (0.06%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Skin abrasion | | | |
| subjects affected / exposed | 1 / 1660 (0.06%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Subdural haematoma | | | |
| subjects affected / exposed | 1 / 1660 (0.06%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Tendon rupture | | | |
| subjects affected / exposed | 1 / 1660 (0.06%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Upper limb fracture | | | |
| subjects affected / exposed | 3 / 1660 (0.18%) | | |
| occurrences causally related to treatment / all | 0 / 3 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cardiac disorders | | | |
| Acute myocardial infarction | | | |

| | | | |
|---|------------------|--|--|
| subjects affected / exposed | 1 / 1660 (0.06%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Angina pectoris | | | |
| subjects affected / exposed | 2 / 1660 (0.12%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Atrial fibrillation | | | |
| subjects affected / exposed | 2 / 1660 (0.12%) | | |
| occurrences causally related to treatment / all | 0 / 3 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Atrial flutter | | | |
| subjects affected / exposed | 1 / 1660 (0.06%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cardiac failure | | | |
| subjects affected / exposed | 1 / 1660 (0.06%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cardiomyopathy | | | |
| subjects affected / exposed | 1 / 1660 (0.06%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Coronary artery disease | | | |
| subjects affected / exposed | 1 / 1660 (0.06%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Left ventricular failure | | | |
| subjects affected / exposed | 1 / 1660 (0.06%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Myocardial infarction | | | |

| | | | |
|---|------------------|--|--|
| subjects affected / exposed | 4 / 1660 (0.24%) | | |
| occurrences causally related to treatment / all | 1 / 4 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Palpitations | | | |
| subjects affected / exposed | 1 / 1660 (0.06%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Ventricular fibrillation | | | |
| subjects affected / exposed | 1 / 1660 (0.06%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Nervous system disorders | | | |
| Carotid arteriosclerosis | | | |
| subjects affected / exposed | 1 / 1660 (0.06%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cerebral infarction | | | |
| subjects affected / exposed | 1 / 1660 (0.06%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Diabetic hyperglycaemic coma | | | |
| subjects affected / exposed | 1 / 1660 (0.06%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Diabetic neuropathy | | | |
| subjects affected / exposed | 1 / 1660 (0.06%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Dizziness | | | |
| subjects affected / exposed | 1 / 1660 (0.06%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Dysaesthesia | | | |

| | | | | |
|---|------------------|--|--|--|
| subjects affected / exposed | 1 / 1660 (0.06%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Facial paralysis | | | | |
| subjects affected / exposed | 1 / 1660 (0.06%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Generalised tonic-clonic seizure | | | | |
| subjects affected / exposed | 1 / 1660 (0.06%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Headache | | | | |
| subjects affected / exposed | 1 / 1660 (0.06%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Intracranial aneurysm | | | | |
| subjects affected / exposed | 1 / 1660 (0.06%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Ischaemic stroke | | | | |
| subjects affected / exposed | 3 / 1660 (0.18%) | | | |
| occurrences causally related to treatment / all | 0 / 3 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Migraine | | | | |
| subjects affected / exposed | 1 / 1660 (0.06%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Radiculopathy | | | | |
| subjects affected / exposed | 1 / 1660 (0.06%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Transient ischaemic attack | | | | |

| | | | |
|---|------------------|--|--|
| subjects affected / exposed | 1 / 1660 (0.06%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Ear and labyrinth disorders | | | |
| Vertigo | | | |
| subjects affected / exposed | 1 / 1660 (0.06%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Eye disorders | | | |
| Pupils unequal | | | |
| subjects affected / exposed | 1 / 1660 (0.06%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Vitreous haemorrhage | | | |
| subjects affected / exposed | 1 / 1660 (0.06%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 1 / 1660 (0.06%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Abdominal pain upper | | | |
| subjects affected / exposed | 1 / 1660 (0.06%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Colitis ulcerative | | | |
| subjects affected / exposed | 2 / 1660 (0.12%) | | |
| occurrences causally related to treatment / all | 1 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Constipation | | | |
| subjects affected / exposed | 1 / 1660 (0.06%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | |
|---|------------------|--|--|
| Crohn's disease | | | |
| subjects affected / exposed | 4 / 1660 (0.24%) | | |
| occurrences causally related to treatment / all | 5 / 5 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Food poisoning | | | |
| subjects affected / exposed | 1 / 1660 (0.06%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Functional gastrointestinal disorder | | | |
| subjects affected / exposed | 1 / 1660 (0.06%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Haemorrhoids | | | |
| subjects affected / exposed | 1 / 1660 (0.06%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Ileus paralytic | | | |
| subjects affected / exposed | 1 / 1660 (0.06%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Inguinal hernia | | | |
| subjects affected / exposed | 1 / 1660 (0.06%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Oedematous pancreatitis | | | |
| subjects affected / exposed | 1 / 1660 (0.06%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hepatobiliary disorders | | | |
| Cholelithiasis | | | |
| subjects affected / exposed | 1 / 1660 (0.06%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hepatic cirrhosis | | | |

| | | | |
|---|------------------|--|--|
| subjects affected / exposed | 1 / 1660 (0.06%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Skin and subcutaneous tissue disorders | | | |
| Angioedema | | | |
| subjects affected / exposed | 2 / 1660 (0.12%) | | |
| occurrences causally related to treatment / all | 1 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Drug eruption | | | |
| subjects affected / exposed | 1 / 1660 (0.06%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Erythema multiforme | | | |
| subjects affected / exposed | 1 / 1660 (0.06%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pruritus | | | |
| subjects affected / exposed | 1 / 1660 (0.06%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Psoriasis | | | |
| subjects affected / exposed | 5 / 1660 (0.30%) | | |
| occurrences causally related to treatment / all | 3 / 5 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Renal and urinary disorders | | | |
| Acute kidney injury | | | |
| subjects affected / exposed | 1 / 1660 (0.06%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hydronephrosis | | | |
| subjects affected / exposed | 1 / 1660 (0.06%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Nephrolithiasis | | | |

| | | | |
|---|------------------|--|--|
| subjects affected / exposed | 3 / 1660 (0.18%) | | |
| occurrences causally related to treatment / all | 0 / 3 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Renal failure | | | |
| subjects affected / exposed | 1 / 1660 (0.06%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Urinary retention | | | |
| subjects affected / exposed | 1 / 1660 (0.06%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Endocrine disorders | | | |
| Thyroid mass | | | |
| subjects affected / exposed | 1 / 1660 (0.06%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 1 / 1660 (0.06%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Bursitis | | | |
| subjects affected / exposed | 1 / 1660 (0.06%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Intervertebral disc protrusion | | | |
| subjects affected / exposed | 3 / 1660 (0.18%) | | |
| occurrences causally related to treatment / all | 0 / 3 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Muscular weakness | | | |
| subjects affected / exposed | 1 / 1660 (0.06%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | | |
|---|------------------|--|--|--|
| Musculoskeletal pain | | | | |
| subjects affected / exposed | 1 / 1660 (0.06%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Osteitis | | | | |
| subjects affected / exposed | 1 / 1660 (0.06%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Osteoarthritis | | | | |
| subjects affected / exposed | 1 / 1660 (0.06%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Osteonecrosis | | | | |
| subjects affected / exposed | 1 / 1660 (0.06%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Rotator cuff syndrome | | | | |
| subjects affected / exposed | 2 / 1660 (0.12%) | | | |
| occurrences causally related to treatment / all | 0 / 2 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Infections and infestations | | | | |
| Appendicitis | | | | |
| subjects affected / exposed | 1 / 1660 (0.06%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Cellulitis | | | | |
| subjects affected / exposed | 3 / 1660 (0.18%) | | | |
| occurrences causally related to treatment / all | 2 / 3 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Clostridium difficile colitis | | | | |
| subjects affected / exposed | 1 / 1660 (0.06%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Dermo-hypodermatitis | | | | |

| | | | | |
|---|------------------|--|--|--|
| subjects affected / exposed | 1 / 1660 (0.06%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Diverticulitis | | | | |
| subjects affected / exposed | 1 / 1660 (0.06%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Erysipelas | | | | |
| subjects affected / exposed | 6 / 1660 (0.36%) | | | |
| occurrences causally related to treatment / all | 4 / 7 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Febrile infection | | | | |
| subjects affected / exposed | 1 / 1660 (0.06%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Gastroenteritis | | | | |
| subjects affected / exposed | 1 / 1660 (0.06%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Herpes virus infection | | | | |
| subjects affected / exposed | 1 / 1660 (0.06%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Infective exacerbation of chronic obstructive airways disease | | | | |
| subjects affected / exposed | 1 / 1660 (0.06%) | | | |
| occurrences causally related to treatment / all | 2 / 2 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Necrotising fasciitis | | | | |
| subjects affected / exposed | 1 / 1660 (0.06%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Oral candidiasis | | | | |

| | | | |
|---|------------------|--|--|
| subjects affected / exposed | 1 / 1660 (0.06%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Otitis media chronic | | | |
| subjects affected / exposed | 1 / 1660 (0.06%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pneumonia | | | |
| subjects affected / exposed | 2 / 1660 (0.12%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Post procedural infection | | | |
| subjects affected / exposed | 1 / 1660 (0.06%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pulmonary sepsis | | | |
| subjects affected / exposed | 1 / 1660 (0.06%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Purulent discharge | | | |
| subjects affected / exposed | 1 / 1660 (0.06%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pyelonephritis | | | |
| subjects affected / exposed | 2 / 1660 (0.12%) | | |
| occurrences causally related to treatment / all | 1 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory tract infection viral | | | |
| subjects affected / exposed | 1 / 1660 (0.06%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Septic shock | | | |

| | | | |
|---|------------------|--|--|
| subjects affected / exposed | 1 / 1660 (0.06%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Tinea pedis | | | |
| subjects affected / exposed | 1 / 1660 (0.06%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Tonsillitis | | | |
| subjects affected / exposed | 2 / 1660 (0.12%) | | |
| occurrences causally related to treatment / all | 1 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Urinary tract infection | | | |
| subjects affected / exposed | 1 / 1660 (0.06%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |
| subjects affected / exposed | 1 / 1660 (0.06%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Diabetic ketoacidosis | | | |
| subjects affected / exposed | 1 / 1660 (0.06%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Type 3 diabetes mellitus | | | |
| subjects affected / exposed | 1 / 1660 (0.06%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

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

| Non-serious adverse events | Subpopulation A (naive) | Subpopulation B (non-biologic) | Subpopulation C (biologic) |
|--|--|--|---|
| Total subjects affected by non-serious adverse events subjects affected / exposed | 450 / 663 (67.87%) | 474 / 673 (70.43%) | 203 / 324 (62.65%) |
| Vascular disorders Hypertension subjects affected / exposed occurrences (all) | 26 / 663 (3.92%) 29 | 31 / 673 (4.61%) 34 | 8 / 324 (2.47%) 8 |
| Nervous system disorders Headache subjects affected / exposed occurrences (all) | 76 / 663 (11.46%) 180 | 79 / 673 (11.74%) 133 | 21 / 324 (6.48%) 31 |
| General disorders and administration site conditions Asthenia subjects affected / exposed occurrences (all) Fatigue subjects affected / exposed occurrences (all) Influenza like illness subjects affected / exposed occurrences (all) Pyrexia subjects affected / exposed occurrences (all) | 16 / 663 (2.41%) 19 17 / 663 (2.56%) 25 8 / 663 (1.21%) 8 11 / 663 (1.66%) 11 | 10 / 673 (1.49%) 12 25 / 673 (3.71%) 29 15 / 673 (2.23%) 16 12 / 673 (1.78%) 13 | 7 / 324 (2.16%) 9 6 / 324 (1.85%) 7 4 / 324 (1.23%) 5 8 / 324 (2.47%) 10 |
| Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all) Toothache subjects affected / exposed occurrences (all) | 35 / 663 (5.28%) 47 14 / 663 (2.11%) 15 | 30 / 673 (4.46%) 34 15 / 673 (2.23%) 16 | 14 / 324 (4.32%) 19 5 / 324 (1.54%) 6 |
| Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) Oropharyngeal pain | 37 / 663 (5.58%) 39 | 31 / 673 (4.61%) 33 | 12 / 324 (3.70%) 15 |

| | | | |
|--|------------------------|------------------------|------------------------|
| subjects affected / exposed occurrences (all) | 34 / 663 (5.13%) 38 | 40 / 673 (5.94%) 47 | 14 / 324 (4.32%) 15 |
| Skin and subcutaneous tissue disorders | | | |
| Alopecia | | | |
| subjects affected / exposed | 3 / 663 (0.45%) | 7 / 673 (1.04%) | 8 / 324 (2.47%) |
| occurrences (all) | 3 | 7 | 8 |
| Eczema | | | |
| subjects affected / exposed | 25 / 663 (3.77%) | 20 / 673 (2.97%) | 5 / 324 (1.54%) |
| occurrences (all) | 27 | 24 | 5 |
| Intertrigo | | | |
| subjects affected / exposed | 12 / 663 (1.81%) | 15 / 673 (2.23%) | 3 / 324 (0.93%) |
| occurrences (all) | 15 | 16 | 3 |
| Pruritus | | | |
| subjects affected / exposed | 31 / 663 (4.68%) | 41 / 673 (6.09%) | 13 / 324 (4.01%) |
| occurrences (all) | 34 | 50 | 15 |
| Psoriasis | | | |
| subjects affected / exposed | 20 / 663 (3.02%) | 36 / 673 (5.35%) | 22 / 324 (6.79%) |
| occurrences (all) | 25 | 40 | 25 |
| Urticaria | | | |
| subjects affected / exposed | 14 / 663 (2.11%) | 7 / 673 (1.04%) | 3 / 324 (0.93%) |
| occurrences (all) | 15 | 7 | 4 |
| Renal and urinary disorders | | | |
| Haematuria | | | |
| subjects affected / exposed | 10 / 663 (1.51%) | 17 / 673 (2.53%) | 5 / 324 (1.54%) |
| occurrences (all) | 12 | 18 | 7 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 26 / 663 (3.92%) | 28 / 673 (4.16%) | 18 / 324 (5.56%) |
| occurrences (all) | 30 | 34 | 25 |
| Back pain | | | |
| subjects affected / exposed | 31 / 663 (4.68%) | 46 / 673 (6.84%) | 15 / 324 (4.63%) |
| occurrences (all) | 35 | 57 | 17 |
| Myalgia | | | |
| subjects affected / exposed | 10 / 663 (1.51%) | 7 / 673 (1.04%) | 7 / 324 (2.16%) |
| occurrences (all) | 14 | 10 | 8 |
| Pain in extremity | | | |

| | | | |
|-----------------------------|--------------------|--------------------|-------------------|
| subjects affected / exposed | 15 / 663 (2.26%) | 17 / 673 (2.53%) | 7 / 324 (2.16%) |
| occurrences (all) | 17 | 17 | 8 |
| Tendonitis | | | |
| subjects affected / exposed | 6 / 663 (0.90%) | 1 / 673 (0.15%) | 7 / 324 (2.16%) |
| occurrences (all) | 7 | 1 | 7 |
| Infections and infestations | | | |
| Bronchitis | | | |
| subjects affected / exposed | 24 / 663 (3.62%) | 27 / 673 (4.01%) | 10 / 324 (3.09%) |
| occurrences (all) | 25 | 30 | 12 |
| Conjunctivitis | | | |
| subjects affected / exposed | 33 / 663 (4.98%) | 21 / 673 (3.12%) | 15 / 324 (4.63%) |
| occurrences (all) | 42 | 26 | 19 |
| Folliculitis | | | |
| subjects affected / exposed | 16 / 663 (2.41%) | 21 / 673 (3.12%) | 7 / 324 (2.16%) |
| occurrences (all) | 19 | 23 | 9 |
| Gastroenteritis | | | |
| subjects affected / exposed | 21 / 663 (3.17%) | 14 / 673 (2.08%) | 6 / 324 (1.85%) |
| occurrences (all) | 22 | 14 | 6 |
| Influenza | | | |
| subjects affected / exposed | 15 / 663 (2.26%) | 17 / 673 (2.53%) | 8 / 324 (2.47%) |
| occurrences (all) | 16 | 20 | 8 |
| Nasopharyngitis | | | |
| subjects affected / exposed | 189 / 663 (28.51%) | 189 / 673 (28.08%) | 66 / 324 (20.37%) |
| occurrences (all) | 296 | 284 | 108 |
| Oral candidiasis | | | |
| subjects affected / exposed | 16 / 663 (2.41%) | 30 / 673 (4.46%) | 14 / 324 (4.32%) |
| occurrences (all) | 23 | 41 | 16 |
| Oral herpes | | | |
| subjects affected / exposed | 16 / 663 (2.41%) | 8 / 673 (1.19%) | 7 / 324 (2.16%) |
| occurrences (all) | 23 | 11 | 10 |
| Otitis externa | | | |
| subjects affected / exposed | 9 / 663 (1.36%) | 7 / 673 (1.04%) | 7 / 324 (2.16%) |
| occurrences (all) | 10 | 8 | 7 |
| Pharyngitis | | | |
| subjects affected / exposed | 28 / 663 (4.22%) | 19 / 673 (2.82%) | 10 / 324 (3.09%) |
| occurrences (all) | 33 | 21 | 11 |

| | | | |
|-----------------------------------|------------------|------------------|------------------|
| Rhinitis | | | |
| subjects affected / exposed | 37 / 663 (5.58%) | 37 / 673 (5.50%) | 11 / 324 (3.40%) |
| occurrences (all) | 47 | 50 | 13 |
| Sinusitis | | | |
| subjects affected / exposed | 11 / 663 (1.66%) | 16 / 673 (2.38%) | 11 / 324 (3.40%) |
| occurrences (all) | 11 | 19 | 14 |
| Tinea pedis | | | |
| subjects affected / exposed | 16 / 663 (2.41%) | 18 / 673 (2.67%) | 7 / 324 (2.16%) |
| occurrences (all) | 16 | 18 | 7 |
| Tonsillitis | | | |
| subjects affected / exposed | 22 / 663 (3.32%) | 34 / 673 (5.05%) | 11 / 324 (3.40%) |
| occurrences (all) | 29 | 39 | 14 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 39 / 663 (5.88%) | 25 / 673 (3.71%) | 20 / 324 (6.17%) |
| occurrences (all) | 51 | 29 | 23 |
| Urinary tract infection | | | |
| subjects affected / exposed | 26 / 663 (3.92%) | 21 / 673 (3.12%) | 13 / 324 (4.01%) |
| occurrences (all) | 38 | 29 | 15 |

| | | | |
|---|----------------------|--|--|
| Non-serious adverse events | All Subjects | | |
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 1127 / 1660 (67.89%) | | |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 65 / 1660 (3.92%) | | |
| occurrences (all) | 71 | | |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 176 / 1660 (10.60%) | | |
| occurrences (all) | 343 | | |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 33 / 1660 (1.99%) | | |
| occurrences (all) | 40 | | |
| Fatigue | | | |

| | | | |
|---|-------------------|--|--|
| subjects affected / exposed | 48 / 1660 (2.89%) | | |
| occurrences (all) | 61 | | |
| Influenza like illness | | | |
| subjects affected / exposed | 27 / 1660 (1.63%) | | |
| occurrences (all) | 29 | | |
| Pyrexia | | | |
| subjects affected / exposed | 31 / 1660 (1.87%) | | |
| occurrences (all) | 34 | | |
| Gastrointestinal disorders | | | |
| Diarrhoea | | | |
| subjects affected / exposed | 79 / 1660 (4.76%) | | |
| occurrences (all) | 100 | | |
| Toothache | | | |
| subjects affected / exposed | 34 / 1660 (2.05%) | | |
| occurrences (all) | 37 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |
| subjects affected / exposed | 80 / 1660 (4.82%) | | |
| occurrences (all) | 87 | | |
| Oropharyngeal pain | | | |
| subjects affected / exposed | 88 / 1660 (5.30%) | | |
| occurrences (all) | 100 | | |
| Skin and subcutaneous tissue disorders | | | |
| Alopecia | | | |
| subjects affected / exposed | 18 / 1660 (1.08%) | | |
| occurrences (all) | 18 | | |
| Eczema | | | |
| subjects affected / exposed | 50 / 1660 (3.01%) | | |
| occurrences (all) | 56 | | |
| Intertrigo | | | |
| subjects affected / exposed | 30 / 1660 (1.81%) | | |
| occurrences (all) | 34 | | |
| Pruritus | | | |
| subjects affected / exposed | 85 / 1660 (5.12%) | | |
| occurrences (all) | 99 | | |
| Psoriasis | | | |

| | | | |
|---|---|--|--|
| <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Urticaria</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>78 / 1660 (4.70%)</p> <p>90</p> <p>24 / 1660 (1.45%)</p> <p>26</p> | | |
| <p>Renal and urinary disorders</p> <p>Haematuria</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>32 / 1660 (1.93%)</p> <p>37</p> | | |
| <p>Musculoskeletal and connective tissue disorders</p> <p>Arthralgia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Back pain</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Myalgia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Pain in extremity</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Tendonitis</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>72 / 1660 (4.34%)</p> <p>89</p> <p>92 / 1660 (5.54%)</p> <p>109</p> <p>24 / 1660 (1.45%)</p> <p>32</p> <p>39 / 1660 (2.35%)</p> <p>42</p> <p>14 / 1660 (0.84%)</p> <p>15</p> | | |
| <p>Infections and infestations</p> <p>Bronchitis</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Conjunctivitis</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Folliculitis</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Gastroenteritis</p> | <p>61 / 1660 (3.67%)</p> <p>67</p> <p>69 / 1660 (4.16%)</p> <p>87</p> <p>44 / 1660 (2.65%)</p> <p>51</p> | | |

| | | | |
|-----------------------------------|------------------------|--|--|
| subjects affected / exposed | 41 / 1660 (2.47%) | | |
| occurrences (all) | 42 | | |
| Influenza | | | |
| subjects affected / exposed | 40 / 1660 (2.41%) | | |
| occurrences (all) | 44 | | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 444 / 1660 (26.75%) | | |
| occurrences (all) | 688 | | |
| Oral candidiasis | | | |
| subjects affected / exposed | 60 / 1660 (3.61%) | | |
| occurrences (all) | 80 | | |
| Oral herpes | | | |
| subjects affected / exposed | 31 / 1660 (1.87%) | | |
| occurrences (all) | 44 | | |
| Otitis externa | | | |
| subjects affected / exposed | 23 / 1660 (1.39%) | | |
| occurrences (all) | 25 | | |
| Pharyngitis | | | |
| subjects affected / exposed | 57 / 1660 (3.43%) | | |
| occurrences (all) | 65 | | |
| Rhinitis | | | |
| subjects affected / exposed | 85 / 1660 (5.12%) | | |
| occurrences (all) | 110 | | |
| Sinusitis | | | |
| subjects affected / exposed | 38 / 1660 (2.29%) | | |
| occurrences (all) | 44 | | |
| Tinea pedis | | | |
| subjects affected / exposed | 41 / 1660 (2.47%) | | |
| occurrences (all) | 41 | | |
| Tonsillitis | | | |
| subjects affected / exposed | 67 / 1660 (4.04%) | | |
| occurrences (all) | 82 | | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 84 / 1660 (5.06%) | | |
| occurrences (all) | 103 | | |

| | | | |
|---|-------------------------|--|--|
| Urinary tract infection subjects affected / exposed occurrences (all) | 60 / 1660 (3.61%) 82 | | |
|---|-------------------------|--|--|

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported