



Clinical trial results:

A Phase III Randomized, Double-blind, Placebo-controlled, Multicenter Study to Determine the Safety and Efficacy of AZD7442 for the Treatment of COVID-19 in Non-hospitalized Adults

Summary

| | |
|--------------------------|-----------------|
| EudraCT number | 2020-005315-44 |
| Trial protocol | DE IT HU PL BG |
| Global end of trial date | 19 October 2022 |

Results information

| | |
|--------------------------------|----------------|
| Result version number | v2 (current) |
| This version publication date | 02 August 2023 |
| First version publication date | 02 June 2023 |
| Version creation reason | |

Trial information

Trial identification

| | |
|-----------------------|-------------|
| Sponsor protocol code | D8851C00001 |
|-----------------------|-------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT04723394 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | AstraZeneca |
| Sponsor organisation address | S-151, Sodertalje, Sweden, |
| Public contact | Global Clinical Lead, AstraZeneca, 1 8772409479, information.center@astrazeneca.com |
| Scientific contact | Global Clinical Lead, AstraZeneca, 1 8772409479, information.center@astrazeneca.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 | 02 December 2022 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 19 October 2022 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To estimate the efficacy of AZD7442 in the prevention of the composite endpoint of either severe COVID-19 or death from any cause through study Day 29

Protection of trial subjects:

This study is conducted in accordance with the protocol and with the following: Consensus ethical principles derived from international guidelines including the Declaration of Helsinki and Council for International Organizations of Medical Sciences International Ethical Guidelines; Applicable International Conference on Harmonisation (ICH)/Good Clinical Practice (GCP) Guidelines; Applicable laws and regulations. The protocol, protocol amendments, Informed Consent Form (ICF), Investigator Brochure, and other relevant documents (e.g. advertisements) must be submitted to an Institutional Review Board/Independent Ethics Committee (IRB/IEC) by the Investigator and reviewed and approved by the IRB/IEC before the study is initiated. Any amendments to the protocol will require IRB/IEC approval before implementation of changes made to the study design, except for changes necessary to eliminate an immediate hazard to study patients. Where applicable as per relevant laws and regulations, amendments will also be submitted to, reviewed and approved by regulatory authorities/national competent authorities.

Background therapy: -

Evidence for comparator: -

| | |
|---|-----------------|
| Actual start date of recruitment | 28 January 2021 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|-------------------------|
| Country: Number of subjects enrolled | Argentina: 60 |
| Country: Number of subjects enrolled | Brazil: 27 |
| Country: Number of subjects enrolled | Czechia: 7 |
| Country: Number of subjects enrolled | Germany: 92 |
| Country: Number of subjects enrolled | Hungary: 3 |
| Country: Number of subjects enrolled | Italy: 73 |
| Country: Number of subjects enrolled | Japan: 42 |
| Country: Number of subjects enrolled | Mexico: 310 |
| Country: Number of subjects enrolled | Poland: 2 |
| Country: Number of subjects enrolled | Russian Federation: 119 |
| Country: Number of subjects enrolled | Spain: 70 |
| Country: Number of subjects enrolled | Ukraine: 16 |
| Country: Number of subjects enrolled | United Kingdom: 44 |
| Country: Number of subjects enrolled | United States: 149 |

| | |
|------------------------------------|------|
| Worldwide total number of subjects | 1014 |
| EEA total number of subjects | 247 |

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) | 890 |
| From 65 to 84 years | 123 |
| 85 years and over | 1 |

Subject disposition

Recruitment

Recruitment details:

910 participants were randomized to receive treatment in study D8851C00001 (TACKLE) with AZD7442 (AZD8895 + AZD1061) or placebo. Of the 910 participants randomized, 903 (99.2%) received treatment with study drug. Of the 903 dosed, 452 (50.1%) participants received AZD7442 and 451 (49.9%) participants received placebo.

Pre-assignment

Screening details:

In TACKLE, at the first visit, ie, the enrollment visit 1, participants were evaluated regarding the protocol mandated inclusion and exclusion criteria. After enrolment, eligible participants were randomized at a 1: 1 ratio to receive a single dose of study provided AZD7442 (AZD8895 + AZD1061) or placebo.

Period 1

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

Arms

| | |
|------------------------------|---------|
| Are arms mutually exclusive? | Yes |
| Arm title | AZD7442 |

Arm description:

Single dose of 600 mg of AZD7442 (2 separate IM injections) on Day 1

| | |
|--|---|
| Arm type | Experimental |
| Investigational medicinal product name | Combination of 2 mAbs (AZD8895 and AZD1061) |
| Investigational medicinal product code | |
| Other name | tixagevimab-cilgavimab |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

Single dose (× 2 separate IM injections) of 600 mg of AZD7442 on Day 1.

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

Arm description:

Single dose of Placebo (2 separate IM injections) on Day 1

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

Dosage and administration details:

Single dose (× 2 separate IM injections) of saline placebo on Day 1.

| Number of subjects in period 1^[1] | AZD7442 | Placebo |
|---|--------------------|---------|
| Started | 452 | 451 |
| Modified Full Analysis Set | 413 | 421 |
| Primary Analysis Population | 410 | 419 |
| Key Secondary Analysis Population | 404 ^[2] | 411 |
| Completed | 407 | 390 |
| Not completed | 45 | 61 |
| Adverse event, serious fatal | 8 | 8 |
| Consent withdrawn by subject | 17 | 33 |
| Adverse event, non-fatal | - | 3 |
| Lost to follow-up | 20 | 17 |

Notes:

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

Justification: These participants are those who have non-missing results of key secondary endpoint.

[2] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: 1014 total participants enrolled in the study but only 903 dosed, and we report results of these dosed participants (Full Analysis Set).

Baseline characteristics

Reporting groups

| | |
|--|---------|
| Reporting group title | AZD7442 |
| Reporting group description: | |
| Single dose of 600 mg of AZD7442 (2 separate IM injections) on Day 1 | |
| Reporting group title | Placebo |
| Reporting group description: | |
| Single dose of Placebo (2 separate IM injections) on Day 1 | |

| Reporting group values | AZD7442 | Placebo | Total |
|--|--------------|--------------|-------|
| Number of subjects | 452 | 451 | 903 |
| Age categorical | | | |
| Units: Subjects | | | |
| In utero | 0 | 0 | 0 |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | 0 |
| Newborns (0-27 days) | 0 | 0 | 0 |
| Infants and toddlers (28 days-23 months) | 0 | 0 | 0 |
| Children (2-11 years) | 0 | 0 | 0 |
| Adolescents (12-17 years) | 0 | 0 | 0 |
| Adults (18-64 years) | 393 | 394 | 787 |
| From 65-84 years | 59 | 56 | 115 |
| 85 years and over | 0 | 1 | 1 |
| Age Continuous | | | |
| Full Analysis Set | | | |
| Units: years | | | |
| median | 46.0 | 46.0 | |
| full range (min-max) | 18.0 to 83.0 | 18.0 to 86.0 | - |
| Sex: Female, Male | | | |
| Units: Participants | | | |
| Female | 239 | 216 | 455 |
| Male | 213 | 235 | 448 |
| Ethnicity (NIH/OMB) | | | |
| Units: Subjects | | | |
| Hispanic or Latino | 230 | 238 | 468 |
| Not Hispanic or Latino | 222 | 213 | 435 |
| Race (NIH/OMB) | | | |
| Units: Subjects | | | |
| American Indian or Alaska Native | 100 | 115 | 215 |
| Asian | 30 | 21 | 51 |
| Black or African American | 16 | 20 | 36 |
| Multiple | 0 | 0 | 0 |
| Native Hawaiian or Other Pacific Islander | 0 | 0 | 0 |
| Not reported | 21 | 21 | 42 |
| White | 285 | 274 | 559 |
| Risk of Progression to Severe COVID-19 | | | |
| Risk of Progression to Severe COVID-19 is assessed based on participant's medical history - based on | | | |

| FDA/CDC guidelines. Summarized in the Full Analysis Set | | | |
|---|---------|---------|-----|
| Units: Subjects | | | |
| High | 405 | 406 | 811 |
| Low | 47 | 45 | 92 |
| Country | | | |
| Units: Subjects | | | |
| Argentina | 29 | 28 | 57 |
| Brazil | 7 | 12 | 19 |
| Czech Republic | 3 | 2 | 5 |
| Germany | 33 | 38 | 71 |
| Hungary | 2 | 1 | 3 |
| Italy | 37 | 33 | 70 |
| Japan | 26 | 14 | 40 |
| Mexico | 139 | 166 | 305 |
| Poland | 1 | 1 | 2 |
| Russian Federation | 55 | 51 | 106 |
| Spain | 31 | 37 | 68 |
| Ukraine | 5 | 10 | 15 |
| United Kingdom | 20 | 18 | 38 |
| United States | 64 | 40 | 104 |
| BMI (kg/m ²) | | | |
| Full Analysis Set | | | |
| Units: kg/m ² | | | |
| arithmetic mean | 28.9 | 29.2 | |
| standard deviation | ± 5.46 | ± 6.56 | - |
| Age Continuous | | | |
| Full Analysis Set | | | |
| Units: Years | | | |
| arithmetic mean | 46.3 | 45.9 | |
| standard deviation | ± 15.42 | ± 14.99 | - |

Subject analysis sets

| | |
|----------------------------|------------------------------------|
| Subject analysis set title | AZD7442 modified Full Analysis Set |
| Subject analysis set type | Full analysis |

Subject analysis set description:

All participants in the full analysis set who received AZD7442 ≤ 7 days from symptom onset and were not hospitalized at baseline (≤ Day 1) for isolation purpose.

| | |
|----------------------------|------------------------------------|
| Subject analysis set title | Placebo modified Full Analysis Set |
| Subject analysis set type | Full analysis |

Subject analysis set description:

All participants in the full analysis set who received placebo ≤ 7 days from symptom onset and were not hospitalized at baseline (≤ Day 1) for isolation purpose.

| Reporting group values | AZD7442 modified Full Analysis Set | Placebo modified Full Analysis Set | |
|--|------------------------------------|------------------------------------|--|
| Number of subjects | 413 | 421 | |
| Age categorical | | | |
| Units: Subjects | | | |
| In utero | | | |
| Preterm newborn infants (gestational age < 37 wks) | | | |
| Newborns (0-27 days) | | | |

| | | | |
|--|-----|-----|--|
| Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over | | | |
| Age Continuous | | | |
| Full Analysis Set | | | |
| Units: years median full range (min-max) | | | |
| Sex: Female, Male | | | |
| Units: Participants | | | |
| Female | 226 | 206 | |
| Male | 187 | 215 | |
| Ethnicity (NIH/OMB) | | | |
| Units: Subjects | | | |
| Hispanic or Latino | | | |
| Not Hispanic or Latino | | | |
| Race (NIH/OMB) | | | |
| Units: Subjects | | | |
| American Indian or Alaska Native Asian Black or African American Multiple Native Hawaiian or Other Pacific Islander Not reported White | | | |
| Risk of Progression to Severe COVID-19 | | | |
| Risk of Progression to Severe COVID-19 is assessed based on participant's medical history - based on FDA/CDC guidelines. Summarized in the Full Analysis Set | | | |
| Units: Subjects | | | |
| High | | | |
| Low | | | |
| Country | | | |
| Units: Subjects | | | |
| Argentina Brazil Czech Republic Germany Hungary Italy Japan Mexico Poland Russian Federation Spain Ukraine United Kingdom United States | | | |

| | | | |
|--------------------------|---|---|--|
| BMI (kg/m ²) | | | |
| Full Analysis Set | | | |
| Units: kg/m ² | | | |
| arithmetic mean | | | |
| standard deviation | ± | ± | |
| Age Continuous | | | |
| Full Analysis Set | | | |
| Units: Years | | | |
| arithmetic mean | | | |
| standard deviation | ± | ± | |

End points

End points reporting groups

| | |
|--|------------------------------------|
| Reporting group title | AZD7442 |
| Reporting group description: | |
| Single dose of 600 mg of AZD7442 (2 separate IM injections) on Day 1 | |
| Reporting group title | Placebo |
| Reporting group description: | |
| Single dose of Placebo (2 separate IM injections) on Day 1 | |
| Subject analysis set title | AZD7442 modified Full Analysis Set |
| Subject analysis set type | Full analysis |
| Subject analysis set description: | |
| All participants in the full analysis set who received AZD7442 ≤ 7 days from symptom onset and were not hospitalized at baseline (\leq Day 1) for isolation purpose. | |
| Subject analysis set title | Placebo modified Full Analysis Set |
| Subject analysis set type | Full analysis |
| Subject analysis set description: | |
| All participants in the full analysis set who received placebo ≤ 7 days from symptom onset and were not hospitalized at baseline (\leq Day 1) for isolation purpose. | |

Primary: A Composite of Either Severe COVID-19 or Death From Any Cause Through Day 29

| | |
|---|--|
| End point title | A Composite of Either Severe COVID-19 or Death From Any Cause Through Day 29 |
| End point description: | |
| Severe COVID-19 is characterized by a minimum of either pneumonia (fever, cough, tachypnea, or dyspnea, and lung infiltrates) or hypoxemia ($\text{SpO}_2 < 90\%$ in room air and/or severe respiratory distress) and a WHO Clinical Progression Scale score of 5 or higher. | |
| End point type | Primary |
| End point timeframe: | |
| Baseline (Day 1) and Day 29 | |

| End point values | AZD7442 modified Full Analysis Set | Placebo modified Full Analysis Set | | |
|-----------------------------|------------------------------------|------------------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 410 | 419 | | |
| Units: Participants | 18 | 37 | | |

Statistical analyses

| | |
|-----------------------------------|---|
| Statistical analysis title | relative risk reduction |
| Statistical analysis description: | |
| AZD7442 vs Placebo | |
| Comparison groups | AZD7442 modified Full Analysis Set v Placebo modified Full Analysis Set |

| | |
|---|--------------------------------------|
| Number of subjects included in analysis | 829 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[1] |
| P-value | = 0.01 |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Relative Risk Reduction (100*[1-RR]) |
| Point estimate | 50.38 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 14.38 |
| upper limit | 71.25 |

Notes:

[1] - The relative risk reduction RRR represents the percent reduction in incidence of severe COVID-19 or death from any cause in the AZD7442 group relative to placebo. A RRR > 0 represents favorable efficacy in the AZD7442 group. A p-value <0.05 indicates a statistically significant result.

Secondary: A Composite of Death From Any Cause or Hospitalization for COVID-19 Complications or Sequelae Through Day 169

| | |
|------------------------|---|
| End point title | A Composite of Death From Any Cause or Hospitalization for COVID-19 Complications or Sequelae Through Day 169 |
| End point description: | Death from Any Cause or Hospitalization for COVID-19 Complications or Sequelae through Day 169 |
| End point type | Secondary |
| End point timeframe: | Baseline (Day 1) and Day 169 |

| End point values | AZD7442 modified Full Analysis Set | Placebo modified Full Analysis Set | | |
|-----------------------------|------------------------------------|------------------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 404 | 411 | | |
| Units: Participants | 20 | 40 | | |

Statistical analyses

| | |
|---|---|
| Statistical analysis title | relative risk reduction |
| Statistical analysis description: | AZD7442 vs Placebo |
| Comparison groups | AZD7442 modified Full Analysis Set v Placebo modified Full Analysis Set |
| Number of subjects included in analysis | 815 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[2] |
| P-value | = 0.009 |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Relative Risk Reduction (100*[1-RR]) |
| Point estimate | 49.24 |

| Confidence interval | |
|---------------------|---------|
| level | 95 % |
| sides | 2-sided |
| lower limit | 14.72 |
| upper limit | 69.79 |

Notes:

[2] - The relative risk reduction RRR represents the percent reduction in incidence of death from any cause or hospitalization for COVID-19 complications or sequelae in the AZD7442 group relative to placebo. A RRR > 0 represents favorable efficacy in the AZD7442 group. A p-value <0.05 indicates a statistically significant result. Participants who discontinued or were lost to follow up prior to Day 169 are considered missing.

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From first dose of study drug until end of study, with an average of 436 days.

Adverse event reporting additional description:

AEs are reported for the Safety Analysis Set, defined as all participants randomized and dosed with IMP.

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 24.0 |
|--------------------|------|

Reporting groups

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

Reporting group description:

Single dose of Placebo (2 separate IM injections) on Day 1

| | |
|-----------------------|---------|
| Reporting group title | AZD7442 |
|-----------------------|---------|

Reporting group description:

Single dose of 600 mg of AZD7442 (2 separate IM injections) on Day 1

| Serious adverse events | Placebo | AZD7442 | |
|---|-------------------|-------------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 65 / 451 (14.41%) | 46 / 452 (10.18%) | |
| number of deaths (all causes) | 8 | 8 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Gastric cancer | | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Colorectal cancer metastatic | | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Vascular disorders | | | |
| Hypertensive emergency | | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Peripheral artery thrombosis | | | |

| | | | |
|--|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypertensive crisis | | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pregnancy, puerperium and perinatal conditions | | | |
| Abortion spontaneous | | | |
| subjects affected / exposed | 2 / 451 (0.44%) | 0 / 452 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General disorders and administration site conditions | | | |
| Sudden cardiac death | | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Death | | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Reproductive system and breast disorders | | | |
| Adenomyosis | | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Acute pulmonary oedema | | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumothorax | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pulmonary embolism | | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Psychiatric disorders | | | |
| Bipolar disorder | | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Disorientation | | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Injury, poisoning and procedural complications | | | |
| Forearm fracture | | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hip fracture | | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Foreign body in gastrointestinal tract | | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Jaw fracture | | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|-----------------|-----------------|--|
| Road traffic accident | | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Cardiac disorders | | | |
| Acute left ventricular failure | | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Acute myocardial infarction | | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 2 / 452 (0.44%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Arrhythmia | | | |
| subjects affected / exposed | 2 / 451 (0.44%) | 0 / 452 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Acute coronary syndrome | | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac failure | | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac arrest | | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Atrial fibrillation | | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Supraventricular extrasystoles | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Myocardial ischaemia | | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nervous system disorders | | | |
| Loss of consciousness | | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Optic neuritis | | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Presyncope | | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Superior sagittal sinus thrombosis | | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Syncope | | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Blood and lymphatic system disorders | | | |
| Anaemia of malignant disease | | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Blood loss anaemia | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Eye disorders | | | |
| Diabetic retinopathy | | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Oesophageal varices haemorrhage | | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastritis erosive | | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Varices oesophageal | | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatobiliary disorders | | | |
| Cholecystitis | | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cholecystitis chronic | | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 2 / 452 (0.44%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|-----------------|-----------------|--|
| Portal vein thrombosis | | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Biliary colic | | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Skin and subcutaneous tissue disorders | | | |
| Actinic keratosis | | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal and urinary disorders | | | |
| Chronic kidney disease | | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nephrolithiasis | | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 1 / 452 (0.22%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ureteric obstruction | | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal and connective tissue disorders | | | |
| Intervertebral disc protrusion | | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Immobilisation syndrome | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Pneumonia bacterial | | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Superinfection bacterial | | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Sinusitis | | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Appendicitis | | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bacterial diarrhoea | | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| COVID-19 | | | |
| subjects affected / exposed | 9 / 451 (2.00%) | 2 / 452 (0.44%) | |
| occurrences causally related to treatment / all | 0 / 9 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 1 | |
| COVID-19 pneumonia | | | |
| subjects affected / exposed | 37 / 451 (8.20%) | 23 / 452 (5.09%) | |
| occurrences causally related to treatment / all | 0 / 37 | 0 / 23 | |
| deaths causally related to treatment / all | 0 / 5 | 0 / 2 | |
| Cellulitis | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Disseminated tuberculosis | | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Septic shock | | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Sepsis | | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pseudomonas infection | | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Post-acute COVID-19 syndrome | | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastroenteritis viral | | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| Non-serious adverse events | Placebo | AZD7442 | |
|---|--------------------|--------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 224 / 451 (49.67%) | 230 / 452 (50.88%) | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Skin papilloma | | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Plasma cell myeloma | | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) | |
| occurrences (all) | 0 | 1 | |
| Bladder cancer | | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) | |
| occurrences (all) | 0 | 1 | |
| Anogenital warts | | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) | |
| occurrences (all) | 0 | 1 | |
| Acrochordon | | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Seborrhoeic keratosis | | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Uterine leiomyoma | | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Vascular disorders | | | |
| Aortic arteriosclerosis | | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Brachiocephalic arteriosclerosis | | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) | |
| occurrences (all) | 0 | 1 | |
| Deep vein thrombosis | | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) | |
| occurrences (all) | 0 | 1 | |
| Essential hypertension | | | |

| | | | |
|--|------------------|------------------|--|
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Hot flush | | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) | |
| occurrences (all) | 0 | 1 | |
| Hypertension | | | |
| subjects affected / exposed | 18 / 451 (3.99%) | 16 / 452 (3.54%) | |
| occurrences (all) | 18 | 16 | |
| Hypertensive crisis | | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Hypertensive urgency | | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) | |
| occurrences (all) | 0 | 1 | |
| Hypotension | | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 1 / 452 (0.22%) | |
| occurrences (all) | 1 | 1 | |
| Lymphostasis | | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Peripheral artery aneurysm | | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Thrombophlebitis | | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Venous thrombosis limb | | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) | |
| occurrences (all) | 0 | 1 | |
| Surgical and medical procedures | | | |
| Abdominal wall operation | | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) | |
| occurrences (all) | 0 | 1 | |
| General disorders and administration site conditions | | | |

| | | |
|-----------------------------|------------------|------------------|
| Asthenia | | |
| subjects affected / exposed | 9 / 451 (2.00%) | 8 / 452 (1.77%) |
| occurrences (all) | 9 | 10 |
| Chest discomfort | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) |
| occurrences (all) | 0 | 1 |
| Decreased activity | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) |
| occurrences (all) | 0 | 1 |
| Energy increased | | |
| subjects affected / exposed | 2 / 451 (0.44%) | 1 / 452 (0.22%) |
| occurrences (all) | 2 | 1 |
| Injection site haematoma | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 1 / 452 (0.22%) |
| occurrences (all) | 1 | 1 |
| Fatigue | | |
| subjects affected / exposed | 15 / 451 (3.33%) | 16 / 452 (3.54%) |
| occurrences (all) | 17 | 16 |
| Feeling hot | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) |
| occurrences (all) | 0 | 1 |
| Gait disturbance | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) |
| occurrences (all) | 0 | 1 |
| Injection site bruising | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 1 / 452 (0.22%) |
| occurrences (all) | 1 | 1 |
| Injection site erythema | | |
| subjects affected / exposed | 2 / 451 (0.44%) | 2 / 452 (0.44%) |
| occurrences (all) | 2 | 2 |
| Face oedema | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) |
| occurrences (all) | 1 | 0 |
| Injection site induration | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) |
| occurrences (all) | 0 | 1 |

| | | |
|-----------------------------|------------------|-----------------|
| Injection site nodule | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) |
| occurrences (all) | 0 | 2 |
| Injection site pain | | |
| subjects affected / exposed | 11 / 451 (2.44%) | 8 / 452 (1.77%) |
| occurrences (all) | 15 | 12 |
| Injection site swelling | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) |
| occurrences (all) | 0 | 2 |
| Injection site warmth | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) |
| occurrences (all) | 2 | 0 |
| Malaise | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 2 / 452 (0.44%) |
| occurrences (all) | 1 | 2 |
| Pain | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 1 / 452 (0.22%) |
| occurrences (all) | 1 | 1 |
| Pyrexia | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 3 / 452 (0.66%) |
| occurrences (all) | 0 | 4 |
| Suprapubic pain | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) |
| occurrences (all) | 1 | 0 |
| Vaccination site pain | | |
| subjects affected / exposed | 2 / 451 (0.44%) | 3 / 452 (0.66%) |
| occurrences (all) | 3 | 6 |
| Vaccination site reaction | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) |
| occurrences (all) | 1 | 0 |
| Injection site inflammation | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) |
| occurrences (all) | 0 | 1 |
| Influenza like illness | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) |
| occurrences (all) | 0 | 1 |

| | | | |
|--|----------------------|----------------------|--|
| Adverse drug reaction subjects affected / exposed occurrences (all) | 1 / 451 (0.22%) 1 | 1 / 452 (0.22%) 1 | |
| Application site haematoma subjects affected / exposed occurrences (all) | 0 / 451 (0.00%) 0 | 1 / 452 (0.22%) 1 | |
| Oedema peripheral subjects affected / exposed occurrences (all) | 2 / 451 (0.44%) 2 | 0 / 452 (0.00%) 0 | |
| Non-cardiac chest pain subjects affected / exposed occurrences (all) | 2 / 451 (0.44%) 2 | 1 / 452 (0.22%) 1 | |
| Injection site discomfort subjects affected / exposed occurrences (all) | 1 / 451 (0.22%) 1 | 2 / 452 (0.44%) 3 | |
| Immune system disorders Allergy to arthropod sting subjects affected / exposed occurrences (all) | 0 / 451 (0.00%) 0 | 1 / 452 (0.22%) 1 | |
| Hypersensitivity subjects affected / exposed occurrences (all) | 0 / 451 (0.00%) 0 | 1 / 452 (0.22%) 1 | |
| Seasonal allergy subjects affected / exposed occurrences (all) | 1 / 451 (0.22%) 1 | 2 / 452 (0.44%) 2 | |
| Drug hypersensitivity subjects affected / exposed occurrences (all) | 1 / 451 (0.22%) 2 | 0 / 452 (0.00%) 0 | |
| Social circumstances Unhealthy diet subjects affected / exposed occurrences (all) | 0 / 451 (0.00%) 0 | 1 / 452 (0.22%) 1 | |
| Reproductive system and breast disorders Bartholin's cyst subjects affected / exposed occurrences (all) | 0 / 451 (0.00%) 0 | 1 / 452 (0.22%) 1 | |

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|--|----------------------|----------------------|
| Benign prostatic hyperplasia subjects affected / exposed occurrences (all) | 1 / 451 (0.22%) 1 | 1 / 452 (0.22%) 1 |
| Breast discharge subjects affected / exposed occurrences (all) | 0 / 451 (0.00%) 0 | 1 / 452 (0.22%) 1 |
| Endometrial thickening subjects affected / exposed occurrences (all) | 1 / 451 (0.22%) 1 | 0 / 452 (0.00%) 0 |
| Erectile dysfunction subjects affected / exposed occurrences (all) | 4 / 451 (0.89%) 4 | 0 / 452 (0.00%) 0 |
| Hypomenorrhoea subjects affected / exposed occurrences (all) | 1 / 451 (0.22%) 1 | 0 / 452 (0.00%) 0 |
| Menopausal symptoms subjects affected / exposed occurrences (all) | 1 / 451 (0.22%) 1 | 1 / 452 (0.22%) 1 |
| Menstruation irregular subjects affected / exposed occurrences (all) | 0 / 451 (0.00%) 0 | 1 / 452 (0.22%) 1 |
| Nipple pain subjects affected / exposed occurrences (all) | 0 / 451 (0.00%) 0 | 1 / 452 (0.22%) 1 |
| Ovarian cyst subjects affected / exposed occurrences (all) | 1 / 451 (0.22%) 1 | 0 / 452 (0.00%) 0 |
| Polycystic ovaries subjects affected / exposed occurrences (all) | 0 / 451 (0.00%) 0 | 1 / 452 (0.22%) 1 |
| Prostatitis subjects affected / exposed occurrences (all) | 2 / 451 (0.44%) 2 | 1 / 452 (0.22%) 1 |
| Prostatomegaly subjects affected / exposed occurrences (all) | 1 / 451 (0.22%) 1 | 0 / 452 (0.00%) 0 |

| | | | |
|---|------------------------|----------------------|--|
| Vaginal haemorrhage subjects affected / exposed occurrences (all) | 0 / 451 (0.00%) 0 | 1 / 452 (0.22%) 1 | |
| Vulvovaginal erythema subjects affected / exposed occurrences (all) | 1 / 451 (0.22%) 1 | 0 / 452 (0.00%) 0 | |
| Dysmenorrhoea subjects affected / exposed occurrences (all) | 1 / 451 (0.22%) 1 | 0 / 452 (0.00%) 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Organising pneumonia subjects affected / exposed occurrences (all) | 0 / 451 (0.00%) 0 | 1 / 452 (0.22%) 1 | |
| Asthma subjects affected / exposed occurrences (all) | 2 / 451 (0.44%) 2 | 2 / 452 (0.44%) 2 | |
| Bronchial hyperreactivity subjects affected / exposed occurrences (all) | 1 / 451 (0.22%) 1 | 0 / 452 (0.00%) 0 | |
| Bronchitis chronic subjects affected / exposed occurrences (all) | 1 / 451 (0.22%) 1 | 0 / 452 (0.00%) 0 | |
| Bronchospasm subjects affected / exposed occurrences (all) | 1 / 451 (0.22%) 1 | 0 / 452 (0.00%) 0 | |
| Chronic obstructive pulmonary disease subjects affected / exposed occurrences (all) | 2 / 451 (0.44%) 2 | 1 / 452 (0.22%) 1 | |
| Cough subjects affected / exposed occurrences (all) | 4 / 451 (0.89%) 4 | 8 / 452 (1.77%) 8 | |
| Dyspnoea subjects affected / exposed occurrences (all) | 11 / 451 (2.44%) 12 | 3 / 452 (0.66%) 3 | |
| Dyspnoea exertional | | | |

| | | |
|-----------------------------|-----------------|-----------------|
| subjects affected / exposed | 3 / 451 (0.67%) | 4 / 452 (0.88%) |
| occurrences (all) | 3 | 5 |
| Epistaxis | | |
| subjects affected / exposed | 2 / 451 (0.44%) | 0 / 452 (0.00%) |
| occurrences (all) | 4 | 0 |
| Hiccups | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 1 / 452 (0.22%) |
| occurrences (all) | 1 | 1 |
| Interstitial lung disease | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) |
| occurrences (all) | 0 | 2 |
| Nasal congestion | | |
| subjects affected / exposed | 3 / 451 (0.67%) | 1 / 452 (0.22%) |
| occurrences (all) | 3 | 1 |
| Nasal obstruction | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) |
| occurrences (all) | 0 | 1 |
| Oropharyngeal pain | | |
| subjects affected / exposed | 3 / 451 (0.67%) | 0 / 452 (0.00%) |
| occurrences (all) | 4 | 0 |
| Pleurisy | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) |
| occurrences (all) | 1 | 0 |
| Productive cough | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 1 / 452 (0.22%) |
| occurrences (all) | 1 | 1 |
| Pulmonary fibrosis | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 1 / 452 (0.22%) |
| occurrences (all) | 1 | 1 |
| Rales | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 1 / 452 (0.22%) |
| occurrences (all) | 1 | 1 |
| Respiratory failure | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) |
| occurrences (all) | 0 | 1 |
| Rhinitis allergic | | |

| | | | |
|--|----------------------|----------------------|--|
| subjects affected / exposed occurrences (all) | 3 / 451 (0.67%) 3 | 1 / 452 (0.22%) 1 | |
| Rhinorrhoea | | | |
| subjects affected / exposed occurrences (all) | 4 / 451 (0.89%) 5 | 0 / 452 (0.00%) 0 | |
| Sleep apnoea syndrome | | | |
| subjects affected / exposed occurrences (all) | 0 / 451 (0.00%) 0 | 1 / 452 (0.22%) 1 | |
| Throat irritation | | | |
| subjects affected / exposed occurrences (all) | 1 / 451 (0.22%) 1 | 0 / 452 (0.00%) 0 | |
| Vocal cord polyp | | | |
| subjects affected / exposed occurrences (all) | 1 / 451 (0.22%) 1 | 0 / 452 (0.00%) 0 | |
| Wheezing | | | |
| subjects affected / exposed occurrences (all) | 0 / 451 (0.00%) 0 | 1 / 452 (0.22%) 1 | |
| Psychiatric disorders | | | |
| Alcohol abuse | | | |
| subjects affected / exposed occurrences (all) | 1 / 451 (0.22%) 1 | 0 / 452 (0.00%) 0 | |
| Alcoholism | | | |
| subjects affected / exposed occurrences (all) | 1 / 451 (0.22%) 1 | 0 / 452 (0.00%) 0 | |
| Anxiety | | | |
| subjects affected / exposed occurrences (all) | 4 / 451 (0.89%) 4 | 3 / 452 (0.66%) 3 | |
| Anxiety disorder | | | |
| subjects affected / exposed occurrences (all) | 1 / 451 (0.22%) 1 | 0 / 452 (0.00%) 0 | |
| Attention deficit hyperactivity disorder | | | |
| subjects affected / exposed occurrences (all) | 0 / 451 (0.00%) 0 | 1 / 452 (0.22%) 1 | |
| Bruxism | | | |

| | | | |
|--|----------------------|----------------------|--|
| subjects affected / exposed occurrences (all) | 0 / 451 (0.00%) 0 | 1 / 452 (0.22%) 1 | |
| Burnout syndrome subjects affected / exposed occurrences (all) | 1 / 451 (0.22%) 1 | 0 / 452 (0.00%) 0 | |
| Confusional state subjects affected / exposed occurrences (all) | 1 / 451 (0.22%) 2 | 1 / 452 (0.22%) 1 | |
| Depression subjects affected / exposed occurrences (all) | 5 / 451 (1.11%) 5 | 5 / 452 (1.11%) 5 | |
| Insomnia subjects affected / exposed occurrences (all) | 2 / 451 (0.44%) 2 | 7 / 452 (1.55%) 7 | |
| Mixed anxiety and depressive disorder subjects affected / exposed occurrences (all) | 0 / 451 (0.00%) 0 | 1 / 452 (0.22%) 1 | |
| Sleep disorder subjects affected / exposed occurrences (all) | 1 / 451 (0.22%) 1 | 2 / 452 (0.44%) 2 | |
| Stress subjects affected / exposed occurrences (all) | 1 / 451 (0.22%) 1 | 0 / 452 (0.00%) 0 | |
| Acute stress disorder subjects affected / exposed occurrences (all) | 2 / 451 (0.44%) 2 | 0 / 452 (0.00%) 0 | |
| Hepatobiliary disorders Non-alcoholic steatohepatitis subjects affected / exposed occurrences (all) | 0 / 451 (0.00%) 0 | 1 / 452 (0.22%) 1 | |
| Biliary colic subjects affected / exposed occurrences (all) | 1 / 451 (0.22%) 1 | 2 / 452 (0.44%) 2 | |
| Cholecystitis | | | |

| | | | |
|--|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Cholecystitis chronic | | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) | |
| occurrences (all) | 0 | 1 | |
| Cholelithiasis | | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 2 / 452 (0.44%) | |
| occurrences (all) | 0 | 2 | |
| Cholestasis | | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Drug-induced liver injury | | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) | |
| occurrences (all) | 0 | 1 | |
| Hepatic failure | | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Hepatic steatosis | | | |
| subjects affected / exposed | 2 / 451 (0.44%) | 2 / 452 (0.44%) | |
| occurrences (all) | 2 | 2 | |
| Hepatitis toxic | | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) | |
| occurrences (all) | 0 | 1 | |
| Investigations | | | |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Blood alkaline phosphatase increased | | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Blood creatine phosphokinase increased | | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Blood urine present | | | |

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|----------------------------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) |
| occurrences (all) | 0 | 1 |
| Body temperature increased | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 2 / 452 (0.44%) |
| occurrences (all) | 0 | 2 |
| Cardiac murmur | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) |
| occurrences (all) | 0 | 1 |
| White blood cell count decreased | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) |
| occurrences (all) | 0 | 1 |
| Transaminases increased | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) |
| occurrences (all) | 0 | 1 |
| Platelet count increased | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) |
| occurrences (all) | 0 | 1 |
| Oxygen saturation decreased | | |
| subjects affected / exposed | 2 / 451 (0.44%) | 1 / 452 (0.22%) |
| occurrences (all) | 2 | 1 |
| Neutrophil count decreased | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) |
| occurrences (all) | 0 | 1 |
| Lipids abnormal | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) |
| occurrences (all) | 1 | 0 |
| Hepatitis A antibody | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) |
| occurrences (all) | 1 | 0 |
| Hepatic enzyme increased | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 1 / 452 (0.22%) |
| occurrences (all) | 1 | 1 |
| C-reactive protein increased | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) |
| occurrences (all) | 0 | 1 |
| Aspartate aminotransferase | | |

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|--|-----------------|-----------------|--|
| increased | | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Injury, poisoning and procedural complications | | | |
| Post-traumatic neck syndrome | | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) | |
| occurrences (all) | 0 | 1 | |
| Post procedural swelling | | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Anaemia postoperative | | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) | |
| occurrences (all) | 0 | 1 | |
| Ankle fracture | | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) | |
| occurrences (all) | 0 | 1 | |
| Complications of transplanted kidney | | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Contusion | | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) | |
| occurrences (all) | 0 | 1 | |
| Head injury | | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) | |
| occurrences (all) | 0 | 1 | |
| Incision site haemorrhage | | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Joint injury | | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Ligament injury | | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Ligament sprain | | | |

| | | | |
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| subjects affected / exposed | 5 / 451 (1.11%) | 1 / 452 (0.22%) | |
| occurrences (all) | 5 | 1 | |
| Limb injury | | | |
| subjects affected / exposed | 2 / 451 (0.44%) | 0 / 452 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Meniscus injury | | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) | |
| occurrences (all) | 0 | 1 | |
| Muscle injury | | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Muscle strain | | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Post-traumatic pain | | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) | |
| occurrences (all) | 0 | 1 | |
| Road traffic accident | | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) | |
| occurrences (all) | 0 | 1 | |
| Skin abrasion | | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) | |
| occurrences (all) | 0 | 1 | |
| Thermal burn | | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) | |
| occurrences (all) | 0 | 1 | |
| Vaccination complication | | | |
| subjects affected / exposed | 13 / 451 (2.88%) | 13 / 452 (2.88%) | |
| occurrences (all) | 33 | 29 | |
| Procedural haemorrhage | | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Fall | | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) | |
| occurrences (all) | 0 | 1 | |
| Congenital, familial and genetic | | | |

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| disorders | | | |
| Azygos lobe | | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) | |
| occurrences (all) | 0 | 1 | |
| Cardiac disorders | | | |
| Angina pectoris | | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) | |
| occurrences (all) | 0 | 1 | |
| Atrial fibrillation | | | |
| subjects affected / exposed | 2 / 451 (0.44%) | 1 / 452 (0.22%) | |
| occurrences (all) | 2 | 1 | |
| Atrioventricular block first degree | | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) | |
| occurrences (all) | 0 | 1 | |
| Bradycardia | | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Cardiac failure acute | | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 1 / 452 (0.22%) | |
| occurrences (all) | 1 | 1 | |
| Cardiac failure chronic | | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Cardiac flutter | | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Coronary artery disease | | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Mitral valve disease | | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Myocardial ischaemia | | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Nodal rhythm | | | |

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| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) | |
| occurrences (all) | 0 | 1 | |
| Palpitations | | | |
| subjects affected / exposed | 2 / 451 (0.44%) | 3 / 452 (0.66%) | |
| occurrences (all) | 2 | 3 | |
| Sinus arrhythmia | | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) | |
| occurrences (all) | 0 | 1 | |
| Sinus bradycardia | | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) | |
| occurrences (all) | 0 | 1 | |
| Sinus tachycardia | | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) | |
| occurrences (all) | 0 | 1 | |
| Ventricular extrasystoles | | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Nervous system disorders | | | |
| Lumbar radiculopathy | | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Loss of consciousness | | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) | |
| occurrences (all) | 0 | 1 | |
| Intercostal neuralgia | | | |
| subjects affected / exposed | 2 / 451 (0.44%) | 0 / 452 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Hyposmia | | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Hypoaesthesia | | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) | |
| occurrences (all) | 0 | 1 | |
| Hypersomnia | | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) | |
| occurrences (all) | 0 | 1 | |

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| Hypergeusia | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) |
| occurrences (all) | 0 | 1 |
| Hemiparaesthesia | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) |
| occurrences (all) | 0 | 1 |
| Headache | | |
| subjects affected / exposed | 11 / 451 (2.44%) | 13 / 452 (2.88%) |
| occurrences (all) | 15 | 14 |
| Head discomfort | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) |
| occurrences (all) | 0 | 1 |
| Facial paralysis | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) |
| occurrences (all) | 0 | 1 |
| Encephalopathy | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 1 / 452 (0.22%) |
| occurrences (all) | 1 | 1 |
| Dysgeusia | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 2 / 452 (0.44%) |
| occurrences (all) | 1 | 2 |
| Dysaesthesia | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) |
| occurrences (all) | 1 | 0 |
| Dizziness | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 8 / 452 (1.77%) |
| occurrences (all) | 1 | 8 |
| Disturbance in attention | | |
| subjects affected / exposed | 2 / 451 (0.44%) | 1 / 452 (0.22%) |
| occurrences (all) | 2 | 1 |
| Cervicobrachial syndrome | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) |
| occurrences (all) | 0 | 1 |
| Cerebrovascular disorder | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) |
| occurrences (all) | 0 | 1 |

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| Cerebral hypoperfusion | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) |
| occurrences (all) | 0 | 1 |
| Cerebral arteriosclerosis | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) |
| occurrences (all) | 0 | 1 |
| Carpal tunnel syndrome | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) |
| occurrences (all) | 1 | 0 |
| Aphasia | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) |
| occurrences (all) | 1 | 0 |
| Apallic syndrome | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) |
| occurrences (all) | 1 | 0 |
| Anosmia | | |
| subjects affected / exposed | 3 / 451 (0.67%) | 8 / 452 (1.77%) |
| occurrences (all) | 3 | 9 |
| Amnesia | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 2 / 452 (0.44%) |
| occurrences (all) | 1 | 2 |
| Ageusia | | |
| subjects affected / exposed | 2 / 451 (0.44%) | 2 / 452 (0.44%) |
| occurrences (all) | 2 | 2 |
| Memory impairment | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) |
| occurrences (all) | 2 | 0 |
| Migraine | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 1 / 452 (0.22%) |
| occurrences (all) | 1 | 1 |
| Neuralgia | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) |
| occurrences (all) | 1 | 0 |
| Paraesthesia | | |
| subjects affected / exposed | 4 / 451 (0.89%) | 0 / 452 (0.00%) |
| occurrences (all) | 4 | 0 |

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| Parosmia | | | |
| subjects affected / exposed | 3 / 451 (0.67%) | 2 / 452 (0.44%) | |
| occurrences (all) | 3 | 2 | |
| Restless legs syndrome | | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) | |
| occurrences (all) | 0 | 1 | |
| Syncope | | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 1 / 452 (0.22%) | |
| occurrences (all) | 1 | 1 | |
| Tarsal tunnel syndrome | | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Taste disorder | | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 1 / 452 (0.22%) | |
| occurrences (all) | 1 | 1 | |
| Blood and lymphatic system disorders | | | |
| Normochromic normocytic anaemia | | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Anaemia | | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 1 / 452 (0.22%) | |
| occurrences (all) | 1 | 1 | |
| Bicytopenia | | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Anaemia of malignant disease | | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) | |
| occurrences (all) | 0 | 1 | |
| Iron deficiency anaemia | | | |
| subjects affected / exposed | 2 / 451 (0.44%) | 1 / 452 (0.22%) | |
| occurrences (all) | 2 | 1 | |
| Nephrogenic anaemia | | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) | |
| occurrences (all) | 0 | 1 | |
| Lymphadenopathy | | | |

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| subjects affected / exposed occurrences (all) | 1 / 451 (0.22%) 1 | 1 / 452 (0.22%) 1 | |
| Leukopenia subjects affected / exposed occurrences (all) | 1 / 451 (0.22%) 1 | 0 / 452 (0.00%) 0 | |
| Thrombocytosis subjects affected / exposed occurrences (all) | 1 / 451 (0.22%) 1 | 0 / 452 (0.00%) 0 | |
| Thrombocytopenia subjects affected / exposed occurrences (all) | 1 / 451 (0.22%) 1 | 1 / 452 (0.22%) 1 | |
| Ear and labyrinth disorders Deafness subjects affected / exposed occurrences (all) | 0 / 451 (0.00%) 0 | 1 / 452 (0.22%) 1 | |
| Ear pain subjects affected / exposed occurrences (all) | 0 / 451 (0.00%) 0 | 1 / 452 (0.22%) 1 | |
| Vertigo subjects affected / exposed occurrences (all) | 3 / 451 (0.67%) 3 | 1 / 452 (0.22%) 1 | |
| Vertigo positional subjects affected / exposed occurrences (all) | 1 / 451 (0.22%) 1 | 0 / 452 (0.00%) 0 | |
| Eye disorders Cataract subjects affected / exposed occurrences (all) | 1 / 451 (0.22%) 1 | 0 / 452 (0.00%) 0 | |
| Conjunctival haemorrhage subjects affected / exposed occurrences (all) | 0 / 451 (0.00%) 0 | 1 / 452 (0.22%) 1 | |
| Conjunctivitis allergic subjects affected / exposed occurrences (all) | 2 / 451 (0.44%) 2 | 1 / 452 (0.22%) 1 | |
| Diabetic retinal oedema | | | |

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| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) | |
| occurrences (all) | 0 | 1 | |
| Diabetic retinopathy | | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) | |
| occurrences (all) | 0 | 1 | |
| Diplopia | | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) | |
| occurrences (all) | 0 | 1 | |
| Eyelid oedema | | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) | |
| occurrences (all) | 0 | 1 | |
| Glaucoma | | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Ocular hyperaemia | | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) | |
| occurrences (all) | 0 | 1 | |
| Retinal detachment | | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) | |
| occurrences (all) | 0 | 1 | |
| Visual impairment | | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) | |
| occurrences (all) | 0 | 1 | |
| Conjunctival disorder | | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Gastrointestinal disorders | | | |
| Abdominal discomfort | | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Abdominal pain | | | |
| subjects affected / exposed | 3 / 451 (0.67%) | 2 / 452 (0.44%) | |
| occurrences (all) | 3 | 2 | |
| Abdominal pain lower | | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 1 / 452 (0.22%) | |
| occurrences (all) | 1 | 1 | |

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| Abdominal pain upper subjects affected / exposed occurrences (all) | 2 / 451 (0.44%) 2 | 2 / 452 (0.44%) 2 |
| Anal fissure subjects affected / exposed occurrences (all) | 1 / 451 (0.22%) 1 | 0 / 452 (0.00%) 0 |
| Anal pruritus subjects affected / exposed occurrences (all) | 0 / 451 (0.00%) 0 | 1 / 452 (0.22%) 1 |
| Chronic gastritis subjects affected / exposed occurrences (all) | 2 / 451 (0.44%) 2 | 2 / 452 (0.44%) 2 |
| Coeliac disease subjects affected / exposed occurrences (all) | 1 / 451 (0.22%) 1 | 0 / 452 (0.00%) 0 |
| Colitis ulcerative subjects affected / exposed occurrences (all) | 0 / 451 (0.00%) 0 | 1 / 452 (0.22%) 1 |
| Constipation subjects affected / exposed occurrences (all) | 1 / 451 (0.22%) 1 | 4 / 452 (0.88%) 4 |
| Diarrhoea subjects affected / exposed occurrences (all) | 6 / 451 (1.33%) 6 | 11 / 452 (2.43%) 12 |
| Diverticulum intestinal subjects affected / exposed occurrences (all) | 1 / 451 (0.22%) 1 | 0 / 452 (0.00%) 0 |
| Vomiting subjects affected / exposed occurrences (all) | 0 / 451 (0.00%) 0 | 1 / 452 (0.22%) 1 |
| Toothache subjects affected / exposed occurrences (all) | 2 / 451 (0.44%) 2 | 0 / 452 (0.00%) 0 |
| Reflux gastritis subjects affected / exposed occurrences (all) | 0 / 451 (0.00%) 0 | 1 / 452 (0.22%) 1 |

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| Pancreatitis chronic | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) |
| occurrences (all) | 0 | 1 |
| Oesophagitis | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) |
| occurrences (all) | 1 | 0 |
| Oesophageal spasm | | |
| subjects affected / exposed | 2 / 451 (0.44%) | 0 / 452 (0.00%) |
| occurrences (all) | 2 | 0 |
| Nausea | | |
| subjects affected / exposed | 3 / 451 (0.67%) | 5 / 452 (1.11%) |
| occurrences (all) | 3 | 5 |
| Irritable bowel syndrome | | |
| subjects affected / exposed | 2 / 451 (0.44%) | 0 / 452 (0.00%) |
| occurrences (all) | 2 | 0 |
| Intra-abdominal haematoma | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) |
| occurrences (all) | 1 | 0 |
| Hiatus hernia | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) |
| occurrences (all) | 1 | 0 |
| Haemorrhoids | | |
| subjects affected / exposed | 2 / 451 (0.44%) | 1 / 452 (0.22%) |
| occurrences (all) | 2 | 1 |
| Haematochezia | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) |
| occurrences (all) | 1 | 0 |
| Gastrooesophageal reflux disease | | |
| subjects affected / exposed | 4 / 451 (0.89%) | 3 / 452 (0.66%) |
| occurrences (all) | 4 | 3 |
| Gastrointestinal haemorrhage | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) |
| occurrences (all) | 0 | 1 |
| Gastrointestinal disorder | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) |
| occurrences (all) | 0 | 1 |

| | | | |
|--|-----------------|-----------------|--|
| Gastritis | | | |
| subjects affected / exposed | 4 / 451 (0.89%) | 3 / 452 (0.66%) | |
| occurrences (all) | 5 | 3 | |
| Functional gastrointestinal disorder | | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) | |
| occurrences (all) | 0 | 1 | |
| Food poisoning | | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Flatulence | | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Duodenitis | | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Diverticulum oesophageal | | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Stomatitis | | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Dyspepsia | | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Glossodynia | | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) | |
| occurrences (all) | 0 | 1 | |
| Inguinal hernia | | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 1 / 452 (0.22%) | |
| occurrences (all) | 1 | 1 | |
| Odynophagia | | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) | |
| occurrences (all) | 0 | 1 | |
| Skin and subcutaneous tissue disorders | | | |
| Dermatitis allergic | | | |

| | | |
|-----------------------------|-----------------|-----------------|
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) |
| occurrences (all) | 1 | 0 |
| Dermatitis | | |
| subjects affected / exposed | 2 / 451 (0.44%) | 0 / 452 (0.00%) |
| occurrences (all) | 2 | 0 |
| Drug eruption | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) |
| occurrences (all) | 1 | 0 |
| Dry skin | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 1 / 452 (0.22%) |
| occurrences (all) | 1 | 1 |
| Eczema | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) |
| occurrences (all) | 0 | 1 |
| Erythema | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 1 / 452 (0.22%) |
| occurrences (all) | 1 | 1 |
| Hyperhidrosis | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) |
| occurrences (all) | 0 | 1 |
| Macule | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) |
| occurrences (all) | 0 | 1 |
| Neurodermatitis | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) |
| occurrences (all) | 1 | 0 |
| Prurigo | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) |
| occurrences (all) | 2 | 0 |
| Pruritus | | |
| subjects affected / exposed | 4 / 451 (0.89%) | 3 / 452 (0.66%) |
| occurrences (all) | 4 | 3 |
| Psoriasis | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) |
| occurrences (all) | 1 | 0 |
| Rash | | |

| | | | |
|--|----------------------|----------------------|--|
| subjects affected / exposed occurrences (all) | 4 / 451 (0.89%) 4 | 4 / 452 (0.88%) 4 | |
| Alopecia subjects affected / exposed occurrences (all) | 7 / 451 (1.55%) 8 | 5 / 452 (1.11%) 5 | |
| Blister subjects affected / exposed occurrences (all) | 1 / 451 (0.22%) 1 | 1 / 452 (0.22%) 1 | |
| Decubitus ulcer subjects affected / exposed occurrences (all) | 1 / 451 (0.22%) 1 | 1 / 452 (0.22%) 1 | |
| Dermatitis contact subjects affected / exposed occurrences (all) | 1 / 451 (0.22%) 1 | 0 / 452 (0.00%) 0 | |
| Rash pruritic subjects affected / exposed occurrences (all) | 1 / 451 (0.22%) 1 | 0 / 452 (0.00%) 0 | |
| Skin ulcer subjects affected / exposed occurrences (all) | 0 / 451 (0.00%) 0 | 1 / 452 (0.22%) 1 | |
| Urticaria subjects affected / exposed occurrences (all) | 0 / 451 (0.00%) 0 | 1 / 452 (0.22%) 1 | |
| Xeroderma subjects affected / exposed occurrences (all) | 1 / 451 (0.22%) 1 | 0 / 452 (0.00%) 0 | |
| Skin reaction subjects affected / exposed occurrences (all) | 0 / 451 (0.00%) 0 | 1 / 452 (0.22%) 1 | |
| Renal and urinary disorders Acute kidney injury subjects affected / exposed occurrences (all) | 2 / 451 (0.44%) 2 | 1 / 452 (0.22%) 1 | |
| Dysuria subjects affected / exposed occurrences (all) | 0 / 451 (0.00%) 0 | 1 / 452 (0.22%) 1 | |

| | | | |
|---|-----------------|-----------------|--|
| Haematuria | | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) | |
| occurrences (all) | 0 | 1 | |
| Oliguria | | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Pollakiuria | | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Endocrine disorders | | | |
| Goitre | | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) | |
| occurrences (all) | 0 | 1 | |
| Hyperthyroidism | | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) | |
| occurrences (all) | 0 | 1 | |
| Hypothyroidism | | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 2 / 452 (0.44%) | |
| occurrences (all) | 0 | 2 | |
| Thyroid mass | | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) | |
| occurrences (all) | 0 | 1 | |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 8 / 451 (1.77%) | 9 / 452 (1.99%) | |
| occurrences (all) | 8 | 10 | |
| Arthritis | | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 1 / 452 (0.22%) | |
| occurrences (all) | 1 | 1 | |
| Arthritis enteropathic | | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) | |
| occurrences (all) | 0 | 1 | |
| Arthropathy | | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Back pain | | | |

| | | |
|--------------------------------|------------------|------------------|
| subjects affected / exposed | 10 / 451 (2.22%) | 10 / 452 (2.21%) |
| occurrences (all) | 10 | 11 |
| Costochondritis | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) |
| occurrences (all) | 1 | 0 |
| Fibromyalgia | | |
| subjects affected / exposed | 2 / 451 (0.44%) | 0 / 452 (0.00%) |
| occurrences (all) | 2 | 0 |
| Intervertebral disc protrusion | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 2 / 452 (0.44%) |
| occurrences (all) | 1 | 2 |
| Tendonitis | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) |
| occurrences (all) | 1 | 0 |
| Tendon pain | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) |
| occurrences (all) | 1 | 0 |
| Synovitis | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) |
| occurrences (all) | 0 | 1 |
| Spinal osteoarthritis | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 1 / 452 (0.22%) |
| occurrences (all) | 1 | 1 |
| Sjogren's syndrome | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) |
| occurrences (all) | 1 | 0 |
| Rhabdomyolysis | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) |
| occurrences (all) | 0 | 1 |
| Plantar fasciitis | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) |
| occurrences (all) | 0 | 1 |
| Pain in extremity | | |
| subjects affected / exposed | 3 / 451 (0.67%) | 1 / 452 (0.22%) |
| occurrences (all) | 4 | 1 |
| Osteoporosis | | |

| | | | |
|-----------------------------|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 451 (0.00%) | 2 / 452 (0.44%) | |
| occurrences (all) | 0 | 2 | |
| Osteochondrosis | | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) | |
| occurrences (all) | 0 | 1 | |
| Osteoarthritis | | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 3 / 452 (0.66%) | |
| occurrences (all) | 2 | 3 | |
| Neck pain | | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 2 / 452 (0.44%) | |
| occurrences (all) | 0 | 2 | |
| Myositis | | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Myalgia | | | |
| subjects affected / exposed | 4 / 451 (0.89%) | 7 / 452 (1.55%) | |
| occurrences (all) | 5 | 7 | |
| Musculoskeletal discomfort | | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) | |
| occurrences (all) | 0 | 1 | |
| Musculoskeletal chest pain | | | |
| subjects affected / exposed | 2 / 451 (0.44%) | 3 / 452 (0.66%) | |
| occurrences (all) | 2 | 3 | |
| Muscle spasms | | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 2 / 452 (0.44%) | |
| occurrences (all) | 1 | 2 | |
| Muscle contracture | | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) | |
| occurrences (all) | 0 | 1 | |
| Mastication disorder | | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Joint stiffness | | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) | |
| occurrences (all) | 0 | 1 | |
| Infections and infestations | | | |

| | | |
|-----------------------------|------------------|-------------------|
| Gastroenteritis viral | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) |
| occurrences (all) | 1 | 0 |
| Acute sinusitis | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 1 / 452 (0.22%) |
| occurrences (all) | 1 | 2 |
| Asymptomatic COVID-19 | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) |
| occurrences (all) | 0 | 1 |
| Bed bug infestation | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) |
| occurrences (all) | 0 | 1 |
| Bronchiolitis | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) |
| occurrences (all) | 1 | 0 |
| Bronchitis | | |
| subjects affected / exposed | 2 / 451 (0.44%) | 1 / 452 (0.22%) |
| occurrences (all) | 2 | 1 |
| Bronchitis bacterial | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) |
| occurrences (all) | 1 | 0 |
| Bronchitis viral | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 2 / 452 (0.44%) |
| occurrences (all) | 0 | 2 |
| COVID-19 | | |
| subjects affected / exposed | 43 / 451 (9.53%) | 49 / 452 (10.84%) |
| occurrences (all) | 44 | 49 |
| COVID-19 pneumonia | | |
| subjects affected / exposed | 12 / 451 (2.66%) | 4 / 452 (0.88%) |
| occurrences (all) | 12 | 4 |
| Cellulitis | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 2 / 452 (0.44%) |
| occurrences (all) | 0 | 2 |
| Cervicitis | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) |
| occurrences (all) | 0 | 1 |

| | | |
|-------------------------------|-----------------|-----------------|
| Chlamydial infection | | |
| subjects affected / exposed | 2 / 451 (0.44%) | 0 / 452 (0.00%) |
| occurrences (all) | 2 | 0 |
| Clostridium difficile colitis | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) |
| occurrences (all) | 1 | 0 |
| Conjunctivitis | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) |
| occurrences (all) | 1 | 0 |
| Cystitis | | |
| subjects affected / exposed | 2 / 451 (0.44%) | 2 / 452 (0.44%) |
| occurrences (all) | 2 | 2 |
| Diarrhoea infectious | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) |
| occurrences (all) | 0 | 1 |
| Ear infection | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) |
| occurrences (all) | 0 | 1 |
| Enterobacter pneumonia | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) |
| occurrences (all) | 1 | 0 |
| Epididymitis | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) |
| occurrences (all) | 1 | 0 |
| Fungal skin infection | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) |
| occurrences (all) | 0 | 1 |
| Furuncle | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) |
| occurrences (all) | 0 | 1 |
| Gastroenteritis | | |
| subjects affected / exposed | 2 / 451 (0.44%) | 6 / 452 (1.33%) |
| occurrences (all) | 2 | 6 |
| Gingivitis | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) |
| occurrences (all) | 1 | 0 |

| | | |
|-----------------------------------|-----------------|-----------------|
| Sinusitis bacterial | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 1 / 452 (0.22%) |
| occurrences (all) | 1 | 1 |
| Gonorrhoea | | |
| subjects affected / exposed | 3 / 451 (0.67%) | 0 / 452 (0.00%) |
| occurrences (all) | 3 | 0 |
| H3N2 influenza | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) |
| occurrences (all) | 0 | 1 |
| Helicobacter gastritis | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) |
| occurrences (all) | 1 | 0 |
| Helicobacter infection | | |
| subjects affected / exposed | 2 / 451 (0.44%) | 0 / 452 (0.00%) |
| occurrences (all) | 2 | 0 |
| Herpes zoster | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 4 / 452 (0.88%) |
| occurrences (all) | 0 | 4 |
| Influenza | | |
| subjects affected / exposed | 2 / 451 (0.44%) | 4 / 452 (0.88%) |
| occurrences (all) | 3 | 5 |
| Lower respiratory tract infection | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 2 / 452 (0.44%) |
| occurrences (all) | 0 | 2 |
| Mastitis | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) |
| occurrences (all) | 1 | 0 |
| Nasopharyngitis | | |
| subjects affected / exposed | 8 / 451 (1.77%) | 4 / 452 (0.88%) |
| occurrences (all) | 10 | 4 |
| Onychomycosis | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) |
| occurrences (all) | 0 | 1 |
| Otitis externa | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 1 / 452 (0.22%) |
| occurrences (all) | 1 | 2 |

| | | |
|-----------------------------------|------------------|------------------|
| Otitis media | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 1 / 452 (0.22%) |
| occurrences (all) | 1 | 1 |
| Pharyngitis | | |
| subjects affected / exposed | 2 / 451 (0.44%) | 0 / 452 (0.00%) |
| occurrences (all) | 2 | 0 |
| Pharyngotonsillitis | | |
| subjects affected / exposed | 2 / 451 (0.44%) | 1 / 452 (0.22%) |
| occurrences (all) | 3 | 1 |
| Pneumonia bacterial | | |
| subjects affected / exposed | 2 / 451 (0.44%) | 1 / 452 (0.22%) |
| occurrences (all) | 2 | 1 |
| Post-acute COVID-19 syndrome | | |
| subjects affected / exposed | 29 / 451 (6.43%) | 38 / 452 (8.41%) |
| occurrences (all) | 30 | 39 |
| Pyelonephritis | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) |
| occurrences (all) | 1 | 0 |
| Pyelonephritis chronic | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) |
| occurrences (all) | 0 | 1 |
| Respiratory tract infection | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) |
| occurrences (all) | 0 | 1 |
| Respiratory tract infection viral | | |
| subjects affected / exposed | 3 / 451 (0.67%) | 1 / 452 (0.22%) |
| occurrences (all) | 3 | 1 |
| Gonococcal infection | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) |
| occurrences (all) | 0 | 1 |
| Tinea pedis | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 2 / 452 (0.44%) |
| occurrences (all) | 0 | 2 |
| Tonsillitis | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 2 / 452 (0.44%) |
| occurrences (all) | 1 | 2 |

| | | |
|---|-----------------|------------------|
| Tooth infection | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) |
| occurrences (all) | 1 | 0 |
| Upper respiratory tract infection | | |
| subjects affected / exposed | 4 / 451 (0.89%) | 4 / 452 (0.88%) |
| occurrences (all) | 4 | 4 |
| Upper respiratory tract infection bacterial | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) |
| occurrences (all) | 0 | 1 |
| Urinary tract infection | | |
| subjects affected / exposed | 9 / 451 (2.00%) | 10 / 452 (2.21%) |
| occurrences (all) | 11 | 11 |
| Vaginal infection | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) |
| occurrences (all) | 0 | 1 |
| Vestibular neuronitis | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) |
| occurrences (all) | 1 | 0 |
| Viral infection | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) |
| occurrences (all) | 0 | 1 |
| Viral rhinitis | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 2 / 452 (0.44%) |
| occurrences (all) | 1 | 2 |
| Viral upper respiratory tract infection | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 3 / 452 (0.66%) |
| occurrences (all) | 0 | 3 |
| Vulvovaginal candidiasis | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 1 / 452 (0.22%) |
| occurrences (all) | 2 | 1 |
| Suspected COVID-19 | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) |
| occurrences (all) | 0 | 1 |
| Syphilis | | |

| | | | |
|--------------------------------------|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Sinusitis | | | |
| subjects affected / exposed | 5 / 451 (1.11%) | 1 / 452 (0.22%) | |
| occurrences (all) | 7 | 1 | |
| Pneumonia | | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Periodontitis | | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Oral herpes | | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 1 / 452 (0.22%) | |
| occurrences (all) | 1 | 1 | |
| Genitourinary chlamydia infection | | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) | |
| occurrences (all) | 0 | 1 | |
| Chronic sinusitis | | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Metabolism and nutrition disorders | | | |
| Glucose tolerance impaired | | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 1 / 452 (0.22%) | |
| occurrences (all) | 1 | 1 | |
| Dyslipidaemia | | | |
| subjects affected / exposed | 5 / 451 (1.11%) | 3 / 452 (0.66%) | |
| occurrences (all) | 5 | 3 | |
| Diabetes mellitus inadequate control | | | |
| subjects affected / exposed | 4 / 451 (0.89%) | 7 / 452 (1.55%) | |
| occurrences (all) | 5 | 10 | |
| Diabetes mellitus | | | |
| subjects affected / exposed | 3 / 451 (0.67%) | 2 / 452 (0.44%) | |
| occurrences (all) | 3 | 2 | |
| Dehydration | | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) | |
| occurrences (all) | 0 | 1 | |

| | | |
|-----------------------------|-----------------|-----------------|
| Gout | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) |
| occurrences (all) | 0 | 1 |
| Hypocalcaemia | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) |
| occurrences (all) | 1 | 0 |
| Hypokalaemia | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 1 / 452 (0.22%) |
| occurrences (all) | 1 | 1 |
| Type 2 diabetes mellitus | | |
| subjects affected / exposed | 7 / 451 (1.55%) | 9 / 452 (1.99%) |
| occurrences (all) | 7 | 9 |
| Vitamin B12 deficiency | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) |
| occurrences (all) | 1 | 0 |
| Vitamin D deficiency | | |
| subjects affected / exposed | 2 / 451 (0.44%) | 1 / 452 (0.22%) |
| occurrences (all) | 2 | 1 |
| Weight gain poor | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) |
| occurrences (all) | 1 | 0 |
| Hypercholesterolaemia | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 1 / 452 (0.22%) |
| occurrences (all) | 0 | 1 |
| Hyperglycaemia | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) |
| occurrences (all) | 1 | 0 |
| Hyperkalaemia | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 1 / 452 (0.22%) |
| occurrences (all) | 1 | 1 |
| Hyperlipidaemia | | |
| subjects affected / exposed | 0 / 451 (0.00%) | 2 / 452 (0.44%) |
| occurrences (all) | 0 | 2 |
| Hypernatraemia | | |
| subjects affected / exposed | 2 / 451 (0.44%) | 0 / 452 (0.00%) |
| occurrences (all) | 2 | 0 |

| | | | |
|-----------------------------|-----------------|-----------------|--|
| Hypertriglyceridaemia | | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Hyperuricaemia | | | |
| subjects affected / exposed | 1 / 451 (0.22%) | 0 / 452 (0.00%) | |
| occurrences (all) | 1 | 0 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|------------------|--|
| 22 December 2020 | Update to the key secondary objective and associated analysis estimand to include as intercurrent events, participants who are unblinded to be considered for COVID-19 vaccination. Consequential consistency change to Section 9.4.2.1 (Primary Endpoint). |
| 26 February 2021 | COVID places pregnant women at increased risk of poor outcomes and poor pregnancy outcomes (CDC, 2021). A fetal TCR study showed no binding of AZD7442 mAbs to any fetal tissues tested. Prior experience with antibody therapy against infectious diseases and with other mAbs suggests low risk in pregnancy. Therefore, the exclusion of pregnant or breast feeding women has been removed from the CSP. |
| 10 March 2021 | Pregnant women and breastfeeding mothers are excluded from the trial (Criterion 16) as there is insufficient data on the drug-associated risk of major birth defects, miscarriage, or adverse maternal or fetal outcomes or effects of the drug on the breastfed infant, or on milk production. All women of child bearing potential must have a negative pregnancy test result at Visit 1 (Criterion 8b). AstraZeneca acknowledges the risk for severe COVID-19 in pregnant women but would like to establish the risk/benefit profile in adults before including pregnant women in the clinical trial. |
| 31 March 2021 | Highly efficacious vaccines against SARS-CoV-2 are being deployed on a mass scale in the participating countries, leading to substantially decreasing attack rates for COVID-19 and reduced potential for study enrollment. Therefore, the interim analysis has been removed and the primary analysis adjusted so that it is completed 30 days after the 52nd event has occurred. This period, of 30 days, allows sufficient time for the 52nd event to be monitored, and any other events occurring during this time interval will also be evaluated. Enrollment will stop after the 52nd event has occurred. |
| 21 April 2021 | Amid a rising number of coronavirus disease 2019 (COVID-19) hospitalizations across the world, leading to a shortage of hospital beds, temporary facilities are being utilized increasingly to manage severe COVID-19 patients who would have usually been treated in a traditional hospital setting. As hospitalizations are an integral component of both the primary and key secondary endpoints in the study, further guidance is provided regarding what constitutes these temporary facility or alternate care sites used for managing participants with severe COVID-19. |
| 05 July 2021 | Due to regional differences in medical practice for COVID-19, the primary analysis population has been clarified to ensure that the efficacy of AZD7442 for the treatment of COVID-19 is assessed only in non-hospitalized adults. |
| 18 March 2022 | Cardiovascular & thrombotic events were added as AESIs which are described as potential risks in the latest IB version. A Cardiovascular Event Adjudication Committee was added to provide an independent, external, systematic, and unbiased assessment of de-identified blinded data to systematically evaluate CV events. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

<http://www.ncbi.nlm.nih.gov/pubmed/36411267>

<http://www.ncbi.nlm.nih.gov/pubmed/35688164>