



Clinical trial results:

Effect of Passive Immunization on the Progression of Mild Alzheimer's Disease: Solanezumab (LY2062430) versus Placebo

Summary

| | |
|--------------------------|------------------|
| EudraCT number | 2013-001119-54 |
| Trial protocol | GB DE IT SE ES |
| Global end of trial date | 17 February 2017 |

Results information

| | |
|--------------------------------|---------------|
| Result version number | v1 (current) |
| This version publication date | 04 March 2018 |
| First version publication date | 04 March 2018 |

Trial information

Trial identification

| | |
|-----------------------|-------------|
| Sponsor protocol code | H8A-MC-LZAX |
|-----------------------|-------------|

Additional study identifiers

| | |
|------------------------------------|---------------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01900665 |
| WHO universal trial number (UTN) | - |
| Other trial identifiers | Trial Number: 15136 |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Eli Lilly and Company |
| Sponsor organisation address | Lilly Corporate Center, Indianapolis, IN, United States, 46285 |
| Public contact | Available Mon - Fri 9 AM - 5 PM EST, Eli Lilly and Company, 1 877CTLilly, |
| Scientific contact | Available Mon - Fri 9 AM - 5 PM EST, Eli Lilly and Company, 1 8772854559, |

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 | 17 February 2017 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 17 February 2017 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to test the idea that solanezumab will slow the cognitive decline of Alzheimer's Disease (AD) as compared with placebo in participants with mild AD.

Protection of trial subjects:

This study was conducted in accordance with International Conference on Harmonization (ICH) Good Clinical Practice, and the principles of the Declaration of Helsinki, in addition to following the laws and regulations of the country or countries in which a study is conducted.

Background therapy: -

Evidence for comparator: -

| | |
|---|----------------|
| Actual start date of recruitment | 12 August 2013 |
| 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 | Canada: 127 |
| Country: Number of subjects enrolled | Sweden: 52 |
| Country: Number of subjects enrolled | United States: 1078 |
| Country: Number of subjects enrolled | Japan: 132 |
| Country: Number of subjects enrolled | Poland: 102 |
| Country: Number of subjects enrolled | Italy: 98 |
| Country: Number of subjects enrolled | United Kingdom: 89 |
| Country: Number of subjects enrolled | Australia: 68 |
| Country: Number of subjects enrolled | France: 173 |
| Country: Number of subjects enrolled | Germany: 96 |
| Country: Number of subjects enrolled | Spain: 114 |
| Worldwide total number of subjects | 2129 |
| EEA total number of subjects | 724 |

Notes:

Subjects enrolled per age group

| | |
|--|---|
| In utero | 0 |
| Preterm newborn - gestational age < 37 | 0 |

| | |
|--|------|
| wk | |
| 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) | 370 |
| From 65 to 84 years | 1636 |
| 85 years and over | 123 |

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Participants were excluded after study enrollment, if PET imaging or CSF results did not show evidence of brain amyloid pathology, a screening MRI with results >4 ARIA-H (amyloid-related imaging abnormality-hemorrhage/hemosiderin deposition) or presence of ARIA-E (amyloid-related imaging abnormality-edema/effusions) and abnormal lab results were found.

Period 1

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

Arms

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

Arm description:

Participants received Solanezumab 400 milligrams (mg) Intravenously (IV) every 4 weeks for 76 weeks with an additional 4 weeks of assessments. Participants who completed the full 80 weeks of treatment/assessment and decide to continue will take this regimen for up to an additional 208 weeks.

| | |
|--|-----------------|
| Arm type | Experimental |
| Investigational medicinal product name | Solanezumab |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Solanezumab 400 mg IV every 4 weeks for 76 weeks with an additional 4 weeks of assessments. Participants who completed the full 80 weeks of treatment/assessment and decide to continue will take this regimen for up to an additional 208 weeks.

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

Arm description:

Participants received Placebo IV every 4 weeks for 76 weeks with an additional 4 weeks of assessments. Participants who complete the full 80 weeks of treatment/assessment and decide to continue will switch to solanezumab 400 mg every 4 weeks for up to an additional 208 weeks.

| | |
|--|-----------------|
| Arm type | Placebo |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Placebo IV every 4 weeks for 76 weeks with an additional 4 weeks of assessments. Participants who complete the full 80 weeks of treatment/assessment and decide to continue will switch to solanezumab 400 mg every 4 weeks for up to an additional 208 weeks

| Number of subjects in period 1 | Solanezumab | Placebo |
|--|-------------|---------|
| Started | 1057 | 1072 |
| Received at Least 1 Dose of Study Drug | 1054 | 1067 |
| Completed | 914 | 908 |
| Not completed | 143 | 164 |
| Adverse event, serious fatal | 9 | 16 |
| Consent withdrawn by subject | 33 | 45 |
| Physician decision | 11 | 7 |
| Adverse event, non-fatal | 48 | 39 |
| Caregiver Decision | 33 | 41 |
| Lost to follow-up | 3 | - |
| Entry Criteria Not Met | 5 | 9 |
| Protocol deviation | 1 | 7 |

Period 2

| | |
|------------------------------|--|
| Period 2 title | Open Label Period |
| Is this the baseline period? | No |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator, Carer, Assessor |

Arms

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

Arm description:

Participants received Solanezumab 400 milligrams (mg) Intravenously (IV) every 4 weeks for 76 weeks with an additional 4 weeks of assessments. Participants who completed the full 80 weeks of treatment/assessment and decide to continue will take this regimen for up to an additional 208 weeks.

| | |
|--|-----------------|
| Arm type | Experimental |
| Investigational medicinal product name | Solanezumab |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Solanezumab 400 mg IV every 4 weeks for 76 weeks with an additional 4 weeks of assessments. Participants who completed the full 80 weeks of treatment/assessment and decide to continue will take this regimen for up to an additional 208 weeks.

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

Arm description:

Participants received Placebo IV every 4 weeks for 76 weeks with an additional 4 weeks of assessments. Participants who complete the full 80 weeks of treatment/assessment and decide to continue will switch to solanezumab 400 mg every 4 weeks for up to an additional 208 weeks.

| | |
|----------|---------|
| Arm type | Placebo |
|----------|---------|

| | |
|--|-----------------|
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Placebo IV every 4 weeks for 76 weeks with an additional 4 weeks of assessments. Participants who complete the full 80 weeks of treatment/assessment and decide to continue will switch to solanezumab 400 mg every 4 weeks for up to an additional 208 weeks.

| Number of subjects in period 2^[1] | Solanezumab | Placebo |
|---|-------------|---------|
| Started | 881 | 859 |
| Completed | 0 | 0 |
| Not completed | 881 | 859 |
| Adverse event, serious fatal | 5 | 6 |
| Parent/Caregiver Decision | 33 | 34 |
| Consent withdrawn by subject | 20 | 28 |
| Physician decision | 4 | 4 |
| Adverse event, non-fatal | 16 | 20 |
| Sponsor Decision | 802 | 765 |
| Lost to follow-up | 1 | 1 |
| Protocol deviation | - | 1 |

Notes:

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

Justification: Subjects from Placebo Controlled Period were not required to enter into Open Label Period.

Baseline characteristics

Reporting groups

| | |
|-----------------------|-------------|
| Reporting group title | Solanezumab |
|-----------------------|-------------|

Reporting group description:

Participants received Solanezumab 400 milligrams (mg) Intravenously (IV) every 4 weeks for 76 weeks with an additional 4 weeks of assessments. Participants who completed the full 80 weeks of treatment/assessment and decide to continue will take this regimen for up to an additional 208 weeks.

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

Reporting group description:

Participants received Placebo IV every 4 weeks for 76 weeks with an additional 4 weeks of assessments. Participants who complete the full 80 weeks of treatment/assessment and decide to continue will switch to solanezumab 400 mg every 4 weeks for up to an additional 208 weeks.

| Reporting group values | Solanezumab | Placebo | Total |
|------------------------------------|-------------|---------|-------|
| Number of subjects | 1057 | 1072 | 2129 |
| Age categorical Units: Subjects | | | |

| | | | |
|---|------------------|------------------|---|
| Age Continuous Units: years arithmetic mean standard deviation | 72.69 ± 7.814 | 73.26 ± 7.966 | - |
|---|------------------|------------------|---|

| | | | |
|---------------------------------------|-----|-----|------|
| Gender categorical Units: Subjects | | | |
| Female | 600 | 631 | 1231 |
| Male | 457 | 441 | 898 |

| | | | |
|--------------------------------------|-----|-----|------|
| Sex: Female, Male Units: Subjects | | | |
| Female | 600 | 631 | 1231 |
| Male | 457 | 441 | 898 |

| | | | |
|--|-----|-----|------|
| Ethnicity (NIH/OMB) | | | |
| All randomized participants who had baseline ethnicity data. | | | |
| Units: Subjects | | | |
| Hispanic or Latino | 49 | 49 | 98 |
| Not Hispanic or Latino | 921 | 937 | 1858 |
| Unknown or Not Reported | 87 | 86 | 173 |

| | | | |
|---|-----|-----|------|
| Race (NIH/OMB) | | | |
| All randomized participants who had baseline race data. | | | |
| Units: Subjects | | | |
| American Indian or Alaska Native | 0 | 0 | 0 |
| Asian | 75 | 71 | 146 |
| Native Hawaiian or Other Pacific Islander | 1 | 0 | 1 |
| Black or African American | 14 | 19 | 33 |
| White | 878 | 894 | 1772 |
| More than one race | 2 | 2 | 4 |
| Unknown or Not Reported | 87 | 86 | 173 |

| | | | |
|---|--|--|--|
| Region of Enrollment Units: Subjects | | | |
|---|--|--|--|

| | | | |
|----------------|-----|-----|------|
| Canada | 61 | 66 | 127 |
| Sweden | 26 | 26 | 52 |
| United States | 537 | 541 | 1078 |
| Japan | 67 | 65 | 132 |
| Poland | 52 | 50 | 102 |
| Italy | 46 | 52 | 98 |
| United Kingdom | 45 | 44 | 89 |
| Australia | 32 | 36 | 68 |
| France | 87 | 86 | 173 |
| Germany | 48 | 48 | 96 |
| Spain | 56 | 58 | 114 |

End points

End points reporting groups

| | |
|--|-------------|
| Reporting group title | Solanezumab |
| Reporting group description: Participants received Solanezumab 400 milligrams (mg) Intravenously (IV) every 4 weeks for 76 weeks with an additional 4 weeks of assessments. Participants who completed the full 80 weeks of treatment/assessment and decide to continue will take this regimen for up to an additional 208 weeks. | |
| Reporting group title | Placebo |
| Reporting group description: Participants received Placebo IV every 4 weeks for 76 weeks with an additional 4 weeks of assessments. Participants who complete the full 80 weeks of treatment/assessment and decide to continue will switch to solanezumab 400 mg every 4 weeks for up to an additional 208 weeks. | |
| Reporting group title | Solanezumab |
| Reporting group description: Participants received Solanezumab 400 milligrams (mg) Intravenously (IV) every 4 weeks for 76 weeks with an additional 4 weeks of assessments. Participants who completed the full 80 weeks of treatment/assessment and decide to continue will take this regimen for up to an additional 208 weeks. | |
| Reporting group title | Placebo |
| Reporting group description: Participants received Placebo IV every 4 weeks for 76 weeks with an additional 4 weeks of assessments. Participants who complete the full 80 weeks of treatment/assessment and decide to continue will switch to solanezumab 400 mg every 4 weeks for up to an additional 208 weeks. | |

Primary: Change from Baseline in Alzheimer's Disease Assessment Scale-Cognitive 14 Item Subscore (ADAS-Cog14)

| | | | |
|---|--|--|--|
| End point title | Change from Baseline in Alzheimer's Disease Assessment Scale-Cognitive 14 Item Subscore (ADAS-Cog14) | | |
| End point description: The ADAS is a rater administered instrument that was designed to assess the severity of the dysfunction in the cognitive and noncognitive behaviors characteristic of persons with AD. The cognitive subscale of the ADAS that was used as the primary efficacy measure consists of 14 items assessing areas of cognitive function most typically impaired in AD: orientation, verbal memory, language, praxis, delayed free recall, digit cancellation, and maze completion measures. The ADAS-Cog14 scale ranges from 0 to 90. Higher scores indicate greater disease severity. Least Squares (LS) Mean value was controlled for baseline value, baseline age, pooled investigator, treatment and visit. Analysis population included all randomized participants who received at least 1 dose of study drug and had baseline and post baseline data. | | | |
| End point type | Primary | | |
| End point timeframe: Baseline, Week 80 | | | |

| End point values | Solanezumab | Placebo | | |
|-------------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 1053 | 1067 | | |
| Units: Units on a scale | | | | |
| least squares mean (standard error) | 6.65 (± 0.355) | 7.44 (± 0.356) | | |

Statistical analyses

| | |
|---|------------------------|
| Statistical analysis title | Statistical analysis 1 |
| Comparison groups | Solanezumab v Placebo |
| Number of subjects included in analysis | 2120 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.095 [1] |
| Method | Mixed models analysis |
| Parameter estimate | Mean difference (net) |
| Point estimate | -0.8 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.73 |
| upper limit | 0.14 |

Notes:

[1] - The Kenward-Roger approximation was used to estimate the denominator degrees of freedom.

Secondary: Change from Baseline in Alzheimer's Disease Cooperative Study- Instrumental Activities of Daily Living (ADCS-iADL)

| | |
|-----------------|--|
| End point title | Change from Baseline in Alzheimer's Disease Cooperative Study- Instrumental Activities of Daily Living (ADCS-iADL) |
|-----------------|--|

End point description:

The ADCS-ADL is a 23-item inventory developed as a rater-administered questionnaire answered by the participant's caregiver. The ADCS-ADL measures both basic and instrumental activities of daily living by participants. The total score ranges from 0 to 78, with lower scores indicating greater disease severity. LS Mean value was controlled for baseline value, baseline age, pooled investigator, treatment and visit. Analysis population included all randomized participants who received at least 1 dose of study drug and had baseline and post baseline data.

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

End point timeframe:

Baseline, Week 80

| End point values | Solanezumab | Placebo | | |
|-------------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 908 | 896 | | |
| Units: Units on a scale | | | | |
| least squares mean (standard error) | -6.17 (± 0.318) | -7.17 (± 0.320) | | |

Statistical analyses

| | |
|-----------------------------------|------------------------|
| Statistical analysis title | Statistical analysis 1 |
| Comparison groups | Solanezumab v Placebo |

| | |
|---|-----------------------|
| Number of subjects included in analysis | 1804 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.019 |
| Method | Mixed models analysis |
| Parameter estimate | Mean difference (net) |
| Point estimate | 1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.17 |
| upper limit | 1.83 |

Secondary: Change from Baseline in Alzheimer's Disease Assessment Scale-Cognitive 11 Item Subscore (ADAS-Cog11)

| | |
|-----------------|--|
| End point title | Change from Baseline in Alzheimer's Disease Assessment Scale-Cognitive 11 Item Subscore (ADAS-Cog11) |
|-----------------|--|

End point description:

The cognitive subscale of ADAS (ADAS Cog11) consists of 11 items assessing areas of function most typically impaired in Alzheimer's disease (AD): orientation, verbal memory, language, and praxis. The scale ranges from 0 to 70, with higher scores indicating greater disease severity. LS Mean value was controlled for baseline value, baseline age, pooled investigator, treatment and visit. Analysis population included all randomized participants who received at least 1 dose of study drug and had baseline and post baseline data.

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

End point timeframe:

Baseline, Week 80

| End point values | Solanezumab | Placebo | | |
|-------------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 1053 | 1067 | | |
| Units: Units on a scale | | | | |
| least squares mean (standard error) | 5.22 (± 0.284) | 5.90 (± 0.285) | | |

Statistical analyses

| | |
|---|------------------------|
| Statistical analysis title | Statistical analysis 1 |
| Comparison groups | Solanezumab v Placebo |
| Number of subjects included in analysis | 2120 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.068 |
| Method | Mixed models analysis |
| Parameter estimate | Mean difference (net) |
| Point estimate | -0.68 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.41 |
| upper limit | 0.05 |

Secondary: Change from Baseline in Mini-Mental State Examination (MMSE)

| | |
|-----------------|--|
| End point title | Change from Baseline in Mini-Mental State Examination (MMSE) |
|-----------------|--|

End point description:

MMSE is a brief screening instrument used to assess cognitive function (orientation, memory, attention, ability to name objects, follow verbal/written commands, write a sentence, and copy figures) in elderly participants. Total score ranges from 0 to 30; lower score indicates greater disease severity. LS Mean value was controlled for baseline value, baseline age, pooled investigator, treatment and visit. Analysis population included all randomized participants who received at least 1 dose of study drug and had baseline and post baseline data.

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

End point timeframe:

Baseline, Week 80

| End point values | Solanezumab | Placebo | | |
|-------------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 893 | 876 | | |
| Units: Units on a scale | | | | |
| least squares mean (standard error) | -3.17 (± 0.154) | -3.66 (± 0.156) | | |

Statistical analyses

| | |
|---|------------------------|
| Statistical analysis title | Statistical analysis 1 |
| Comparison groups | Solanezumab v Placebo |
| Number of subjects included in analysis | 1769 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.014 |
| Method | Mixed models analysis |
| Parameter estimate | Mean difference (net) |
| Point estimate | 0.49 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.1 |
| upper limit | 0.88 |

Secondary: Change from Baseline in Alzheimer's Disease Cooperative Study Activities of Daily Living Inventory (ADCS-ADL)

| | |
|-----------------|---|
| End point title | Change from Baseline in Alzheimer's Disease Cooperative Study Activities of Daily Living Inventory (ADCS-ADL) |
|-----------------|---|

End point description:

The ADCS-ADL is a 23-item inventory developed as a rater-administered questionnaire answered by the participant's caregiver. The ADCS-ADL measures both basic and instrumental activities of daily living by participants. The total score ranges from 0 to 78, with lower scores indicating greater disease severity. LS Mean value was controlled for baseline value, baseline age, pooled investigator, treatment and visit. Analysis population included all randomized participants who received at least 1 dose of study drug and had baseline and post baseline data.

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

End point timeframe:

Baseline, Week 80

| End point values | Solanezumab | Placebo | | |
|-------------------------------------|----------------------|----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 908 | 897 | | |
| Units: Units on a scale | | | | |
| least squares mean (standard error) | -7.42 (\pm 0.386) | -8.77 (\pm 0.387) | | |

Statistical analyses

| | |
|---|------------------------|
| Statistical analysis title | Statistical analysis 1 |
| Comparison groups | Solanezumab v Placebo |
| Number of subjects included in analysis | 1805 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.009 |
| Method | Mixed models analysis |
| Parameter estimate | Mean difference (net) |
| Point estimate | 1.35 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.33 |
| upper limit | 2.37 |

Secondary: Change from Baseline in Functional Activities Questionnaire (FAQ)

| | |
|-----------------|---|
| End point title | Change from Baseline in Functional Activities Questionnaire (FAQ) |
|-----------------|---|

End point description:

FAQ is a 10-item, caregiver-based questionnaire and was administered to the study partner who was asked to rate the participant's ability to perform a variety of activities ranging from financial management, shopping, playing games, food preparation, traveling, keeping appointments, keeping track of current events, and understanding media. FAQ total score was calculated by adding the scores from each of the 10 items. A negative change indicated an improvement from baseline. FAQ Total Score is the sum of 10 items, ranging from 0 (best possible outcome) to 100 (worst possible outcome). LS Mean value was controlled for baseline value, baseline age, pooled investigator, treatment and visit. Analysis population included all randomized participants who received at least 1 dose of study drug and had baseline and post baseline data.

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Baseline, Week 80 | |

| End point values | Solanezumab | Placebo | | |
|-------------------------------------|---------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 907 | 892 | | |
| Units: Units on a scale | | | | |
| least squares mean (standard error) | 5.17 (\pm 0.212) | 5.57 (\pm 0.213) | | |

Statistical analyses

| | |
|---|------------------------|
| Statistical analysis title | Statistical analysis 1 |
| Comparison groups | Solanezumab v Placebo |
| Number of subjects included in analysis | 1799 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.14 |
| Method | Mixed models analysis |
| Parameter estimate | Mean difference (net) |
| Point estimate | -0.4 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.93 |
| upper limit | 0.13 |

Secondary: Change from Baseline in Clinical Dementia Rating-Sum of Boxes (CDR-SB)

| | |
|-----------------|--|
| End point title | Change from Baseline in Clinical Dementia Rating-Sum of Boxes (CDR-SB) |
|-----------------|--|

End point description:

CDR-SB is a semi-structured interview of participants and their caregivers. Participant's cognitive status is rated across 6 domains of functioning, including memory, orientation, judgment/problem solving, community affairs, home/hobbies, and personal care. Severity score assigned for each of 6 domains; total score (SB) ranges from 0 to 18. Higher scores indicate greater disease severity. LS Mean value was controlled for baseline value, baseline age, pooled investigator, treatment and visit. Analysis population included all randomized participants who received at least 1 dose of study drug and had baseline and

post baseline data.

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Baseline, Week 80 | |

| End point values | Solanezumab | Placebo | | |
|--------------------------------------|---------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 903 | 895 | | |
| Units: Units on a scale | | | | |
| arithmetic mean (standard deviation) | 1.91 (\pm 2.442) | 2.23 (\pm 2.692) | | |

Statistical analyses

| | |
|---|------------------------|
| Statistical analysis title | Statistical Analysis 1 |
| Comparison groups | Solanezumab v Placebo |
| Number of subjects included in analysis | 1798 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.004 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (net) |

Secondary: Change from Baseline in Neuropsychiatric Inventory (NPI)

| | |
|------------------------|---|
| End point title | Change from Baseline in Neuropsychiatric Inventory (NPI) |
| End point description: | NPI assesses psychopathology in participants with dementia and other neurologic disorders. Information is obtained from a caregiver familiar with the participant's behavior. Total score ranges from 12 to 144; Higher scores indicate greater disease severity. LS Mean value was controlled for baseline value, baseline age, pooled investigator, treatment and visit. Analysis population included all randomized participants who received at least 1 dose of study drug and had baseline and post baseline data. |
| End point type | Secondary |
| End point timeframe: | |
| Baseline, Week 80 | |

| End point values | Solanezumab | Placebo | | |
|-------------------------------------|--------------------|----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 909 | 891 | | |
| Units: Units on a scale | | | | |
| least squares mean (standard error) | 2.26 (\pm 3.11) | 0.382 (\pm 0.387) | | |

Statistical analyses

| | |
|---|------------------------|
| Statistical analysis title | Statistical analysis 1 |
| Comparison groups | Solanezumab v Placebo |
| Number of subjects included in analysis | 1800 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.082 |
| Method | Mixed models analysis |
| Parameter estimate | Mean difference (net) |
| Point estimate | -0.85 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.82 |
| upper limit | 0.11 |

Secondary: Change from Baseline in Resource Utilization in Dementia-Lite (RUD-Lite)

| | |
|------------------------|--|
| End point title | Change from Baseline in Resource Utilization in Dementia-Lite (RUD-Lite) |
| End point description: | Assesses healthcare resource utilization (formal and informal care). Information gathered on both caregivers (care-giving time, work status) and participants (accommodation and healthcare resource utilization) was gathered from baseline and follow-up interviews. Reported number of hospitalizations per participant up to 76 weeks. LS Mean value was controlled for baseline value, baseline age, pooled investigator, treatment and visit. Analysis population included all randomized participants who received at least 1 dose of study drug and had baseline and post baseline data. |
| End point type | Secondary |
| End point timeframe: | Baseline, Week 80 |

| End point values | Solanezumab | Placebo | | |
|-------------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 909 | 891 | | |
| Units: Number of hospitalizations | | | | |
| least squares mean (standard error) | | | | |
| Basic ADL | 0.34 (± 0.058) | 0.35 (± 0.058) | | |
| Instrumental ADL | 0.55 (± 0.099) | 0.50 (± 0.100) | | |
| Sum of Basic and Instrumental ADL | 0.91 (± 0.132) | 0.86 (± 0.134) | | |
| Supervision | 0.72 (± 0.125) | 0.88 (± 0.127) | | |

Statistical analyses

| | |
|---|-----------------------------------|
| Statistical analysis title | Statistical analysis 1: Basic ADL |
| Comparison groups | Solanezumab v Placebo |
| Number of subjects included in analysis | 1800 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.97 |
| Method | Mixed models analysis |
| Parameter estimate | Mean difference (net) |
| Point estimate | 0 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.15 |
| upper limit | 0.14 |

| | |
|---|--|
| Statistical analysis title | Statistical analysis 2: Instrumental ADL |
| Comparison groups | Solanezumab v Placebo |
| Number of subjects included in analysis | 1800 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.69 |
| Method | Mixed models analysis |
| Parameter estimate | Mean difference (net) |
| Point estimate | 0.05 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.2 |
| upper limit | 0.3 |

| | |
|-----------------------------------|--|
| Statistical analysis title | Statistical analysis 3: Basic and Instrumental ADL |
| Comparison groups | Solanezumab v Placebo |

| | |
|---|-----------------------|
| Number of subjects included in analysis | 1800 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.786 |
| Method | Mixed models analysis |
| Parameter estimate | Mean difference (net) |
| Point estimate | 0.05 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.29 |
| upper limit | 0.38 |

| | |
|---|-------------------------------------|
| Statistical analysis title | Statistical analysis 4: Supervision |
| Comparison groups | Solanezumab v Placebo |
| Number of subjects included in analysis | 1800 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.329 |
| Method | Mixed models analysis |
| Parameter estimate | Mean difference (net) |
| Point estimate | -0.16 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.48 |
| upper limit | 0.16 |

Secondary: Change from Baseline in Quality of Life in Alzheimer's Disease (QoL-AD)

| | |
|-----------------|---|
| End point title | Change from Baseline in Quality of Life in Alzheimer's Disease (QoL-AD) |
|-----------------|---|

End point description:

Assesses QoL for AD: participant rates mood, relationships, memory, finances, physical condition, and overall QoL assessment. Each of 13 items, rated on a 4-point scale. Sum of items=total score (range: 13 to 52). Higher scores indicate greater QoL. Participant's primary caregiver asked to complete same measure. LS Mean value was controlled for baseline value, baseline age, pooled investigator, treatment and visit. Analysis population included all randomized participants who received at least 1 dose of study drug and had baseline and post baseline data. QoL-AD self- report score was reported.

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

End point timeframe:

Baseline, Week 80

| End point values | Solanezumab | Placebo | | |
|-------------------------------------|--------------------|--------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 853 | 812 | | |
| Units: Units on a scale | | | | |
| least squares mean (standard error) | -0.55 (± 0.158) | -0.72 (± 0.161) | | |

Statistical analyses

| Statistical analysis title | Statistical analysis 1 |
|---|------------------------|
| Comparison groups | Solanezumab v Placebo |
| Number of subjects included in analysis | 1665 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.381 |
| Method | Mixed models analysis |
| Parameter estimate | Mean difference (net) |
| Point estimate | 0.17 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.21 |
| upper limit | 0.56 |

Secondary: Change from Baseline in 5-Dimensional EuroQol Quality of Life Scale Proxy Version (EQ-5D Proxy)

| | |
|------------------------|---|
| End point title | Change from Baseline in 5-Dimensional EuroQol Quality of Life Scale Proxy Version (EQ-5D Proxy) |
| End point description: | EQ-5D (proxy version) measures mobility, self-care, usual activities, pain/discomfort, anxiety/depression. 3 severity levels: no, some, severe problems. Visual analog scale (VAS) assesses caregiver's impression of participant's health state; score ranges: 0 to 100 millimeter (mm). Lower scores=greater disease severity LS Mean value was controlled for baseline value, baseline age, pooled investigator, treatment and visit. Analysis population included all randomized participants who received at least 1 dose of study drug and had baseline and post baseline data. |
| End point type | Secondary |
| End point timeframe: | Baseline, Week 80 |

| End point values | Solanezumab | Placebo | | |
|-------------------------------------|--------------------|--------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 904 | 892 | | |
| Units: mm | | | | |
| least squares mean (standard error) | -1.10 (± 0.556) | -2.61 (± 0.562) | | |

Statistical analyses

| | |
|---|------------------------|
| Statistical analysis title | Statistical analysis 1 |
| Comparison groups | Solanezumab v Placebo |
| Number of subjects included in analysis | 1796 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.031 |
| Method | Mixed models analysis |
| Parameter estimate | Mean difference (net) |
| Point estimate | 1.5 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.13 |
| upper limit | 2.87 |

Secondary: Change from Baseline in Integrated Alzheimer's Disease Rating Scale (iADRS)

| | |
|-----------------|---|
| End point title | Change from Baseline in Integrated Alzheimer's Disease Rating Scale (iADRS) |
|-----------------|---|

End point description:

Integrated Alzheimer's Disease Rating Scale is used to assess that solanezumab slows down the cognitive and functional decline associated with AD compared with placebo. iADRS is a simple linear combination of ADAS-Cog 13 or 14 and the ADCS-iADL. The scale ranges from 0 to 146, where lower scores indicate worse performance. LS Mean value was controlled for baseline value, baseline age, pooled investigator, treatment and visit. Analysis population included all randomized participants who received at least 1 dose of study drug and had baseline and post baseline data.

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

End point timeframe:

Baseline, Week 80

| End point values | Solanezumab | Placebo | | |
|-------------------------------------|-----------------------|-----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 903 | 883 | | |
| Units: units on a scale | | | | |
| least squares mean (standard error) | -12.92 (\pm 0.533) | -14.59 (\pm 0.537) | | |

Statistical analyses

| | |
|---|------------------------|
| Statistical analysis title | Statistical analysis 1 |
| Comparison groups | Solanezumab v Placebo |
| Number of subjects included in analysis | 1786 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.017 |
| Method | Mixed models analysis |
| Parameter estimate | Mean difference (net) |
| Point estimate | 1.68 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.29 |
| upper limit | 3.06 |

Secondary: Percentage of Participants of Cognitive and Functional Responders

| | |
|-----------------|---|
| End point title | Percentage of Participants of Cognitive and Functional Responders |
|-----------------|---|

End point description:

Assess the proportion of participants who reach certain levels of cognitive and functional decline. Decline in cognition was defined as worsening from baseline by at least 6 or 9 points on the ADAS Cog14. If there is a cognitive decline of a specified cut-off or more at any time then the participant is considered a nonresponder. Functional nonresponders are participants who have not had any of the following at any time point: Clinically evident decline in ability to perform one or more basic ADL present at baseline; A clinically evident decline in ability to perform 20% or more of the instrumental ADL present at baseline; An increase in global CDR score of 1 point or more compared with baseline. A decline from no impairment to mild impairment (bADL, iADL is not considered clinically significant, but other declines of 1 or more points and any participant discontinuation within the first 6 months will be considered a non-responder. Analysis population included all randomized participants.

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

End point timeframe:

Baseline through Week 80

| End point values | Solanezumab | Placebo | | |
|-----------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 1057 | 1072 | | |
| Units: percentage of participants | | | | |
| number (not applicable) | | | | |
| Cognitive Responders: Cut-off 6 | 35.7 | 35.3 | | |
| Cognitive Responders: Cut-off 9 | 55.2 | 52.3 | | |
| Functional Responders | 38.0 | 36.8 | | |

Statistical analyses

| | |
|---|---|
| Statistical analysis title | Statistical analysis 1:Cognitive: Cut-off 6 |
| Comparison groups | Solanezumab v Placebo |
| Number of subjects included in analysis | 2129 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.891 |
| Method | Fisher exact |
| Parameter estimate | Fishers exact test |

| | |
|---|---|
| Statistical analysis title | Statistical analysis 2:Cognitive: Cut-off 9 |
| Comparison groups | Solanezumab v Placebo |
| Number of subjects included in analysis | 2129 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.203 |
| Method | Fisher exact |
| Parameter estimate | Fishers exact test |

| | |
|---|--|
| Statistical analysis title | Statistical analysis 3:Functional Responders |
| Comparison groups | Solanezumab v Placebo |
| Number of subjects included in analysis | 2129 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.588 |
| Method | Fisher exact |
| Parameter estimate | Fishers exact test |

| | |
|---|--|
| Secondary: Change from Baseline in Plasma Amyloid-Beta (Aβ) Species | |
| End point title | Change from Baseline in Plasma Amyloid-Beta (A β) Species |
| End point description: Concentration of amino acid peptide known as A β 1-42 in plasma. The change in plasma A β analytes after treatment were assessed separately for each plasma A β parameter. LS Mean value was controlled for baseline value, baseline age, pooled investigator, treatment and visit. Analysis population included all randomized participants. | |
| End point type | Secondary |
| End point timeframe: Baseline, Week 80 | |

| End point values | Solanezumab | Placebo | | |
|-------------------------------------|-----------------------------|--------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 1057 | 1072 | | |
| Units: Picogram/milliliter | | | | |
| least squares mean (standard error) | | | | |
| Modified amyloid beta 1-40 | 172754.36 (\pm 1613.534) | 262.98 (\pm 1609.006) | | |
| Modified amyloid beta1-42 | 18485.26 (\pm 104.913) | 15.75 (\pm 105.237) | | |

Statistical analyses

| Statistical analysis title | Statistical analysis 1: Modified amyloid beta 1-40 |
|---|--|
| Comparison groups | Solanezumab v Placebo |
| Number of subjects included in analysis | 2129 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Mixed models analysis |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 172491.38 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 168131.33 |
| upper limit | 176851.43 |

| Statistical analysis title | Statistical analysis 2: Modified amyloid beta 1-42 |
|---|--|
| Comparison groups | Solanezumab v Placebo |
| Number of subjects included in analysis | 2129 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Mixed models analysis |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 18469.51 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 18187.59 |
| upper limit | 18751.44 |

Secondary: Change from Baseline in volumetric Magnetic Resonance Imaging (vMRI)

| | |
|-----------------|---|
| End point title | Change from Baseline in volumetric Magnetic Resonance |
|-----------------|---|

End point description:

The vMRI assessment of right and left hippocampal atrophy, is reported. LS Mean value was controlled for baseline value, baseline age, pooled investigator, treatment and visit. Analysis population included all randomized participants.

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

End point timeframe:

Baseline, Week 80

| End point values | Solanezumab | Placebo | | |
|--|-----------------------|-----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 1057 | 1072 | | |
| Units: Cubic millimeter (mm ³) | | | | |
| arithmetic mean (standard deviation) | | | | |
| Right hippocampal atrophy | -145.7 (± 75.42) | -154.1 (± 81.06) | | |
| Left hippocampal atrophy | -142.3 (± 74.27) | -146.3 (± 78.04) | | |
| Right hippocampal atrophy+Left hippocampal atrophy | -288.0 (± 135.19) | -300.4 (± 138.52) | | |
| Right entorhinal cortex atrophy | -77.3 (± 45.18) | -80.8 (± 45.16) | | |
| Left entorhinal cortex atrophy | -91.6 (± 47.60) | -95.2 (± 53.46) | | |
| Right+Left entorhinal cortex atrophy | -169.0 (± 79.65) | -176.0 (± 86.11) | | |
| Atrophy of whole brain volume | -22725.6 (± 11920.78) | -23500.5 (± 12000.09) | | |
| Enlargement of Ventricular volume | 7055.4 (± 4580.36) | 7226.6 (± 4545.73) | | |

Statistical analyses

| Statistical analysis title | Statistical analysis 1: Right hippocampal atrophy |
|---|---|
| Comparison groups | Solanezumab v Placebo |
| Number of subjects included in analysis | 2129 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.032 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (net) |

| Statistical analysis title | Statistical analysis 2: Left hippocampal atrophy |
|----------------------------|--|
| Comparison groups | Solanezumab v Placebo |

| | |
|---|-----------------------|
| Number of subjects included in analysis | 2129 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.32 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (net) |

| | |
|--|--|
| Statistical analysis title | SA 3: Right + Left hippocampal atrophy |
| Statistical analysis description: Statistical Analysis 3 (SA 3) | |
| Comparison groups | Solanezumab v Placebo |
| Number of subjects included in analysis | 2129 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.077 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (net) |

| | |
|--|---------------------------------------|
| Statistical analysis title | SA 4: Right entorhinal cortex atrophy |
| Statistical analysis description: Statistical analysis 4 (SA 4) | |
| Comparison groups | Solanezumab v Placebo |
| Number of subjects included in analysis | 2129 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.186 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (net) |

| | |
|--|--------------------------------------|
| Statistical analysis title | SA 5: Left entorhinal cortex atrophy |
| Statistical analysis description: Statistical analysis 5 (SA 5) | |
| Comparison groups | Solanezumab v Placebo |
| Number of subjects included in analysis | 2129 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.126 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (net) |

| | |
|-----------------------------------|--|
| Statistical analysis title | SA 6: Right + Left entorhinal cortex atrophy |
|-----------------------------------|--|

Statistical analysis description:

Statistical analysis 6 (SA 6)

| | |
|---|-----------------------|
| Comparison groups | Solanezumab v Placebo |
| Number of subjects included in analysis | 2129 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.099 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (net) |

Statistical analysis title

SA 7: Atrophy of whole brain volume

Statistical analysis description:

Statistical analysis 7 (SA 7)

| | |
|---|-----------------------|
| Comparison groups | Solanezumab v Placebo |
| Number of subjects included in analysis | 2129 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.095 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (net) |

Statistical analysis title

SA 8: Enlargement of Ventricular volume

Statistical analysis description:

Statistical analysis 8 (SA 8)

| | |
|---|-----------------------|
| Comparison groups | Solanezumab v Placebo |
| Number of subjects included in analysis | 2129 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.227 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (net) |

Secondary: Pharmacokinetics (PK): Area Under the Concentration Time Curve (AUC) of Solanezumab (LY2062430)

| | |
|-----------------|--|
| End point title | Pharmacokinetics (PK): Area Under the Concentration Time Curve (AUC) of Solanezumab (LY2062430) ^[2] |
|-----------------|--|

End point description:

Area Under the Concentration versus Time Curve was evaluated for Solanezumab. Analysis population included all randomized participants who received at least 1 dose of study medication (Solanezumab) with evaluable Solanezumab PK data.

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

End point timeframe:

Visit 2 (Post-dose), Visit 5, 9, 15 (Pre-dose, Post-dose) and Visit 22 (Pre-dose): Pre-dose before the infusion, Post-dose 30 minutes End of Infusion

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: No inferential statistics were planned or conducted for this endpoint.

| | | | | |
|---|-----------------|--|--|--|
| End point values | Solanezumab | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 1044 | | | |
| Units: milligram*hour per milliliter (mg*h/mL) | | | | |
| geometric mean (geometric coefficient of variation) | 43.2 (± 24.3) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Florbetapir Positron Emission Tomography (PET) Scan

| | |
|-----------------|---|
| End point title | Change from Baseline in Florbetapir Positron Emission Tomography (PET) Scan |
|-----------------|---|

End point description:

Florbetapir PET imaging was used to confirm the presence of amyloid pathology consistent with AD. Change from baseline was done to test the hypothesis that amyloid burden was reduced in participants in the treatment group. The change from baseline to the postbaseline visit of the composite summary standard uptake value ratio of florbetapir F18 standardized to subject-specific white matter. LS Mean value was controlled for baseline value, baseline age, pooled investigator, treatment and visit. Analysis population included all randomized participants who received at least 1 dose of study drug and had baseline and post baseline data.

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

End point timeframe:

Baseline, Week 80

| | | | | |
|---|-----------------------------------|----------------------------------|--|--|
| End point values | Solanezumab | Placebo | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 915 | 924 | | |
| Units: Composite summary | | | | |
| least squares mean (standard error) | | | | |
| Subject specific white matter corrected Mean whole cerebellum | 0.02 (± 0.002) -0.01 (± 0.005) | 0.02 (± 0.002) 0.00 (± 0.005) | | |

Statistical analyses

| | |
|-----------------------------------|--|
| Statistical analysis title | SA1: Subject specific white matter corrected |
|-----------------------------------|--|

Statistical analysis description:

Statistical analysis 1 (SA1)

| | |
|---|-----------------------|
| Comparison groups | Solanezumab v Placebo |
| Number of subjects included in analysis | 1839 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.131 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (net) |

| | |
|---|----------------------------|
| Statistical analysis title | SA2: Mean whole cerebellum |
| Statistical analysis description: Statistical analysis 2 (SA2) | |
| Comparison groups | Solanezumab v Placebo |
| Number of subjects included in analysis | 1839 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.181 |
| Method | ANCOVA |
| Parameter estimate | Median difference (net) |

Secondary: Change from Baseline in Cerebrospinal Fluid (CSF) A β Levels

| | |
|--|--|
| End point title | Change from Baseline in Cerebrospinal Fluid (CSF) A β Levels |
| End point description: Concentration of CSF parameters includes amino acid peptide known as A β 1-40 and A β 1-42. Analyses of these CSF biomarkers was conducted in a subset of participants (as an addendum to the protocol). The dependent variable for each CSF parameter was its change from baseline to endpoint. LS Mean value was controlled for baseline value, baseline age, pooled investigator, treatment and visit. Analysis population included all randomized participants who received at least 1 dose of study drug and had baseline and post baseline data. | |
| End point type | Secondary |
| End point timeframe: Baseline, Week 80 | |

| End point values | Solanezumab | Placebo | | |
|-------------------------------------|--------------------------|---------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 1057 | 1072 | | |
| Units: picogram/milliliter | | | | |
| least squares mean (standard error) | | | | |
| Free amyloid beta 1-40, CSF | -714.60 (\pm 177.828) | -319.97 (\pm 182.519) | | |
| Free amyloid beta 1-42, CSF | -37.33 (\pm 7.507) | -9.27 (\pm 8.175) | | |
| Modified amyloid beta 1-40, CSF | 1093.81 (\pm 624.059) | -2336.68 (\pm 637.126) | | |
| Modified amyloid beta 1-42, CSF | 315.69 (\pm 42.620) | -107.91 (\pm 42.907) | | |

Statistical analyses

| | |
|--|-----------------------------------|
| Statistical analysis title | SA 1: Free amyloid beta 1-40, CSF |
| Statistical analysis description: Statistical analysis 1 (SA 1) | |
| Comparison groups | Solanezumab v Placebo |
| Number of subjects included in analysis | 2129 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.073 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (net) |

| | |
|--|-----------------------------------|
| Statistical analysis title | SA 2: Free amyloid beta 1-42, CSF |
| Statistical analysis description: Statistical analysis 2 (SA 2) | |
| Comparison groups | Solanezumab v Placebo |
| Number of subjects included in analysis | 2129 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.005 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (net) |

| | |
|--|---------------------------------------|
| Statistical analysis title | SA 3: Modified amyloid beta 1-40, CSF |
| Statistical analysis description: Statistical analysis 3 (SA 3) | |
| Comparison groups | Solanezumab v Placebo |
| Number of subjects included in analysis | 2129 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (net) |

| | |
|-----------------------------------|---------------------------------------|
| Statistical analysis title | SA 4: Modified amyloid beta 1-42, CSF |
|-----------------------------------|---------------------------------------|

Statistical analysis description:

Statistical analysis 4 (SA 4)

| | |
|---|-----------------------|
| Comparison groups | Solanezumab v Placebo |
| Number of subjects included in analysis | 2129 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (net) |

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up To 80 Weeks

Adverse event reporting additional description:

All randomized participants who received at least 1 dose of study drug.

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 19.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|--|
| Reporting group title | Solanezumab 400mg - Double-Blind Phase |
|-----------------------|--|

Reporting group description:

Participants received Solanezumab 400 mg IV every 4 weeks for 76 weeks with an additional 4 weeks of assessments. Participants who completed the full 80 weeks of treatment/assessment and decide to continue will take this regimen for up to an additional 208 weeks.

| | |
|-----------------------|------------------------------|
| Reporting group title | Placebo - Double-Blind Phase |
|-----------------------|------------------------------|

Reporting group description:

Participants received Placebo IV every 4 weeks for 76 weeks with an additional 4 weeks of assessments. Participants who complete the full 80 weeks of treatment/assessment and decide to continue will switch to solanezumab 400 mg every 4 weeks for up to an additional 208 weeks.

| | |
|-----------------------|---|
| Reporting group title | Solanezumab 400mg: Solanezumab 400mg Open Label |
|-----------------------|---|

Reporting group description:

Participants who complete 80 weeks treatment/assessment of the double-blind period were entered into open-label period. Participants received Solanezumab 400 mg IV every 4 weeks for 180 weeks with an additional 4 weeks of assessments.

| | |
|-----------------------|---------------------------------------|
| Reporting group title | Placebo: Solanezumab 400mg Open Label |
|-----------------------|---------------------------------------|

Reporting group description:

Participants who complete 80 weeks treatment/assessment of the double-blind period were entered into open-label period. Participants received Placebo IV every 4 weeks for 180 weeks with an additional 4 weeks of assessments.

| Serious adverse events | Solanezumab 400mg - Double-Blind Phase | Placebo - Double-Blind Phase | Solanezumab 400mg: Solanezumab 400mg Open Label |
|--|--|------------------------------|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 175 / 1054 (16.60%) | 203 / 1067 (19.03%) | 102 / 879 (11.60%) |
| number of deaths (all causes) | 9 | 17 | 5 |
| number of deaths resulting from adverse events | 2 | 2 | 2 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) abdominal neoplasm alternative dictionary used: MedDRA 19.0 | | | |

| | | | |
|---|------------------|------------------|-----------------|
| subjects affected / exposed | 0 / 1054 (0.00%) | 1 / 1067 (0.09%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| adenocarcinoma of colon | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 1054 (0.09%) | 2 / 1067 (0.19%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| b-cell lymphoma | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 1054 (0.09%) | 0 / 1067 (0.00%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| basal cell carcinoma | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 2 / 1054 (0.19%) | 2 / 1067 (0.19%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 3 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| benign small intestinal neoplasm | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 1054 (0.09%) | 0 / 1067 (0.00%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| bladder cancer | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 1054 (0.09%) | 0 / 1067 (0.00%) | 1 / 879 (0.11%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| bladder neoplasm | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 0 / 1067 (0.00%) | 1 / 879 (0.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|--|------------------|------------------|-----------------|
| breast cancer alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 1 / 1067 (0.09%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| breast cancer metastatic alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 1054 (0.09%) | 0 / 1067 (0.00%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| cardiac myxoma alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 1054 (0.09%) | 0 / 1067 (0.00%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| clear cell renal cell carcinoma alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 1054 (0.09%) | 0 / 1067 (0.00%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| colon adenoma alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 1 / 1067 (0.09%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| colon cancer alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 1054 (0.09%) | 1 / 1067 (0.09%) | 1 / 879 (0.11%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| endometrial adenocarcinoma alternative dictionary used: MedDRA 19.0 | | | |

| | | | |
|---|------------------|------------------|-----------------|
| subjects affected / exposed ^[1] | 0 / 599 (0.00%) | 1 / 627 (0.16%) | 0 / 501 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| glioblastoma | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 1054 (0.09%) | 0 / 1067 (0.00%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| glioblastoma multiforme | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 1054 (0.09%) | 0 / 1067 (0.00%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| hepatic neoplasm | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 0 / 1067 (0.00%) | 1 / 879 (0.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| intraductal proliferative breast lesion | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 1054 (0.09%) | 0 / 1067 (0.00%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| invasive ductal breast carcinoma | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 1054 (0.09%) | 0 / 1067 (0.00%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| lip squamous cell carcinoma | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 1 / 1067 (0.09%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

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| lung adenocarcinoma alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 1 / 1067 (0.09%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| lung cancer metastatic alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 1 / 1067 (0.09%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| lung neoplasm malignant alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 1054 (0.09%) | 2 / 1067 (0.19%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| malignant melanoma alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 2 / 1067 (0.19%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| malignant melanoma in situ alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 1 / 1067 (0.09%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| metastases to central nervous system alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 1 / 1067 (0.09%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| metastatic neoplasm alternative dictionary used: MedDRA 19.0 | | | |

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|---|------------------|------------------|-----------------|
| subjects affected / exposed | 0 / 1054 (0.00%) | 1 / 1067 (0.09%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| oesophageal adenocarcinoma | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 1 / 1067 (0.09%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| ovarian cancer stage iv | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed ^[2] | 0 / 599 (0.00%) | 1 / 627 (0.16%) | 0 / 501 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| pancreatic neoplasm | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 0 / 1067 (0.00%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| parathyroid tumour benign | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 1 / 1067 (0.09%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| plasma cell myeloma | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 1054 (0.09%) | 0 / 1067 (0.00%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| prostate cancer | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed ^[3] | 2 / 455 (0.44%) | 0 / 440 (0.00%) | 2 / 378 (0.53%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

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|---|------------------|------------------|-----------------|
| prostate cancer metastatic alternative dictionary used: MedDRA 19.0 subjects affected / exposed ^[4] | 1 / 455 (0.22%) | 1 / 440 (0.23%) | 0 / 378 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| rectal adenocarcinoma alternative dictionary used: MedDRA 19.0 subjects affected / exposed | 0 / 1054 (0.00%) | 0 / 1067 (0.00%) | 1 / 879 (0.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| renal cell carcinoma alternative dictionary used: MedDRA 19.0 subjects affected / exposed | 0 / 1054 (0.00%) | 1 / 1067 (0.09%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| small cell lung cancer alternative dictionary used: MedDRA 19.0 subjects affected / exposed | 1 / 1054 (0.09%) | 0 / 1067 (0.00%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| squamous cell carcinoma of the tongue alternative dictionary used: MedDRA 19.0 subjects affected / exposed | 1 / 1054 (0.09%) | 0 / 1067 (0.00%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| transitional cell cancer of renal pelvis and ureter metastatic alternative dictionary used: MedDRA 19.0 subjects affected / exposed | 0 / 1054 (0.00%) | 0 / 1067 (0.00%) | 1 / 879 (0.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| transitional cell carcinoma alternative dictionary used: MedDRA 19.0 | | | |

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|---|------------------|------------------|-----------------|
| subjects affected / exposed | 0 / 1054 (0.00%) | 1 / 1067 (0.09%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| uterine cancer alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed ^[5] | 1 / 599 (0.17%) | 0 / 627 (0.00%) | 0 / 501 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vascular disorders | | | |
| aortic aneurysm alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 3 / 1054 (0.28%) | 0 / 1067 (0.00%) | 2 / 879 (0.23%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| aortic stenosis alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 1054 (0.09%) | 0 / 1067 (0.00%) | 1 / 879 (0.11%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deep vein thrombosis alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 1054 (0.09%) | 0 / 1067 (0.00%) | 1 / 879 (0.11%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| hypertension alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 1054 (0.09%) | 0 / 1067 (0.00%) | 2 / 879 (0.23%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| hypertensive crisis alternative dictionary used: MedDRA 19.0 | | | |

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|--|------------------|------------------|-----------------|
| subjects affected / exposed | 0 / 1054 (0.00%) | 1 / 1067 (0.09%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| hypotension alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 1054 (0.09%) | 1 / 1067 (0.09%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| lymphoedema alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 1054 (0.09%) | 0 / 1067 (0.00%) | 1 / 879 (0.11%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| orthostatic hypotension alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 1054 (0.09%) | 1 / 1067 (0.09%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| peripheral arterial occlusive disease alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 1 / 1067 (0.09%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pregnancy, puerperium and perinatal conditions cephalhaematoma alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 1054 (0.09%) | 0 / 1067 (0.00%) | 1 / 879 (0.11%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General disorders and administration site conditions asthenia alternative dictionary used: MedDRA 19.0 | | | |

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|---|------------------|------------------|-----------------|
| subjects affected / exposed | 0 / 1054 (0.00%) | 2 / 1067 (0.19%) | 2 / 879 (0.23%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| chest discomfort | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 1 / 1067 (0.09%) | 1 / 879 (0.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| chest pain | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 3 / 1054 (0.28%) | 0 / 1067 (0.00%) | 1 / 879 (0.11%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| death | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 1054 (0.09%) | 2 / 1067 (0.19%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 2 | 0 / 0 |
| gait disturbance | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 0 / 1067 (0.00%) | 1 / 879 (0.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| general physical health deterioration | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 1054 (0.09%) | 1 / 1067 (0.09%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| generalised oedema | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 1054 (0.09%) | 0 / 1067 (0.00%) | 1 / 879 (0.11%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

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| multiple organ dysfunction syndrome | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 1 / 1067 (0.09%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| non-cardiac chest pain | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 7 / 1054 (0.66%) | 5 / 1067 (0.47%) | 1 / 879 (0.11%) |
| occurrences causally related to treatment / all | 1 / 8 | 0 / 7 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| pain | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 0 / 1067 (0.00%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| pyrexia | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 3 / 1054 (0.28%) | 0 / 1067 (0.00%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| stent-graft endoleak | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 1054 (0.09%) | 0 / 1067 (0.00%) | 1 / 879 (0.11%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| sudden death | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 1054 (0.09%) | 0 / 1067 (0.00%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| systemic inflammatory response syndrome | | | |
| alternative dictionary used: MedDRA 19.0 | | | |

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|--|------------------|------------------|-----------------|
| subjects affected / exposed | 2 / 1054 (0.19%) | 1 / 1067 (0.09%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Social circumstances | | | |
| immobilisation prolonged | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 1054 (0.09%) | 0 / 1067 (0.00%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| respite care | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 1054 (0.09%) | 0 / 1067 (0.00%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| acute respiratory failure | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 1 / 1067 (0.09%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| asthma | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 1054 (0.09%) | 1 / 1067 (0.09%) | 2 / 879 (0.23%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| benign prostatic hyperplasia | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed ^[6] | 1 / 455 (0.22%) | 1 / 440 (0.23%) | 3 / 378 (0.79%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| chronic obstructive pulmonary disease | | | |
| alternative dictionary used: MedDRA 19.0 | | | |

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|---|------------------|------------------|-----------------|
| subjects affected / exposed | 1 / 1054 (0.09%) | 1 / 1067 (0.09%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| dyspnoea | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 1054 (0.09%) | 0 / 1067 (0.00%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| epistaxis | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 1054 (0.09%) | 0 / 1067 (0.00%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| organising pneumonia | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 0 / 1067 (0.00%) | 1 / 879 (0.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| pharyngeal mass | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 1 / 1067 (0.09%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| pleural effusion | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 1 / 1067 (0.09%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| pleurisy | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 1054 (0.09%) | 0 / 1067 (0.00%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

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|--|------------------|------------------|-----------------|
| pneumonia aspiration alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 1054 (0.09%) | 1 / 1067 (0.09%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| pneumothorax alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 1054 (0.09%) | 0 / 1067 (0.00%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| prostatitis alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed ^[7] | 1 / 455 (0.22%) | 0 / 440 (0.00%) | 0 / 378 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| pulmonary embolism alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 4 / 1054 (0.38%) | 2 / 1067 (0.19%) | 1 / 879 (0.11%) |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 2 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| respiratory arrest alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 1054 (0.09%) | 0 / 1067 (0.00%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| sleep apnoea syndrome alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 1 / 1067 (0.09%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| vulvar dysplasia alternative dictionary used: MedDRA 19.0 | | | |

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|--|------------------|------------------|-----------------|
| subjects affected / exposed ^[8] | 0 / 599 (0.00%) | 1 / 627 (0.16%) | 0 / 501 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Psychiatric disorders | | | |
| abnormal behaviour | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 1 / 1067 (0.09%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| affective disorder | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 1054 (0.09%) | 0 / 1067 (0.00%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| aggression | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 2 / 1067 (0.19%) | 1 / 879 (0.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| agitation | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 3 / 1054 (0.28%) | 2 / 1067 (0.19%) | 1 / 879 (0.11%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 2 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| anxiety | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 2 / 1054 (0.19%) | 2 / 1067 (0.19%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| behavioural and psychiatric symptoms of dementia | | | |
| alternative dictionary used: MedDRA 19.0 | | | |

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|---|------------------|------------------|-----------------|
| subjects affected / exposed | 0 / 1054 (0.00%) | 1 / 1067 (0.09%) | 2 / 879 (0.23%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| confusional state | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 3 / 1054 (0.28%) | 1 / 1067 (0.09%) | 2 / 879 (0.23%) |
| occurrences causally related to treatment / all | 1 / 3 | 0 / 1 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| delirium | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 1054 (0.09%) | 5 / 1067 (0.47%) | 1 / 879 (0.11%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 5 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| delusion | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 1 / 1067 (0.09%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| depression | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 2 / 1054 (0.19%) | 1 / 1067 (0.09%) | 1 / 879 (0.11%) |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| disorientation | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 1 / 1067 (0.09%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| hallucination | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 0 / 1067 (0.00%) | 1 / 879 (0.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

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| mental status changes alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 2 / 1054 (0.19%) | 4 / 1067 (0.37%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 1 / 2 | 1 / 4 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| phobia alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 1054 (0.09%) | 0 / 1067 (0.00%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| psychotic disorder alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 2 / 1067 (0.19%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| suicide attempt alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 2 / 1054 (0.19%) | 0 / 1067 (0.00%) | 1 / 879 (0.11%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Investigations | | | |
| heart rate irregular alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 0 / 1067 (0.00%) | 1 / 879 (0.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| troponin t increased alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 1 / 1067 (0.09%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| weight decreased alternative dictionary used: MedDRA 19.0 | | | |

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|---|------------------|------------------|-----------------|
| subjects affected / exposed | 1 / 1054 (0.09%) | 0 / 1067 (0.00%) | 1 / 879 (0.11%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Injury, poisoning and procedural complications | | | |
| alcohol poisoning | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 1 / 1067 (0.09%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| animal bite | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 1 / 1067 (0.09%) | 1 / 879 (0.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| ankle fracture | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 0 / 1067 (0.00%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| arthropod sting | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 1 / 1067 (0.09%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| cervical vertebral fracture | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 2 / 1054 (0.19%) | 1 / 1067 (0.09%) | 1 / 879 (0.11%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| chest injury | | | |
| alternative dictionary used: MedDRA 19.0 | | | |

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|--|-------------------|-------------------|-----------------|
| subjects affected / exposed | 1 / 1054 (0.09%) | 1 / 1067 (0.09%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| clavicle fracture alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 1054 (0.09%) | 0 / 1067 (0.00%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| concussion alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 0 / 1067 (0.00%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| contusion alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 1 / 1067 (0.09%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| coronary vascular graft occlusion alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 1 / 1067 (0.09%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| craniocerebral injury alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 1054 (0.09%) | 0 / 1067 (0.00%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| fall alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 24 / 1054 (2.28%) | 24 / 1067 (2.25%) | 5 / 879 (0.57%) |
| occurrences causally related to treatment / all | 2 / 26 | 1 / 27 | 0 / 5 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

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|--|------------------|------------------|-----------------|
| femoral neck fracture alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 1054 (0.09%) | 1 / 1067 (0.09%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| femur fracture alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 6 / 1054 (0.57%) | 5 / 1067 (0.47%) | 3 / 879 (0.34%) |
| occurrences causally related to treatment / all | 0 / 7 | 0 / 5 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| fibula fracture alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 1054 (0.09%) | 0 / 1067 (0.00%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| fracture displacement alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 0 / 1067 (0.00%) | 1 / 879 (0.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| fractured coccyx alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 1 / 1067 (0.09%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| gastrointestinal stoma complication alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 1054 (0.09%) | 0 / 1067 (0.00%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| gun shot wound alternative dictionary used: MedDRA 19.0 | | | |

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|---|------------------|------------------|-----------------|
| subjects affected / exposed | 0 / 1054 (0.00%) | 1 / 1067 (0.09%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| head injury | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 2 / 1054 (0.19%) | 0 / 1067 (0.00%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| hip fracture | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 5 / 1054 (0.47%) | 6 / 1067 (0.56%) | 3 / 879 (0.34%) |
| occurrences causally related to treatment / all | 1 / 5 | 1 / 6 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| humerus fracture | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 1 / 1067 (0.09%) | 1 / 879 (0.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| joint dislocation | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 1054 (0.09%) | 0 / 1067 (0.00%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| laceration | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 1054 (0.09%) | 1 / 1067 (0.09%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| ligament sprain | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 1054 (0.09%) | 0 / 1067 (0.00%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

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| lumbar vertebral fracture alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 0 / 1067 (0.00%) | 1 / 879 (0.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| pelvic fracture alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 2 / 1067 (0.19%) | 1 / 879 (0.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| periprosthetic fracture alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 1054 (0.09%) | 0 / 1067 (0.00%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| postoperative ileus alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 1054 (0.09%) | 0 / 1067 (0.00%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| pubis fracture alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 1054 (0.09%) | 1 / 1067 (0.09%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| radius fracture alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 2 / 1054 (0.19%) | 1 / 1067 (0.09%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| rib fracture alternative dictionary used: MedDRA 19.0 | | | |

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|--|------------------|------------------|-----------------|
| subjects affected / exposed | 1 / 1054 (0.09%) | 4 / 1067 (0.37%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 4 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| road traffic accident alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 1054 (0.09%) | 1 / 1067 (0.09%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| skull fracture alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 1 / 1067 (0.09%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| spinal compression fracture alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 2 / 1067 (0.19%) | 1 / 879 (0.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| spinal fracture alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 0 / 1067 (0.00%) | 1 / 879 (0.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| sternal fracture alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 0 / 1067 (0.00%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| subdural haematoma alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 2 / 1054 (0.19%) | 4 / 1067 (0.37%) | 1 / 879 (0.11%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 4 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |

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| upper limb fracture alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 1054 (0.09%) | 2 / 1067 (0.19%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| wound alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 1 / 1067 (0.09%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| wrist fracture alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 2 / 1054 (0.19%) | 1 / 1067 (0.09%) | 1 / 879 (0.11%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac disorders | | | |
| acute myocardial infarction alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 1054 (0.09%) | 2 / 1067 (0.19%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| adams-stokes syndrome alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 1 / 1067 (0.09%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| angina pectoris alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 3 / 1054 (0.28%) | 2 / 1067 (0.19%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 1 / 3 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| aortic valve stenosis alternative dictionary used: MedDRA 19.0 | | | |

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|---|------------------|------------------|-----------------|
| subjects affected / exposed | 1 / 1054 (0.09%) | 0 / 1067 (0.00%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| arrhythmia supraventricular alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 1054 (0.09%) | 0 / 1067 (0.00%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| atrial fibrillation alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 5 / 1054 (0.47%) | 9 / 1067 (0.84%) | 4 / 879 (0.46%) |
| occurrences causally related to treatment / all | 2 / 5 | 2 / 9 | 1 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| atrioventricular block alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 1 / 1067 (0.09%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| atrioventricular block complete alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 2 / 1067 (0.19%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| atrioventricular block second degree alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 1 / 1067 (0.09%) | 1 / 879 (0.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| bradycardia alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 2 / 1054 (0.19%) | 2 / 1067 (0.19%) | 2 / 879 (0.23%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

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| cardiac arrest | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 1054 (0.09%) | 3 / 1067 (0.28%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 3 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 3 | 0 / 0 |
| cardiac failure | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 3 / 1067 (0.28%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 3 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| cardiac failure congestive | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 1054 (0.09%) | 1 / 1067 (0.09%) | 2 / 879 (0.23%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| cardio-respiratory arrest | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 1054 (0.09%) | 1 / 1067 (0.09%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 1 / 1 | 0 / 0 |
| coronary artery disease | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 0 / 1067 (0.00%) | 1 / 879 (0.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| myocardial infarction | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 2 / 1054 (0.19%) | 4 / 1067 (0.37%) | 2 / 879 (0.23%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 4 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 2 | 0 / 2 | 0 / 0 |
| myocardial ischaemia | | | |
| alternative dictionary used: MedDRA 19.0 | | | |

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|---|------------------|------------------|-----------------|
| subjects affected / exposed | 0 / 1054 (0.00%) | 1 / 1067 (0.09%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| sinus bradycardia | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 2 / 1067 (0.19%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| sinus node dysfunction | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 1054 (0.09%) | 1 / 1067 (0.09%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| altered state of consciousness | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 1 / 1067 (0.09%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| basal ganglia infarction | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 0 / 1067 (0.00%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| carotid artery stenosis | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 1 / 1067 (0.09%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| cerebellar haemorrhage | | | |
| alternative dictionary used: MedDRA 19.0 | | | |

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|---|------------------|------------------|-----------------|
| subjects affected / exposed | 1 / 1054 (0.09%) | 0 / 1067 (0.00%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| cerebellar infarction | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 1 / 1067 (0.09%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| cerebral haemorrhage | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 1 / 1067 (0.09%) | 1 / 879 (0.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| cerebral infarction | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 1054 (0.09%) | 1 / 1067 (0.09%) | 3 / 879 (0.34%) |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 1 | 0 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| cerebrovascular accident | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 5 / 1067 (0.47%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 7 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| cognitive disorder | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 1054 (0.09%) | 0 / 1067 (0.00%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| coma | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 0 / 1067 (0.00%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

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| dementia | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 0 / 1067 (0.00%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| dementia alzheimer's type | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 1054 (0.09%) | 2 / 1067 (0.19%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| dementia of the alzheimer's type, with delirium | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 1054 (0.09%) | 0 / 1067 (0.00%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| dizziness | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 1054 (0.09%) | 1 / 1067 (0.09%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| embolic stroke | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 1054 (0.09%) | 0 / 1067 (0.00%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| encephalopathy | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 1054 (0.09%) | 2 / 1067 (0.19%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| epilepsy | | | |
| alternative dictionary used: MedDRA 19.0 | | | |

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|---|------------------|------------------|-----------------|
| subjects affected / exposed | 0 / 1054 (0.00%) | 1 / 1067 (0.09%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| generalised tonic-clonic seizure alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 0 / 1067 (0.00%) | 1 / 879 (0.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| haemorrhage intracranial alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 1054 (0.09%) | 0 / 1067 (0.00%) | 1 / 879 (0.11%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| haemorrhagic stroke alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 1054 (0.09%) | 0 / 1067 (0.00%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| headache alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 1054 (0.09%) | 3 / 1067 (0.28%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 3 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| hypertensive encephalopathy alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 1054 (0.09%) | 0 / 1067 (0.00%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| hypoesthesia alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 1 / 1067 (0.09%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

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| ischaemic stroke | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 1054 (0.09%) | 1 / 1067 (0.09%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| lacunar infarction | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 0 / 1067 (0.00%) | 1 / 879 (0.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| loss of consciousness | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 2 / 1054 (0.19%) | 1 / 1067 (0.09%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| metabolic encephalopathy | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 1054 (0.09%) | 1 / 1067 (0.09%) | 1 / 879 (0.11%) |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| presyncope | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 3 / 1054 (0.28%) | 1 / 1067 (0.09%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| seizure | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 4 / 1067 (0.37%) | 1 / 879 (0.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 4 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| somnolence | | | |
| alternative dictionary used: MedDRA 19.0 | | | |

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|---|------------------|-------------------|-----------------|
| subjects affected / exposed | 1 / 1054 (0.09%) | 0 / 1067 (0.00%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| spinal cord compression | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 0 / 1067 (0.00%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| spinal epidural haematoma | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 1054 (0.09%) | 0 / 1067 (0.00%) | 1 / 879 (0.11%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| subarachnoid haemorrhage | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 1054 (0.09%) | 1 / 1067 (0.09%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| syncope | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 8 / 1054 (0.76%) | 14 / 1067 (1.31%) | 5 / 879 (0.57%) |
| occurrences causally related to treatment / all | 3 / 11 | 4 / 14 | 1 / 5 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| thalamic infarction | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 1 / 1067 (0.09%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| thalamus haemorrhage | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 1 / 1067 (0.09%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

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| thrombotic cerebral infarction alternative dictionary used: MedDRA 19.0 subjects affected / exposed | 0 / 1054 (0.00%) | 0 / 1067 (0.00%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| tonic convulsion alternative dictionary used: MedDRA 19.0 subjects affected / exposed | 0 / 1054 (0.00%) | 0 / 1067 (0.00%) | 1 / 879 (0.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| transient ischaemic attack alternative dictionary used: MedDRA 19.0 subjects affected / exposed | 2 / 1054 (0.19%) | 0 / 1067 (0.00%) | 1 / 879 (0.11%) |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood and lymphatic system disorders anaemia alternative dictionary used: MedDRA 19.0 subjects affected / exposed | 1 / 1054 (0.09%) | 0 / 1067 (0.00%) | 1 / 879 (0.11%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| lymphadenitis alternative dictionary used: MedDRA 19.0 subjects affected / exposed | 0 / 1054 (0.00%) | 1 / 1067 (0.09%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ear and labyrinth disorders vertigo alternative dictionary used: MedDRA 19.0 subjects affected / exposed | 0 / 1054 (0.00%) | 1 / 1067 (0.09%) | 2 / 879 (0.23%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| vertigo positional alternative dictionary used: MedDRA 19.0 | | | |

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|---|------------------|------------------|-----------------|
| subjects affected / exposed | 0 / 1054 (0.00%) | 0 / 1067 (0.00%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Eye disorders | | | |
| cataract | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 1054 (0.09%) | 1 / 1067 (0.09%) | 1 / 879 (0.11%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| glaucoma | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 1 / 1067 (0.09%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| open angle glaucoma | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 0 / 1067 (0.00%) | 1 / 879 (0.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| retinal detachment | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 0 / 1067 (0.00%) | 1 / 879 (0.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| abdominal pain | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 3 / 1054 (0.28%) | 3 / 1067 (0.28%) | 1 / 879 (0.11%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 3 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| abdominal pain upper | | | |
| alternative dictionary used: MedDRA 19.0 | | | |

| | | | |
|---|------------------|------------------|-----------------|
| subjects affected / exposed | 0 / 1054 (0.00%) | 1 / 1067 (0.09%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| colitis ulcerative | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 1 / 1067 (0.09%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| diarrhoea | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 1054 (0.09%) | 1 / 1067 (0.09%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| duodenal perforation | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 0 / 1067 (0.00%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| gastric ulcer | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 1054 (0.09%) | 0 / 1067 (0.00%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| gastrointestinal disorder | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 1 / 1067 (0.09%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| gastrointestinal haemorrhage | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 2 / 1054 (0.19%) | 2 / 1067 (0.19%) | 1 / 879 (0.11%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

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| gastroesophageal reflux disease alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 1 / 1067 (0.09%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| haemorrhoidal haemorrhage alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 0 / 1067 (0.00%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| haemorrhoids alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 0 / 1067 (0.00%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| hernial eventration alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 0 / 1067 (0.00%) | 1 / 879 (0.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| hiatus hernia alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 1 / 1067 (0.09%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| inguinal hernia alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 1 / 1067 (0.09%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| intestinal obstruction alternative dictionary used: MedDRA 19.0 | | | |

| | | | |
|---|------------------|------------------|-----------------|
| subjects affected / exposed | 2 / 1054 (0.19%) | 0 / 1067 (0.00%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| intestinal perforation alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 1054 (0.09%) | 0 / 1067 (0.00%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| intestinal polyp alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 1 / 1067 (0.09%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| large intestine polyp alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 1 / 1067 (0.09%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| lower gastrointestinal haemorrhage alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 1054 (0.09%) | 1 / 1067 (0.09%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| mallory-weiss syndrome alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 1 / 1067 (0.09%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| nausea alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 2 / 1054 (0.19%) | 0 / 1067 (0.00%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

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| oesophageal rupture | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 1 / 1067 (0.09%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| pancreatitis acute | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 2 / 1054 (0.19%) | 0 / 1067 (0.00%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| peptic ulcer haemorrhage | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 1 / 1067 (0.09%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| rectal prolapse | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 1 / 1067 (0.09%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| retroperitoneal haematoma | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 0 / 1067 (0.00%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| small intestinal obstruction | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 1054 (0.09%) | 3 / 1067 (0.28%) | 1 / 879 (0.11%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 3 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| upper gastrointestinal haemorrhage | | | |
| alternative dictionary used: MedDRA 19.0 | | | |

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|---|------------------|------------------|-----------------|
| subjects affected / exposed | 0 / 1054 (0.00%) | 3 / 1067 (0.28%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| vomiting | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 2 / 1067 (0.19%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 3 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatobiliary disorders | | | |
| bile duct stone | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 2 / 1054 (0.19%) | 0 / 1067 (0.00%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| cholangitis | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 1 / 1067 (0.09%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| cholecystitis | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 1 / 1067 (0.09%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| cholecystitis acute | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 2 / 1054 (0.19%) | 2 / 1067 (0.19%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| cholelithiasis | | | |
| alternative dictionary used: MedDRA 19.0 | | | |

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|---|------------------|------------------|-----------------|
| subjects affected / exposed | 2 / 1054 (0.19%) | 0 / 1067 (0.00%) | 2 / 879 (0.23%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| gallbladder perforation | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 1054 (0.09%) | 0 / 1067 (0.00%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| hepatotoxicity | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 1 / 1067 (0.09%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| jaundice cholestatic | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 1054 (0.09%) | 0 / 1067 (0.00%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| portal vein thrombosis | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 1054 (0.09%) | 0 / 1067 (0.00%) | 1 / 879 (0.11%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Skin and subcutaneous tissue disorders | | | |
| angioedema | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 1 / 1067 (0.09%) | 1 / 879 (0.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| Renal and urinary disorders | | | |
| acute kidney injury | | | |
| alternative dictionary used: MedDRA 19.0 | | | |

| | | | |
|---|------------------|------------------|-----------------|
| subjects affected / exposed | 2 / 1054 (0.19%) | 3 / 1067 (0.28%) | 2 / 879 (0.23%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 3 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| nephrolithiasis | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 1 / 1067 (0.09%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| renal colic | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 0 / 1067 (0.00%) | 2 / 879 (0.23%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| renal failure | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 2 / 1067 (0.19%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| urinary bladder polyp | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 1054 (0.09%) | 0 / 1067 (0.00%) | 1 / 879 (0.11%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| urinary incontinence | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 1 / 1067 (0.09%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| urinary retention | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 1054 (0.09%) | 0 / 1067 (0.00%) | 2 / 879 (0.23%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

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| Endocrine disorders | | | |
| toxic nodular goitre | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 1054 (0.09%) | 0 / 1067 (0.00%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal and connective tissue disorders | | | |
| back pain | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 1 / 1067 (0.09%) | 1 / 879 (0.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| foot deformity | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 1054 (0.09%) | 0 / 1067 (0.00%) | 1 / 879 (0.11%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| lumbar spinal stenosis | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 1054 (0.09%) | 0 / 1067 (0.00%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| musculoskeletal chest pain | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 0 / 1067 (0.00%) | 1 / 879 (0.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| osteoarthritis | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 2 / 1054 (0.19%) | 3 / 1067 (0.28%) | 2 / 879 (0.23%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 3 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| osteonecrosis | | | |

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|--|------------------|------------------|-----------------|
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 3 / 1054 (0.28%) | 0 / 1067 (0.00%) | 1 / 879 (0.11%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| rhabdomyolysis | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 1 / 1067 (0.09%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| spinal osteoarthritis | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 1054 (0.09%) | 0 / 1067 (0.00%) | 1 / 879 (0.11%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| spondylolisthesis | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 1054 (0.09%) | 0 / 1067 (0.00%) | 1 / 879 (0.11%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| tenosynovitis | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 1 / 1067 (0.09%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| abdominal abscess | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 2 / 1054 (0.19%) | 0 / 1067 (0.00%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| appendicitis perforated | | | |
| alternative dictionary used: MedDRA 19.0 | | | |

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|---|------------------|------------------|-----------------|
| subjects affected / exposed | 0 / 1054 (0.00%) | 1 / 1067 (0.09%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| atypical mycobacterial pneumonia alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 1 / 1067 (0.09%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| atypical pneumonia alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 0 / 1067 (0.00%) | 1 / 879 (0.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| bacteraemia alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 1 / 1067 (0.09%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| bacterial infection alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 0 / 1067 (0.00%) | 1 / 879 (0.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| bacterial sepsis alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 1054 (0.09%) | 0 / 1067 (0.00%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| bronchitis alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 1054 (0.09%) | 1 / 1067 (0.09%) | 2 / 879 (0.23%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

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| cellulitis | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 1054 (0.09%) | 2 / 1067 (0.19%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| chronic sinusitis | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 0 / 1067 (0.00%) | 1 / 879 (0.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| clostridium difficile infection | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 2 / 1067 (0.19%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 4 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| escherichia sepsis | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 2 / 1067 (0.19%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| extradural abscess | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 1 / 1067 (0.09%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| furuncle | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 1 / 1067 (0.09%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| gastroenteritis | | | |
| alternative dictionary used: MedDRA 19.0 | | | |

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|---|------------------|------------------|-----------------|
| subjects affected / exposed | 1 / 1054 (0.09%) | 1 / 1067 (0.09%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| gastroenteritis viral | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 0 / 1067 (0.00%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| hepatitis e | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 1054 (0.09%) | 0 / 1067 (0.00%) | 1 / 879 (0.11%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| herpes zoster | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 1 / 1067 (0.09%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| influenza | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 2 / 1054 (0.19%) | 1 / 1067 (0.09%) | 1 / 879 (0.11%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| intervertebral discitis | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 1 / 1067 (0.09%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| localised infection | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 0 / 1067 (0.00%) | 1 / 879 (0.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

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|--|------------------|------------------|-----------------|
| lung abscess | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 1 / 1067 (0.09%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| meningoencephalitis herpetic | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 1 / 1067 (0.09%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| oesophageal candidiasis | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 1 / 1067 (0.09%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| ophthalmic herpes zoster | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 0 / 1067 (0.00%) | 1 / 879 (0.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| orchitis | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed ^[9] | 0 / 455 (0.00%) | 0 / 440 (0.00%) | 0 / 378 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| osteomyelitis bacterial | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 1 / 1067 (0.09%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| paraspinal abscess | | | |
| alternative dictionary used: MedDRA 19.0 | | | |

| | | | |
|---|-------------------|------------------|-----------------|
| subjects affected / exposed | 0 / 1054 (0.00%) | 1 / 1067 (0.09%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| pelvic abscess | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 1054 (0.09%) | 1 / 1067 (0.09%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| peritonitis | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 1054 (0.09%) | 1 / 1067 (0.09%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| pneumonia | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 11 / 1054 (1.04%) | 8 / 1067 (0.75%) | 3 / 879 (0.34%) |
| occurrences causally related to treatment / all | 0 / 11 | 0 / 8 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| pneumonia influenzal | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 0 / 1067 (0.00%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| pyelonephritis | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 1054 (0.09%) | 3 / 1067 (0.28%) | 1 / 879 (0.11%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 3 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| sepsis | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 2 / 1067 (0.19%) | 1 / 879 (0.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 1 / 1 |

| | | | |
|--|------------------|------------------|-----------------|
| septic shock | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 2 / 1054 (0.19%) | 0 / 1067 (0.00%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| tooth infection | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 0 / 1067 (0.00%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| upper respiratory tract infection | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 1 / 1067 (0.09%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| urinary tract infection | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 2 / 1054 (0.19%) | 8 / 1067 (0.75%) | 2 / 879 (0.23%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 9 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| urosepsis | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 1054 (0.09%) | 1 / 1067 (0.09%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| viral infection | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 0 / 1067 (0.00%) | 3 / 879 (0.34%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| wound infection | | | |
| alternative dictionary used: MedDRA 19.0 | | | |

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|---|------------------|------------------|-----------------|
| subjects affected / exposed | 0 / 1054 (0.00%) | 0 / 1067 (0.00%) | 1 / 879 (0.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolism and nutrition disorders | | | |
| cachexia | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 0 / 1067 (0.00%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| decreased appetite | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 2 / 1067 (0.19%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| dehydration | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 3 / 1054 (0.28%) | 4 / 1067 (0.37%) | 3 / 879 (0.34%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 4 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| diabetic ketoacidosis | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 1 / 1067 (0.09%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| hyponatraemia | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 1 / 1067 (0.09%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| hypovolaemia | | | |
| alternative dictionary used: MedDRA 19.0 | | | |

| | | | |
|---|------------------|------------------|-----------------|
| subjects affected / exposed | 1 / 1054 (0.09%) | 0 / 1067 (0.00%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| metabolic acidosis alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 1054 (0.00%) | 0 / 1067 (0.00%) | 0 / 879 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| Serious adverse events | Placebo: Solanezumab 400mg Open Label | | |
|--|---|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 114 / 856 (13.32%) | | |
| number of deaths (all causes) | 5 | | |
| number of deaths resulting from adverse events | 0 | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) abdominal neoplasm alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| adenocarcinoma of colon alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| b-cell lymphoma alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| basal cell carcinoma alternative dictionary used: MedDRA 19.0 | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| benign small intestinal neoplasm alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| bladder cancer alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| bladder neoplasm alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| breast cancer alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 2 / 856 (0.23%) | | |
| occurrences causally related to treatment / all | 1 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| breast cancer metastatic alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| cardiac myxoma alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

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|---|-----------------|--|--|--|
| clear cell renal cell carcinoma alternative dictionary used: MedDRA 19.0 subjects affected / exposed | 0 / 856 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| colon adenoma alternative dictionary used: MedDRA 19.0 subjects affected / exposed | 0 / 856 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| colon cancer alternative dictionary used: MedDRA 19.0 subjects affected / exposed | 0 / 856 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| endometrial adenocarcinoma alternative dictionary used: MedDRA 19.0 subjects affected / exposed ^[1] | 0 / 508 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| glioblastoma alternative dictionary used: MedDRA 19.0 subjects affected / exposed | 0 / 856 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| glioblastoma multiforme alternative dictionary used: MedDRA 19.0 subjects affected / exposed | 0 / 856 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| hepatic neoplasm alternative dictionary used: MedDRA 19.0 | | | | |

| | | | |
|--|-----------------|--|--|
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| intraductal proliferative breast lesion alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| invasive ductal breast carcinoma alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| lip squamous cell carcinoma alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| lung adenocarcinoma alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 856 (0.12%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| lung cancer metastatic alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| lung neoplasm malignant alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

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|--|-----------------|--|--|--|
| malignant melanoma | | | | |
| alternative dictionary used: MedDRA 19.0 | | | | |
| subjects affected / exposed | 1 / 856 (0.12%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| malignant melanoma in situ | | | | |
| alternative dictionary used: MedDRA 19.0 | | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| metastases to central nervous system | | | | |
| alternative dictionary used: MedDRA 19.0 | | | | |
| subjects affected / exposed | 1 / 856 (0.12%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| metastatic neoplasm | | | | |
| alternative dictionary used: MedDRA 19.0 | | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| oesophageal adenocarcinoma | | | | |
| alternative dictionary used: MedDRA 19.0 | | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| ovarian cancer stage iv | | | | |
| alternative dictionary used: MedDRA 19.0 | | | | |
| subjects affected / exposed ^[2] | 0 / 508 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| pancreatic neoplasm | | | | |
| alternative dictionary used: MedDRA 19.0 | | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 1 / 856 (0.12%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| parathyroid tumour benign alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| plasma cell myeloma alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| prostate cancer alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed ^[3] | 0 / 348 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| prostate cancer metastatic alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed ^[4] | 1 / 348 (0.29%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| rectal adenocarcinoma alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| renal cell carcinoma alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

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|---|-----------------|--|--|
| small cell lung cancer alternative dictionary used: MedDRA 19.0 subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| squamous cell carcinoma of the tongue alternative dictionary used: MedDRA 19.0 subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| transitional cell cancer of renal pelvis and ureter metastatic alternative dictionary used: MedDRA 19.0 subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| transitional cell carcinoma alternative dictionary used: MedDRA 19.0 subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| uterine cancer alternative dictionary used: MedDRA 19.0 subjects affected / exposed ^[5] | 0 / 508 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Vascular disorders aortic aneurysm alternative dictionary used: MedDRA 19.0 subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| aortic stenosis alternative dictionary used: | | | |

| | | | | |
|---|-----------------|--|--|--|
| MedDRA 19.0 | | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| deep vein thrombosis | | | | |
| alternative dictionary used: MedDRA 19.0 | | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| hypertension | | | | |
| alternative dictionary used: MedDRA 19.0 | | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| hypertensive crisis | | | | |
| alternative dictionary used: MedDRA 19.0 | | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| hypotension | | | | |
| alternative dictionary used: MedDRA 19.0 | | | | |
| subjects affected / exposed | 2 / 856 (0.23%) | | | |
| occurrences causally related to treatment / all | 0 / 2 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| lymphoedema | | | | |
| alternative dictionary used: MedDRA 19.0 | | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| orthostatic hypotension | | | | |
| alternative dictionary used: MedDRA 19.0 | | | | |

| | | | |
|--|-----------------|--|--|
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| peripheral arterial occlusive disease alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pregnancy, puerperium and perinatal conditions cephalhaematoma alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| General disorders and administration site conditions asthenia alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| chest discomfort alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| chest pain alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 856 (0.12%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| death alternative dictionary used: MedDRA 19.0 | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| gait disturbance | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| general physical health deterioration | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| generalised oedema | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| multiple organ dysfunction syndrome | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| non-cardiac chest pain | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 856 (0.12%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| pain | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 856 (0.12%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | |
|---|--|--|--|
| <p>pyrexia</p> <p>alternative dictionary used: MedDRA 19.0</p> <p>subjects affected / exposed</p> <p>occurrences causally related to treatment / all</p> <p>deaths causally related to treatment / all</p> | <p>2 / 856 (0.23%)</p> <p>0 / 2</p> <p>0 / 0</p> | | |
| <p>stent-graft endoleak</p> <p>alternative dictionary used: MedDRA 19.0</p> <p>subjects affected / exposed</p> <p>occurrences causally related to treatment / all</p> <p>deaths causally related to treatment / all</p> | <p>0 / 856 (0.00%)</p> <p>0 / 0</p> <p>0 / 0</p> | | |
| <p>sudden death</p> <p>alternative dictionary used: MedDRA 19.0</p> <p>subjects affected / exposed</p> <p>occurrences causally related to treatment / all</p> <p>deaths causally related to treatment / all</p> | <p>0 / 856 (0.00%)</p> <p>0 / 0</p> <p>0 / 0</p> | | |
| <p>systemic inflammatory response syndrome</p> <p>alternative dictionary used: MedDRA 19.0</p> <p>subjects affected / exposed</p> <p>occurrences causally related to treatment / all</p> <p>deaths causally related to treatment / all</p> | <p>0 / 856 (0.00%)</p> <p>0 / 0</p> <p>0 / 0</p> | | |
| <p>Social circumstances</p> <p>immobilisation prolonged</p> <p>alternative dictionary used: MedDRA 19.0</p> <p>subjects affected / exposed</p> <p>occurrences causally related to treatment / all</p> <p>deaths causally related to treatment / all</p> | <p>0 / 856 (0.00%)</p> <p>0 / 0</p> <p>0 / 0</p> | | |
| <p>respite care</p> <p>alternative dictionary used: MedDRA 19.0</p> <p>subjects affected / exposed</p> <p>occurrences causally related to treatment / all</p> <p>deaths causally related to treatment / all</p> | <p>0 / 856 (0.00%)</p> <p>0 / 0</p> <p>0 / 0</p> | | |
| <p>Respiratory, thoracic and mediastinal disorders</p> | | | |

| | | | | |
|--|-----------------|--|--|--|
| acute respiratory failure | | | | |
| alternative dictionary used: MedDRA 19.0 | | | | |
| subjects affected / exposed | 1 / 856 (0.12%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| asthma | | | | |
| alternative dictionary used: MedDRA 19.0 | | | | |
| subjects affected / exposed | 1 / 856 (0.12%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| benign prostatic hyperplasia | | | | |
| alternative dictionary used: MedDRA 19.0 | | | | |
| subjects affected / exposed ^[6] | 0 / 348 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| chronic obstructive pulmonary disease | | | | |
| alternative dictionary used: MedDRA 19.0 | | | | |
| subjects affected / exposed | 1 / 856 (0.12%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| dyspnoea | | | | |
| alternative dictionary used: MedDRA 19.0 | | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| epistaxis | | | | |
| alternative dictionary used: MedDRA 19.0 | | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| organising pneumonia | | | | |
| alternative dictionary used: MedDRA 19.0 | | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| pharyngeal mass | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| pleural effusion | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 856 (0.12%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| pleurisy | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| pneumonia aspiration | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| pneumothorax | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 856 (0.12%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| prostatitis | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed ^[7] | 0 / 348 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | |
|---|-----------------|--|--|
| pulmonary embolism alternative dictionary used: MedDRA 19.0 subjects affected / exposed | 2 / 856 (0.23%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| respiratory arrest alternative dictionary used: MedDRA 19.0 subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| sleep apnoea syndrome alternative dictionary used: MedDRA 19.0 subjects affected / exposed | 1 / 856 (0.12%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| vulvar dysplasia alternative dictionary used: MedDRA 19.0 subjects affected / exposed ^[8] | 0 / 508 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Psychiatric disorders abnormal behaviour alternative dictionary used: MedDRA 19.0 subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| affective disorder alternative dictionary used: MedDRA 19.0 subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| aggression alternative dictionary used: MedDRA 19.0 | | | |

| | | | |
|--|-----------------|--|--|
| subjects affected / exposed | 2 / 856 (0.23%) | | |
| occurrences causally related to treatment / all | 1 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| agitation | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 856 (0.12%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| anxiety | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 856 (0.12%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| behavioural and psychiatric symptoms of dementia | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| confusional state | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 856 (0.12%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| delirium | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 856 (0.12%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| delusion | | | |
| alternative dictionary used: MedDRA 19.0 | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| depression | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| disorientation | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 856 (0.12%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| hallucination | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| mental status changes | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 2 / 856 (0.23%) | | |
| occurrences causally related to treatment / all | 0 / 3 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| phobia | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| psychotic disorder | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | |
|--|--|--|--|
| <p>suicide attempt</p> <p>alternative dictionary used: MedDRA 19.0</p> <p>subjects affected / exposed</p> <p>occurrences causally related to treatment / all</p> <p>deaths causally related to treatment / all</p> | <p>0 / 856 (0.00%)</p> <p>0 / 0</p> <p>0 / 0</p> | | |
| <p>Investigations</p> <p>heart rate irregular</p> <p>alternative dictionary used: MedDRA 19.0</p> <p>subjects affected / exposed</p> <p>occurrences causally related to treatment / all</p> <p>deaths causally related to treatment / all</p> | <p>0 / 856 (0.00%)</p> <p>0 / 0</p> <p>0 / 0</p> | | |
| <p>troponin t increased</p> <p>alternative dictionary used: MedDRA 19.0</p> <p>subjects affected / exposed</p> <p>occurrences causally related to treatment / all</p> <p>deaths causally related to treatment / all</p> | <p>1 / 856 (0.12%)</p> <p>0 / 1</p> <p>0 / 0</p> | | |
| <p>weight decreased</p> <p>alternative dictionary used: MedDRA 19.0</p> <p>subjects affected / exposed</p> <p>occurrences causally related to treatment / all</p> <p>deaths causally related to treatment / all</p> | <p>1 / 856 (0.12%)</p> <p>0 / 1</p> <p>0 / 0</p> | | |
| <p>Injury, poisoning and procedural complications</p> <p>alcohol poisoning</p> <p>alternative dictionary used: MedDRA 19.0</p> <p>subjects affected / exposed</p> <p>occurrences causally related to treatment / all</p> <p>deaths causally related to treatment / all</p> | <p>0 / 856 (0.00%)</p> <p>0 / 0</p> <p>0 / 0</p> | | |
| <p>animal bite</p> <p>alternative dictionary used: MedDRA 19.0</p> <p>subjects affected / exposed</p> <p>occurrences causally related to treatment / all</p> <p>deaths causally related to treatment / all</p> | <p>0 / 856 (0.00%)</p> <p>0 / 0</p> <p>0 / 0</p> | | |
| <p>ankle fracture</p> | | | |

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|--|-----------------|--|--|--|
| alternative dictionary used: MedDRA 19.0 | | | | |
| subjects affected / exposed | 1 / 856 (0.12%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| arthropod sting | | | | |
| alternative dictionary used: MedDRA 19.0 | | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| cervical vertebral fracture | | | | |
| alternative dictionary used: MedDRA 19.0 | | | | |
| subjects affected / exposed | 1 / 856 (0.12%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| chest injury | | | | |
| alternative dictionary used: MedDRA 19.0 | | | | |
| subjects affected / exposed | 1 / 856 (0.12%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| clavicle fracture | | | | |
| alternative dictionary used: MedDRA 19.0 | | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| concussion | | | | |
| alternative dictionary used: MedDRA 19.0 | | | | |
| subjects affected / exposed | 1 / 856 (0.12%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| contusion | | | | |
| alternative dictionary used: MedDRA 19.0 | | | | |

| | | | |
|--|------------------|--|--|
| subjects affected / exposed | 2 / 856 (0.23%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| coronary vascular graft occlusion alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| craniocerebral injury alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| fall alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 12 / 856 (1.40%) | | |
| occurrences causally related to treatment / all | 0 / 12 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| femoral neck fracture alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 2 / 856 (0.23%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| femur fracture alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 856 (0.12%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| fibula fracture alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | | |
|--|-----------------|--|--|--|
| fracture displacement | | | | |
| alternative dictionary used: MedDRA 19.0 | | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| fractured coccyx | | | | |
| alternative dictionary used: MedDRA 19.0 | | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| gastrointestinal stoma complication | | | | |
| alternative dictionary used: MedDRA 19.0 | | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| gun shot wound | | | | |
| alternative dictionary used: MedDRA 19.0 | | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| head injury | | | | |
| alternative dictionary used: MedDRA 19.0 | | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| hip fracture | | | | |
| alternative dictionary used: MedDRA 19.0 | | | | |
| subjects affected / exposed | 3 / 856 (0.35%) | | | |
| occurrences causally related to treatment / all | 0 / 3 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| humerus fracture | | | | |
| alternative dictionary used: MedDRA 19.0 | | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| joint dislocation | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| laceration | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| ligament sprain | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| lumbar vertebral fracture | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| pelvic fracture | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 2 / 856 (0.23%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| periprosthetic fracture | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | | |
|--|-----------------|--|--|--|
| postoperative ileus | | | | |
| alternative dictionary used: MedDRA 19.0 | | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| pubis fracture | | | | |
| alternative dictionary used: MedDRA 19.0 | | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| radius fracture | | | | |
| alternative dictionary used: MedDRA 19.0 | | | | |
| subjects affected / exposed | 1 / 856 (0.12%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| rib fracture | | | | |
| alternative dictionary used: MedDRA 19.0 | | | | |
| subjects affected / exposed | 1 / 856 (0.12%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| road traffic accident | | | | |
| alternative dictionary used: MedDRA 19.0 | | | | |
| subjects affected / exposed | 1 / 856 (0.12%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| skull fracture | | | | |
| alternative dictionary used: MedDRA 19.0 | | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| spinal compression fracture | | | | |
| alternative dictionary used: MedDRA 19.0 | | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 3 / 856 (0.35%) | | |
| occurrences causally related to treatment / all | 0 / 3 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| spinal fracture | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 856 (0.12%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| sternal fracture | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 856 (0.12%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| subdural haematoma | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 856 (0.12%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| upper limb fracture | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 856 (0.12%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| wound | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| wrist fracture | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | |
|--|-----------------|--|--|
| Cardiac disorders | | | |
| acute myocardial infarction | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| adams-stokes syndrome | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| angina pectoris | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 856 (0.12%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| aortic valve stenosis | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| arrhythmia supraventricular | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| atrial fibrillation | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 5 / 856 (0.58%) | | |
| occurrences causally related to treatment / all | 0 / 5 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| atrioventricular block | | | |
| alternative dictionary used: MedDRA 19.0 | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| atrioventricular block complete alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| atrioventricular block second degree alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| bradycardia alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 3 / 856 (0.35%) | | |
| occurrences causally related to treatment / all | 0 / 3 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| cardiac arrest alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 856 (0.12%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| cardiac failure alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 856 (0.12%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| cardiac failure congestive alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 2 / 856 (0.23%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 1 | | |

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|---|-----------------|--|--|
| cardio-respiratory arrest alternative dictionary used: MedDRA 19.0 subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| coronary artery disease alternative dictionary used: MedDRA 19.0 subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| myocardial infarction alternative dictionary used: MedDRA 19.0 subjects affected / exposed | 1 / 856 (0.12%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| myocardial ischaemia alternative dictionary used: MedDRA 19.0 subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| sinus bradycardia alternative dictionary used: MedDRA 19.0 subjects affected / exposed | 3 / 856 (0.35%) | | |
| occurrences causally related to treatment / all | 1 / 3 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| sinus node dysfunction alternative dictionary used: MedDRA 19.0 subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Nervous system disorders altered state of consciousness alternative dictionary used: MedDRA 19.0 | | | |

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|---|-----------------|--|--|
| subjects affected / exposed | 1 / 856 (0.12%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| basal ganglia infarction | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 856 (0.12%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| carotid artery stenosis | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| cerebellar haemorrhage | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| cerebellar infarction | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| cerebral haemorrhage | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| cerebral infarction | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

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|--|-----------------|--|--|--|
| cerebrovascular accident | | | | |
| alternative dictionary used: MedDRA 19.0 | | | | |
| subjects affected / exposed | 3 / 856 (0.35%) | | | |
| occurrences causally related to treatment / all | 2 / 3 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| cognitive disorder | | | | |
| alternative dictionary used: MedDRA 19.0 | | | | |
| subjects affected / exposed | 1 / 856 (0.12%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| coma | | | | |
| alternative dictionary used: MedDRA 19.0 | | | | |
| subjects affected / exposed | 1 / 856 (0.12%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| dementia | | | | |
| alternative dictionary used: MedDRA 19.0 | | | | |
| subjects affected / exposed | 2 / 856 (0.23%) | | | |
| occurrences causally related to treatment / all | 0 / 2 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| dementia alzheimer's type | | | | |
| alternative dictionary used: MedDRA 19.0 | | | | |
| subjects affected / exposed | 4 / 856 (0.47%) | | | |
| occurrences causally related to treatment / all | 2 / 5 | | | |
| deaths causally related to treatment / all | 0 / 1 | | | |
| dementia of the alzheimer's type, with delirium | | | | |
| alternative dictionary used: MedDRA 19.0 | | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| dizziness | | | | |
| alternative dictionary used: MedDRA 19.0 | | | | |

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|---|-----------------|--|--|
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| embolic stroke | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| encephalopathy | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 856 (0.12%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| epilepsy | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 2 / 856 (0.23%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| generalised tonic-clonic seizure | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| haemorrhage intracranial | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| haemorrhagic stroke | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

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|--|-----------------|--|--|--|
| headache | | | | |
| alternative dictionary used: MedDRA 19.0 | | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| hypertensive encephalopathy | | | | |
| alternative dictionary used: MedDRA 19.0 | | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| hypoesthesia | | | | |
| alternative dictionary used: MedDRA 19.0 | | | | |
| subjects affected / exposed | 1 / 856 (0.12%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| ischaemic stroke | | | | |
| alternative dictionary used: MedDRA 19.0 | | | | |
| subjects affected / exposed | 1 / 856 (0.12%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| lacunar infarction | | | | |
| alternative dictionary used: MedDRA 19.0 | | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| loss of consciousness | | | | |
| alternative dictionary used: MedDRA 19.0 | | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| metabolic encephalopathy | | | | |
| alternative dictionary used: MedDRA 19.0 | | | | |

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|---|-----------------|--|--|
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| presyncope | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 2 / 856 (0.23%) | | |
| occurrences causally related to treatment / all | 1 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| seizure | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 856 (0.12%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| somnolence | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| spinal cord compression | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 856 (0.12%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| spinal epidural haematoma | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| subarachnoid haemorrhage | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 856 (0.12%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

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|--|-----------------|--|--|
| syncope alternative dictionary used: MedDRA 19.0 subjects affected / exposed | 7 / 856 (0.82%) | | |
| occurrences causally related to treatment / all | 0 / 7 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| thalamic infarction alternative dictionary used: MedDRA 19.0 subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| thalamus haemorrhage alternative dictionary used: MedDRA 19.0 subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| thrombotic cerebral infarction alternative dictionary used: MedDRA 19.0 subjects affected / exposed | 1 / 856 (0.12%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| tonic convulsion alternative dictionary used: MedDRA 19.0 subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| transient ischaemic attack alternative dictionary used: MedDRA 19.0 subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Blood and lymphatic system disorders anaemia alternative dictionary used: MedDRA 19.0 | | | |

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|---|-----------------|--|--|
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| lymphadenitis | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Ear and labyrinth disorders | | | |
| vertigo | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 856 (0.12%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| vertigo positional | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 856 (0.12%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Eye disorders | | | |
| cataract | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 856 (0.12%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| glaucoma | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 856 (0.12%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| open angle glaucoma | | | |
| alternative dictionary used: MedDRA 19.0 | | | |

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|---|-----------------|--|--|
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| retinal detachment | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrointestinal disorders | | | |
| abdominal pain | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| abdominal pain upper | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| colitis ulcerative | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| diarrhoea | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| duodenal perforation | | | |
| alternative dictionary used: MedDRA 19.0 | | | |

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|---|-----------------|--|--|
| subjects affected / exposed | 1 / 856 (0.12%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| gastric ulcer | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 856 (0.12%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| gastrointestinal disorder | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| gastrointestinal haemorrhage | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| gastroesophageal reflux disease | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| haemorrhoidal haemorrhage | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 856 (0.12%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| haemorrhoids | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 856 (0.12%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

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|--|-----------------|--|--|--|
| hernial eventration | | | | |
| alternative dictionary used: MedDRA 19.0 | | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| hiatus hernia | | | | |
| alternative dictionary used: MedDRA 19.0 | | | | |
| subjects affected / exposed | 1 / 856 (0.12%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| inguinal hernia | | | | |
| alternative dictionary used: MedDRA 19.0 | | | | |
| subjects affected / exposed | 1 / 856 (0.12%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| intestinal obstruction | | | | |
| alternative dictionary used: MedDRA 19.0 | | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| intestinal perforation | | | | |
| alternative dictionary used: MedDRA 19.0 | | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| intestinal polyp | | | | |
| alternative dictionary used: MedDRA 19.0 | | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| large intestine polyp | | | | |
| alternative dictionary used: MedDRA 19.0 | | | | |

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|---|-----------------|--|--|
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| lower gastrointestinal haemorrhage alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| mallory-weiss syndrome alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| nausea alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| oesophageal rupture alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| pancreatitis acute alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| peptic ulcer haemorrhage alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

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|--|-----------------|--|--|--|
| rectal prolapse | | | | |
| alternative dictionary used: MedDRA 19.0 | | | | |
| subjects affected / exposed | 1 / 856 (0.12%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| retroperitoneal haematoma | | | | |
| alternative dictionary used: MedDRA 19.0 | | | | |
| subjects affected / exposed | 1 / 856 (0.12%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| small intestinal obstruction | | | | |
| alternative dictionary used: MedDRA 19.0 | | | | |
| subjects affected / exposed | 1 / 856 (0.12%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| upper gastrointestinal haemorrhage | | | | |
| alternative dictionary used: MedDRA 19.0 | | | | |
| subjects affected / exposed | 1 / 856 (0.12%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| vomiting | | | | |
| alternative dictionary used: MedDRA 19.0 | | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Hepatobiliary disorders | | | | |
| bile duct stone | | | | |
| alternative dictionary used: MedDRA 19.0 | | | | |
| subjects affected / exposed | 1 / 856 (0.12%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| cholangitis | | | | |
| alternative dictionary used: MedDRA 19.0 | | | | |

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|---|-----------------|--|--|
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| cholecystitis | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 856 (0.12%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| cholecystitis acute | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 856 (0.12%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| cholelithiasis | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| gallbladder perforation | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| hepatotoxicity | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| jaundice cholestatic | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | |
|---|-----------------------------------|--|--|
| portal vein thrombosis alternative dictionary used: MedDRA 19.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 856 (0.00%) 0 / 0 0 / 0 | | |
| Skin and subcutaneous tissue disorders angioedema alternative dictionary used: MedDRA 19.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 856 (0.00%) 0 / 0 0 / 0 | | |
| Renal and urinary disorders acute kidney injury alternative dictionary used: MedDRA 19.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 3 / 856 (0.35%) 0 / 3 0 / 0 | | |
| nephrolithiasis alternative dictionary used: MedDRA 19.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 856 (0.12%) 0 / 1 0 / 0 | | |
| renal colic alternative dictionary used: MedDRA 19.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 856 (0.12%) 0 / 1 0 / 0 | | |
| renal failure alternative dictionary used: MedDRA 19.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 856 (0.00%) 0 / 0 0 / 0 | | |
| urinary bladder polyp alternative dictionary used: MedDRA 19.0 | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| urinary incontinence | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| urinary retention | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Endocrine disorders | | | |
| toxic nodular goitre | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Musculoskeletal and connective tissue disorders | | | |
| back pain | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| foot deformity | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| lumbar spinal stenosis | | | |
| alternative dictionary used: MedDRA 19.0 | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| musculoskeletal chest pain | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| osteoarthritis | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 856 (0.12%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| osteonecrosis | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| rhabdomyolysis | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 856 (0.12%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| spinal osteoarthritis | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| spondylolisthesis | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | |
|---|-----------------------------------|--|--|
| tenosynovitis alternative dictionary used: MedDRA 19.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 856 (0.12%) 0 / 1 0 / 0 | | |
| Infections and infestations | | | |
| abdominal abscess alternative dictionary used: MedDRA 19.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 856 (0.00%) 0 / 0 0 / 0 | | |
| appendicitis perforated alternative dictionary used: MedDRA 19.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 856 (0.00%) 0 / 0 0 / 0 | | |
| atypical mycobacterial pneumonia alternative dictionary used: MedDRA 19.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 856 (0.00%) 0 / 0 0 / 0 | | |
| atypical pneumonia alternative dictionary used: MedDRA 19.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 856 (0.00%) 0 / 0 0 / 0 | | |
| bacteraemia alternative dictionary used: MedDRA 19.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 856 (0.00%) 0 / 0 0 / 0 | | |
| bacterial infection alternative dictionary used: MedDRA 19.0 | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| bacterial sepsis | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| bronchitis | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| cellulitis | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 856 (0.12%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| chronic sinusitis | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| clostridium difficile infection | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| escherichia sepsis | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | | |
|--|-----------------|--|--|--|
| extradural abscess | | | | |
| alternative dictionary used: MedDRA 19.0 | | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| furuncle | | | | |
| alternative dictionary used: MedDRA 19.0 | | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| gastroenteritis | | | | |
| alternative dictionary used: MedDRA 19.0 | | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| gastroenteritis viral | | | | |
| alternative dictionary used: MedDRA 19.0 | | | | |
| subjects affected / exposed | 1 / 856 (0.12%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| hepatitis e | | | | |
| alternative dictionary used: MedDRA 19.0 | | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| herpes zoster | | | | |
| alternative dictionary used: MedDRA 19.0 | | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| influenza | | | | |
| alternative dictionary used: MedDRA 19.0 | | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| intervertebral discitis | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| localised infection | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| lung abscess | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 856 (0.12%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| meningoencephalitis herpetic | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| oesophageal candidiasis | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| ophthalmic herpes zoster | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | | |
|--|-----------------|--|--|--|
| orchitis | | | | |
| alternative dictionary used: MedDRA 19.0 | | | | |
| subjects affected / exposed ^[9] | 1 / 348 (0.29%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| osteomyelitis bacterial | | | | |
| alternative dictionary used: MedDRA 19.0 | | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| paraspinal abscess | | | | |
| alternative dictionary used: MedDRA 19.0 | | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| pelvic abscess | | | | |
| alternative dictionary used: MedDRA 19.0 | | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| peritonitis | | | | |
| alternative dictionary used: MedDRA 19.0 | | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| pneumonia | | | | |
| alternative dictionary used: MedDRA 19.0 | | | | |
| subjects affected / exposed | 5 / 856 (0.58%) | | | |
| occurrences causally related to treatment / all | 0 / 5 | | | |
| deaths causally related to treatment / all | 0 / 1 | | | |
| pneumonia influenzal | | | | |
| alternative dictionary used: MedDRA 19.0 | | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 1 / 856 (0.12%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| pyelonephritis | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 856 (0.12%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| sepsis | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| septic shock | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| tooth infection | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 856 (0.12%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| upper respiratory tract infection | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| urinary tract infection | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 3 / 856 (0.35%) | | |
| occurrences causally related to treatment / all | 0 / 3 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | |
|--|-----------------|--|--|
| urosepsis | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| viral infection | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| wound infection | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Metabolism and nutrition disorders | | | |
| cachexia | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 856 (0.12%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| decreased appetite | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| dehydration | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 2 / 856 (0.23%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| diabetic ketoacidosis | | | |
| alternative dictionary used: MedDRA 19.0 | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| hyponatraemia | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| hypovolaemia | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 0 / 856 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| metabolic acidosis | | | |
| alternative dictionary used: MedDRA 19.0 | | | |
| subjects affected / exposed | 1 / 856 (0.12%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.

Justification: This event is gender specific, only occurring in male or female participants. The number of participants exposed has been adjusted accordingly.

[2] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.

Justification: This event is gender specific, only occurring in male or female participants. The number of participants exposed has been adjusted accordingly.

[3] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.

Justification: This event is gender specific, only occurring in male or female participants. The number of participants exposed has been adjusted accordingly.

[4] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.

Justification: This event is gender specific, only occurring in male or female participants. The number of participants exposed has been adjusted accordingly.

[5] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.

Justification: This event is gender specific, only occurring in male or female participants. The number of participants exposed has been adjusted accordingly.

[6] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.

Justification: This event is gender specific, only occurring in male or female participants. The number of participants exposed has been adjusted accordingly.

[7] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.

Justification: This event is gender specific, only occurring in male or female participants. The number of

participants exposed has been adjusted accordingly.

[8] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.

Justification: This event is gender specific, only occurring in male or female participants. The number of participants exposed has been adjusted accordingly.

[9] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.

Justification: This event is gender specific, only occurring in male or female participants. The number of participants exposed has been adjusted accordingly.

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

| Non-serious adverse events | Solanezumab 400mg - Double- Blind Phase | Placebo - Double- Blind Phase | Solanezumab 400mg: Solanezumab 400mg Open Label |
|---|--|---|--|
| Total subjects affected by non-serious adverse events subjects affected / exposed | 536 / 1054 (50.85%) | 530 / 1067 (49.67%) | 255 / 879 (29.01%) |
| Injury, poisoning and procedural complications fall alternative dictionary used: MedDRA 19.0 subjects affected / exposed occurrences (all) | 146 / 1054 (13.85%) 195 | 144 / 1067 (13.50%) 207 | 67 / 879 (7.62%) 97 |
| Nervous system disorders dizziness alternative dictionary used: MedDRA 19.0 subjects affected / exposed occurrences (all) headache alternative dictionary used: MedDRA 19.0 subjects affected / exposed occurrences (all) | 61 / 1054 (5.79%) 66 86 / 1054 (8.16%) 96 | 57 / 1067 (5.34%) 65 86 / 1067 (8.06%) 151 | 23 / 879 (2.62%) 24 28 / 879 (3.19%) 34 |
| Gastrointestinal disorders diarrhoea alternative dictionary used: MedDRA 19.0 subjects affected / exposed occurrences (all) nausea alternative dictionary used: MedDRA 19.0 subjects affected / exposed occurrences (all) | 76 / 1054 (7.21%) 86 54 / 1054 (5.12%) 69 | 87 / 1067 (8.15%) 109 46 / 1067 (4.31%) 63 | 23 / 879 (2.62%) 24 23 / 879 (2.62%) 32 |
| Respiratory, thoracic and mediastinal disorders | | | |

| | | | |
|---|--|--|--|
| cough alternative dictionary used: MedDRA 19.0 subjects affected / exposed occurrences (all) | 44 / 1054 (4.17%) 53 | 58 / 1067 (5.44%) 69 | 25 / 879 (2.84%) 27 |
| Psychiatric disorders anxiety alternative dictionary used: MedDRA 19.0 subjects affected / exposed occurrences (all) depression alternative dictionary used: MedDRA 19.0 subjects affected / exposed occurrences (all) | 54 / 1054 (5.12%) 57 60 / 1054 (5.69%) 62 | 58 / 1067 (5.44%) 59 57 / 1067 (5.34%) 57 | 15 / 879 (1.71%) 18 18 / 879 (2.05%) 18 |
| Musculoskeletal and connective tissue disorders arthralgia alternative dictionary used: MedDRA 19.0 subjects affected / exposed occurrences (all) back pain alternative dictionary used: MedDRA 19.0 subjects affected / exposed occurrences (all) | 44 / 1054 (4.17%) 51 63 / 1054 (5.98%) 70 | 56 / 1067 (5.25%) 62 60 / 1067 (5.62%) 67 | 21 / 879 (2.39%) 23 26 / 879 (2.96%) 26 |
| Infections and infestations nasopharyngitis alternative dictionary used: MedDRA 19.0 subjects affected / exposed occurrences (all) upper respiratory tract infection alternative dictionary used: MedDRA 19.0 subjects affected / exposed occurrences (all) urinary tract infection alternative dictionary used: MedDRA 19.0 subjects affected / exposed occurrences (all) | 89 / 1054 (8.44%) 114 64 / 1054 (6.07%) 74 58 / 1054 (5.50%) 79 | 80 / 1067 (7.50%) 99 54 / 1067 (5.06%) 61 72 / 1067 (6.75%) 103 | 29 / 879 (3.30%) 31 23 / 879 (2.62%) 25 38 / 879 (4.32%) 47 |

| Non-serious adverse events | Placebo: Solanezumab 400mg Open Label | | |
|---|--|--|--|
| Total subjects affected by non-serious adverse events subjects affected / exposed | 260 / 856 (30.37%) | | |
| Injury, poisoning and procedural complications fall alternative dictionary used: MedDRA 19.0 subjects affected / exposed occurrences (all) | 80 / 856 (9.35%) 109 | | |
| Nervous system disorders dizziness alternative dictionary used: MedDRA 19.0 subjects affected / exposed occurrences (all) headache alternative dictionary used: MedDRA 19.0 subjects affected / exposed occurrences (all) | 29 / 856 (3.39%) 31 29 / 856 (3.39%) 42 | | |
| Gastrointestinal disorders diarrhoea alternative dictionary used: MedDRA 19.0 subjects affected / exposed occurrences (all) nausea alternative dictionary used: MedDRA 19.0 subjects affected / exposed occurrences (all) | 17 / 856 (1.99%) 18 15 / 856 (1.75%) 18 | | |
| Respiratory, thoracic and mediastinal disorders cough alternative dictionary used: MedDRA 19.0 subjects affected / exposed occurrences (all) | 18 / 856 (2.10%) 22 | | |
| Psychiatric disorders anxiety alternative dictionary used: MedDRA 19.0 | | | |

| | | | |
|--|--|--|--|
| <p>subjects affected / exposed occurrences (all)</p> <p>depression alternative dictionary used: MedDRA 19.0 subjects affected / exposed occurrences (all)</p> | <p>17 / 856 (1.99%) 17</p> <p>20 / 856 (2.34%) 20</p> | | |
| <p>Musculoskeletal and connective tissue disorders</p> <p>arthralgia alternative dictionary used: MedDRA 19.0 subjects affected / exposed occurrences (all)</p> <p>back pain alternative dictionary used: MedDRA 19.0 subjects affected / exposed occurrences (all)</p> | <p>22 / 856 (2.57%) 22</p> <p>23 / 856 (2.69%) 23</p> | | |
| <p>Infections and infestations</p> <p>nasopharyngitis alternative dictionary used: MedDRA 19.0 subjects affected / exposed occurrences (all)</p> <p>upper respiratory tract infection alternative dictionary used: MedDRA 19.0 subjects affected / exposed occurrences (all)</p> <p>urinary tract infection alternative dictionary used: MedDRA 19.0 subjects affected / exposed occurrences (all)</p> | <p>32 / 856 (3.74%) 36</p> <p>21 / 856 (2.45%) 23</p> <p>36 / 856 (4.21%) 46</p> | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|-------------------|---|
| 02 September 2014 | The duration of the protocol was extended to include a 24-month open-label period, which followed the initial 18-month treatment period. Added secondary objectives and corresponding statistical analyses for the open-label period including the delayed-start-analyses. |
| 29 January 2016 | Changed from cognitive and functional coprimary endpoints (ADAS-Cog14 and ADCS-iADL) to a single primary cognitive endpoint (ADAS-Cog14) with function (ADCS-iADL) as a key secondary endpoint. Added a secondary objective and corresponding analysis for the iADRS to incorporate an additional measure of both cognition and function. |
| 03 August 2016 | The open-label extension period was extended to include a second 24-month open-label period. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported