



Clinical trial results:

A Clinical Outcomes Study to Compare the Incidence of Major Adverse Cardiovascular Events in Subjects Presenting with Acute Coronary Syndrome Treated with Losmapimod Compared to Placebo (PM1116197) Losmapimod To Inhibit p38 MAP kinase as a Therapeutic target and modify outcomes after an acute coronary syndrome (LATITUDE)-TIMI 60 Summary

| | |
|--------------------------|--|
| EudraCT number | 2013-000657-50 |
| Trial protocol | SE NL IT DE BE SK DK ES NO GB CZ HU EE GR PL BG RO |
| Global end of trial date | 14 December 2015 |

Results information

| | |
|--------------------------------|--------------|
| Result version number | v1 (current) |
| This version publication date | 13 May 2016 |
| First version publication date | 13 May 2016 |

Trial information

Trial identification

| | |
|-----------------------|-----------|
| Sponsor protocol code | PM1116197 |
|-----------------------|-----------|

Additional study identifiers

| | |
|------------------------------------|-----------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02145468 |
| WHO universal trial number (UTN) | U1111-1150-5007 |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | GlaxoSmithKline |
| Sponsor organisation address | 980 Great West Road, Brentford, Middlesex, United Kingdom, |
| Public contact | GSK Response Center, GlaxoSmithKline, 1 866-435-7343, |
| Scientific contact | GSK Response Center, GlaxoSmithKline, 1 866-435-7343, |

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 | 18 February 2016 |
| Is this the analysis of the primary completion data? | No |

| | |
|----------------------------------|------------------|
| Global end of trial reached? | Yes |
| Global end of trial date | 14 December 2015 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The primary objective is to evaluate the efficacy of oral losmapimod 7.5 mg BID compared to placebo when added to standard of care in subjects with acute coronary syndrome (ACS) on the time to first occurrence of adjudicated Major Adverse Cardiovascular Events (MACE; defined as CV death, MI, or severe recurrent ischemia [SRI-UR]) through 12 weeks of therapy.

Protection of trial subjects:

Not applicable

Background therapy:

Investigators managed the subjects according to standard of care, following local prescribing information. Close adherence to professional society guidelines for standard of care therapies in ACS was emphasized during study conduct, including anti-platelet therapy, statin medications, use of appropriate revascularization, ACE inhibitors and beta blockers.

Evidence for comparator: -

| | |
|---|--------------|
| Actual start date of recruitment | 03 June 2014 |
| 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 | Australia: 130 |
| Country: Number of subjects enrolled | Canada: 52 |
| Country: Number of subjects enrolled | Chile: 33 |
| Country: Number of subjects enrolled | Hong Kong: 14 |
| Country: Number of subjects enrolled | Korea, Republic of: 62 |
| Country: Number of subjects enrolled | Mexico: 12 |
| Country: Number of subjects enrolled | New Zealand: 67 |
| Country: Number of subjects enrolled | Philippines: 16 |
| Country: Number of subjects enrolled | Russian Federation: 233 |
| Country: Number of subjects enrolled | South Africa: 25 |
| Country: Number of subjects enrolled | Taiwan: 54 |
| Country: Number of subjects enrolled | Thailand: 30 |
| Country: Number of subjects enrolled | Ukraine: 90 |
| Country: Number of subjects enrolled | United States: 417 |
| Country: Number of subjects enrolled | Israel: 38 |
| Country: Number of subjects enrolled | Argentina: 42 |
| Country: Number of subjects enrolled | Netherlands: 223 |

| | |
|--------------------------------------|---------------------|
| Country: Number of subjects enrolled | Norway: 39 |
| Country: Number of subjects enrolled | Poland: 215 |
| Country: Number of subjects enrolled | Romania: 58 |
| Country: Number of subjects enrolled | Slovakia: 231 |
| Country: Number of subjects enrolled | Spain: 229 |
| Country: Number of subjects enrolled | Sweden: 92 |
| Country: Number of subjects enrolled | United Kingdom: 62 |
| Country: Number of subjects enrolled | Belgium: 72 |
| Country: Number of subjects enrolled | Bulgaria: 73 |
| Country: Number of subjects enrolled | Czech Republic: 228 |
| Country: Number of subjects enrolled | Denmark: 51 |
| Country: Number of subjects enrolled | Estonia: 99 |
| Country: Number of subjects enrolled | France: 97 |
| Country: Number of subjects enrolled | Germany: 186 |
| Country: Number of subjects enrolled | Greece: 76 |
| Country: Number of subjects enrolled | Hungary: 87 |
| Country: Number of subjects enrolled | Italy: 56 |
| Worldwide total number of subjects | 3489 |
| EEA total number of subjects | 2174 |

Notes:

Subjects enrolled per age group

| | |
|---|------|
| In utero | 0 |
| Preterm newborn - gestational age < 37 wk | 0 |
| Newborns (0-27 days) | 0 |
| Infants and toddlers (28 days-23 months) | 0 |
| Children (2-11 years) | 0 |
| Adolescents (12-17 years) | 0 |
| Adults (18-64 years) | 1437 |
| From 65 to 84 years | 1942 |
| 85 years and over | 110 |

Subject disposition

Recruitment

Recruitment details:

The study was planned in 2 parts (Part A, N=3500 & Part B, N=22,000). Upon completion of Part A, a decision was made not to progress to Part B because of lack of efficacy. 3503 participants (par.) were randomized to Part A. 14 par. were excluded due to concerns over data integrity. 3489 par. were randomized & included in the ITT Population.

Pre-assignment

Screening details:

Eligible: ≥ 35 yrs & hospitalized with type 1 MI & 1 additional predictor of CV risk. Excluded: unstable, known liver disease, life-threatening or opportunistic infection, severe renal impairment, NYHA III/ IV or Killip III/ IV CHF. All participants were followed through the end of the study unless they withdrew consent to participate.

Period 1

| | |
|------------------------------|-------------------------|
| Period 1 title | Part A (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator |

Arms

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

Arm description:

Participants received matching placebo twice daily (BID) according to the randomization schedule for 12 weeks in addition to standard of care, and were followed for an additional 12 weeks after completing treatment, for a total study duration of 24 weeks.

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

Dosage and administration details:

Oral doses to be taken twice daily with or without food and swallowed whole (not chewed).

| | |
|------------------|-----------------------|
| Arm title | Losmapimod 7.5 mg BID |
|------------------|-----------------------|

Arm description:

Participants received oral losmapimod 7.5 milligrams (mg) BID according to the randomization schedule for 12 weeks in addition to standard of care, and were followed for an additional 12 weeks after completing treatment, for a total study duration of 24 weeks.

| | |
|--|--------------|
| Arm type | Experimental |
| Investigational medicinal product name | Losmapimod |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Oral doses to be taken twice daily with or without food and swallowed whole (not chewed).

| Number of subjects in period 1 | Placebo | Losmapimod 7.5 mg BID |
|---------------------------------------|---------|--------------------------|
| Started | 1758 | 1731 |
| Completed | 1753 | 1722 |
| Not completed | 5 | 9 |
| Consent withdrawn by subject | 5 | 8 |
| Lost to follow-up | - | 1 |

Baseline characteristics

Reporting groups

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

Reporting group description:

Participants received matching placebo twice daily (BID) according to the randomization schedule for 12 weeks in addition to standard of care, and were followed for an additional 12 weeks after completing treatment, for a total study duration of 24 weeks.

| | |
|-----------------------|-----------------------|
| Reporting group title | Losmapimod 7.5 mg BID |
|-----------------------|-----------------------|

Reporting group description:

Participants received oral losmapimod 7.5 milligrams (mg) BID according to the randomization schedule for 12 weeks in addition to standard of care, and were followed for an additional 12 weeks after completing treatment, for a total study duration of 24 weeks.

| Reporting group values | Placebo | Losmapimod 7.5 mg BID | Total |
|------------------------------------|---------|-----------------------|-------|
| Number of subjects | 1758 | 1731 | 3489 |
| Age categorical Units: Subjects | | | |

| | | | |
|---|----------------|--------------|------|
| Age continuous Units: years arithmetic mean standard deviation | 66.5 ± 9.72 | 66.7 ± 10 | - |
| Gender categorical Units: Subjects | | | |
| Female | 532 | 500 | 1032 |
| Male | 1226 | 1231 | 2457 |
| Race, customized Units: Subjects | | | |
| American Indian or Alaskan Native | 8 | 8 | 16 |
| Asian | 99 | 105 | 204 |
| Black | 25 | 20 | 45 |
| White | 1616 | 1585 | 3201 |
| Native Hawaiian or Other Pacific Islander | 5 | 10 | 15 |
| Mixed Race | 2 | 3 | 5 |
| Missing | 3 | 0 | 3 |

End points

End points reporting groups

| | |
|--|-----------------------|
| Reporting group title | Placebo |
| Reporting group description: Participants received matching placebo twice daily (BID) according to the randomization schedule for 12 weeks in addition to standard of care, and were followed for an additional 12 weeks after completing treatment, for a total study duration of 24 weeks. | |
| Reporting group title | Losmapimod 7.5 mg BID |
| Reporting group description: Participants received oral losmapimod 7.5 milligrams (mg) BID according to the randomization schedule for 12 weeks in addition to standard of care, and were followed for an additional 12 weeks after completing treatment, for a total study duration of 24 weeks. | |

Primary: Number of participants with first occurrence of MACE through Week 12

| | |
|---|--|
| End point title | Number of participants with first occurrence of MACE through Week 12 |
| End point description: Number of participants with first occurrence of major adverse cardiovascular events (MACE) through Week 12 including cardiovascular (CV) death, myocardial infarction (MI) or severe recurrent ischemia requiring urgent coronary artery revascularization (SRI-UR) are summarized. Death for which the clinical events committee (CEC) or investigator were unable to establish cause were analyzed as CV deaths. As losmapimod on MACE shown a statistically significant benefit compared to placebo, time to first occurrence analyzed by cox model with log-rank test. Hazard ratio and confidence interval (CI) were estimated using a cox proportional hazard regression model stratified by Baseline ST-segment elevation myocardial infarction (STEMI)/ non-ST-segment elevation myocardial infarction (NSTEMI) status with treatment as the only covariate. A hazard ratio <1 indicates a lower risk with the treatment compared with placebo. | |
| End point type | Primary |
| End point timeframe: Week 12 | |

| End point values | Placebo | Losmapimod 7.5 mg BID | | |
|-----------------------------|---------------------|-----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 1758 ^[1] | 1731 ^[2] | | |
| Units: Participants | | | | |
| First occurrence of MACE | 123 | 139 | | |
| CV Death | 34 | 31 | | |
| MI | 74 | 90 | | |
| SRI-UR | 15 | 18 | | |

Notes:

[1] - All Randomized (ITT) Population: all participants randomized to study treatment.

[2] - All Randomized (ITT) Population: all participants randomized to study treatment.

Statistical analyses

| | |
|----------------------------|---------------------------------|
| Statistical analysis title | Statistical Analysis 1 |
| Comparison groups | Losmapimod 7.5 mg BID v Placebo |

| | |
|---|----------------------------|
| Number of subjects included in analysis | 3489 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[3] |
| P-value | = 0.238 |
| Method | Regression, Cox |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 1.16 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.91 |
| upper limit | 1.47 |

Notes:

[3] - Log rank test

Secondary: Number of participants with first occurrence of MACE through Week 24

| | |
|-----------------|--|
| End point title | Number of participants with first occurrence of MACE through Week 24 |
|-----------------|--|

End point description:

Number of participants with first occurrence of MACE through Week 24 including CV death, MI or SRI-UR are presented. Death for which the CEC or investigator were unable to establish cause were analyzed as CV deaths. Time to first occurrence analyzed by cox model with log-rank test. Hazard ratio and CI were estimated using a cox proportional hazard regression model stratified by Baseline STEMI/NSTEMI status with treatment as the only covariate. A hazard ratio <1 indicates a lower risk with the treatment compared with placebo.

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

End point timeframe:

Week 24

| End point values | Placebo | Losmapimod 7.5 mg BID | | |
|-----------------------------|---------------------|-----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 1758 ^[4] | 1731 ^[5] | | |
| Units: Participants | | | | |
| First occurrence of MACE | 162 | 176 | | |
| CV Death | 45 | 38 | | |
| MI | 98 | 117 | | |
| SRI-UR | 19 | 21 | | |

Notes:

[4] - All Randomized (ITT) Population

[5] - All Randomized (ITT) Population

Statistical analyses

| | |
|----------------------------|---------------------------------|
| Statistical analysis title | Statistical Analysis 1 |
| Comparison groups | Placebo v Losmapimod 7.5 mg BID |

| | |
|---|------------------------|
| Number of subjects included in analysis | 3489 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.329 ^[6] |
| Method | Regression, Cox |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 1.11 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.9 |
| upper limit | 1.38 |

Notes:

[6] - Log rank test

Secondary: Number of participants with first occurrence of the composite of CV death or MI through to Week 12 and Week 24

| | |
|-----------------|--|
| End point title | Number of participants with first occurrence of the composite of CV death or MI through to Week 12 and Week 24 |
|-----------------|--|

End point description:

Week 12 results are considered the principal secondary endpoint. Number of participants with first occurrence of the composite of CV death or MI through to Week 12 and Week 24 are summarized. Time to first occurrence analyzed by cox model with log-rank test. Hazard ratio and CI were estimated using a cox proportional hazard regression model stratified by Baseline STEMI/NSTEMI status with treatment as the only covariate. A hazard ratio <1 indicates a lower risk with the treatment compared with placebo.

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

End point timeframe:

Week 12, Week 24

| End point values | Placebo | Losmapimod 7.5 mg BID | | |
|-----------------------------|---------------------|-----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 1758 ^[7] | 1731 ^[8] | | |
| Units: Participants | | | | |
| Week 12 | 110 | 122 | | |
| Week 24 | 145 | 156 | | |

Notes:

[7] - All Randomized (ITT) Population

[8] - All Randomized (ITT) Population

Statistical analyses

| | |
|-----------------------------------|---------------------------------|
| Statistical analysis title | Statistical Analysis 1 |
| Statistical analysis description: | |
| Week 12 estimates | |
| Comparison groups | Losmapimod 7.5 mg BID v Placebo |

| | |
|---|------------------------|
| Number of subjects included in analysis | 3489 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.338 ^[9] |
| Method | Regression, Cox |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 1.13 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.88 |
| upper limit | 1.47 |

Notes:

[9] - Log rank test

| | |
|---|---------------------------------|
| Statistical analysis title | Statistical Analysis 2 |
| Statistical analysis description: | |
| Week 24 estimates | |
| Comparison groups | Placebo v Losmapimod 7.5 mg BID |
| Number of subjects included in analysis | 3489 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.41 ^[10] |
| Method | Regression, Cox |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 1.1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.88 |
| upper limit | 1.38 |

Notes:

[10] - Log rank test

Secondary: Number of participants with first occurrence of the composite of CV death, MI or hospitalization for heart failure (HF) through to Week 12 and Week 24

| | |
|---|--|
| End point title | Number of participants with first occurrence of the composite of CV death, MI or hospitalization for heart failure (HF) through to Week 12 and Week 24 |
| End point description: | |
| Number of participants with first occurrence of the composite of CV death, MI or hospitalization for HF through to Week 12 and Week 24 are presented. Time to first occurrence at Week 12 analyzed by cox model with log-rank test. Hazard ratio and CI were estimated using a cox proportional hazard regression model stratified by Baseline STEMI/NSTEMI status with treatment as the only covariate. A hazard ratio <1 indicates a lower risk with the treatment compared with placebo. | |
| End point type | Secondary |
| End point timeframe: | |
| Week 12, Week 24 | |

| End point values | Placebo | Losmapimod 7.5 mg BID | | |
|-----------------------------|----------------------|--------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 1758 ^[11] | 1731 ^[12] | | |
| Units: Participants | | | | |
| Week 12 | 131 | 140 | | |
| Week 24 | 169 | 178 | | |

Notes:

[11] - All Randomized (ITT) Population

[12] - All Randomized (ITT) Population

Statistical analyses

| Statistical analysis title | Statistical Analysis 1 |
|---|---------------------------------|
| Statistical analysis description: | |
| Week 12 estimates | |
| Comparison groups | Placebo v Losmapimod 7.5 mg BID |
| Number of subjects included in analysis | 3489 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.472 ^[13] |
| Method | Regression, Cox |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 1.09 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.86 |
| upper limit | 1.38 |

Notes:

[13] - Log rank test

Secondary: Number of participants with first occurrence of the expanded composite of arterial CV events defined as CV death, MI, SRI-UR or stroke through to Week 12 and Week 24

| | |
|---|---|
| End point title | Number of participants with first occurrence of the expanded composite of arterial CV events defined as CV death, MI, SRI-UR or stroke through to Week 12 and Week 24 |
| End point description: | |
| Number of participants with first occurrence of the expanded composite of arterial CV events defined as CV death, MI, SRI-UR or stroke through to Week 12 and Week 24 are presented. Time to first occurrence at Week 12 analyzed by cox model with log-rank test. Hazard ratio and CI were estimated using a cox proportional hazard regression model stratified by Baseline STEMI/ NSTEMI status with treatment as the only covariate. A hazard ratio <1 indicates a lower risk with the treatment compared with placebo. | |
| End point type | Secondary |
| End point timeframe: | |
| Week 12, Week 24 | |

| End point values | Placebo | Losmapimod 7.5 mg BID | | |
|-----------------------------|----------------------|-----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 1758 ^[14] | 1731 ^[15] | | |
| Units: Participants | | | | |
| Week 12 | 135 | 151 | | |
| Week 24 | 174 | 190 | | |

Notes:

[14] - All Randomized (ITT) Population

[15] - All Randomized (ITT) Population

Statistical analyses

| Statistical analysis title | Statistical Analysis 1 |
|---|---------------------------------|
| Statistical analysis description: | |
| Week 12 estimates | |
| Comparison groups | Placebo v Losmapimod 7.5 mg BID |
| Number of subjects included in analysis | 3489 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.255 ^[16] |
| Method | Regression, Cox |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 1.14 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.91 |
| upper limit | 1.44 |

Notes:

[16] - Log rank test

Secondary: Number of participants with first occurrence of the composite of coronary events defined as CHD death, MI, SRI-UR or any unplanned coronary artery revascularization through to Week 12 and Week 24

| | |
|--|---|
| End point title | Number of participants with first occurrence of the composite of coronary events defined as CHD death, MI, SRI-UR or any unplanned coronary artery revascularization through to Week 12 and Week 24 |
| End point description: | |
| Number of participants with first occurrence of the composite of coronary events defined as coronary heart disease (CHD) death, MI, SRI-UR or any unplanned coronary artery revascularization through to Week 12 and Week 24 are presented. Time to first occurrence at Week 12 analyzed by cox model with log-rank test. Hazard ratio and CI were estimated using a cox proportional hazard regression model stratified by Baseline STEMI/ NSTEMI status with treatment as the only covariate. A hazard ratio <1 indicates a lower risk with the treatment compared with placebo. | |
| End point type | Secondary |
| End point timeframe: | |
| Week 12, Week 24 | |

| End point values | Placebo | Losmapimod 7.5 mg BID | | |
|-----------------------------|----------------------|--------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 1758 ^[17] | 1731 ^[18] | | |
| Units: Participants | | | | |
| Week 12 | 144 | 152 | | |
| Week 24 | 186 | 194 | | |

Notes:

[17] - All Randomized (ITT) Population

[18] - All Randomized (ITT) Population

Statistical analyses

| Statistical analysis title | Statistical Analysis 1 |
|---|---------------------------------|
| Statistical analysis description: | |
| Week 12 estimates | |
| Comparison groups | Placebo v Losmapimod 7.5 mg BID |
| Number of subjects included in analysis | 3489 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.505 ^[19] |
| Method | Regression, Cox |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 1.08 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.86 |
| upper limit | 1.36 |

Notes:

[19] - Log rank test

Secondary: Number of participants with first occurrence of the composite of CV death or hospitalization for HF through to Week 12 and Week 24

| | |
|--|--|
| End point title | Number of participants with first occurrence of the composite of CV death or hospitalization for HF through to Week 12 and Week 24 |
| End point description: | |
| Number of participants with first occurrence of the composite of CV death or hospitalization for HF through to Week 12 and Week 24 are presented. Time to first occurrence at Week 12 analyzed by cox model with log-rank test. Hazard ratio and CI were estimated using a cox proportional hazard regression model stratified by Baseline STEMI/ NSTEMI status with treatment as the only covariate. A hazard ratio <1 indicates a lower risk with the treatment compared with placebo. | |
| End point type | Secondary |
| End point timeframe: | |
| Week 12, Week 24 | |

| End point values | Placebo | Losmapimod 7.5 mg BID | | |
|-----------------------------|----------------------|--------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 1758 ^[20] | 1731 ^[21] | | |
| Units: Participants | | | | |
| Week 12 | 72 | 64 | | |
| Week 24 | 94 | 86 | | |

Notes:

[20] - All Randomized (ITT) Population

[21] - All Randomized (ITT) Population

Statistical analyses

| Statistical analysis title | Statistical Analysis 1 |
|---|---------------------------------|
| Statistical analysis description: | |
| Week 12 estimates | |
| Comparison groups | Placebo v Losmapimod 7.5 mg BID |
| Number of subjects included in analysis | 3489 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.536 ^[22] |
| Method | Regression, Cox |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.9 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.64 |
| upper limit | 1.26 |

Notes:

[22] - Log rank test

| Statistical analysis title | Statistical Analysis 2 |
|---|---------------------------------|
| Statistical analysis description: | |
| Week 24 estimates | |
| Comparison groups | Placebo v Losmapimod 7.5 mg BID |
| Number of subjects included in analysis | 3489 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.6 ^[23] |
| Method | Regression, Cox |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.92 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.69 |
| upper limit | 1.24 |

Notes:

[23] - Log rank test

Secondary: Number of participants with first occurrence of the composite of CV death, MI or stroke through to Week 12 and Week 24

| | |
|-----------------|--|
| End point title | Number of participants with first occurrence of the composite of CV death, MI or stroke through to Week 12 and Week 24 |
|-----------------|--|

End point description:

Number of participants with first occurrence of the composite of CV death, MI or stroke through to Week 12 and Week 24 are presented. Time to first occurrence at Week 12 analyzed by cox model with log-rank test. Hazard ratio and CI were estimated using a cox proportional hazard regression model stratified by Baseline STEMI/ NSTEMI status with treatment as the only covariate. A hazard ratio <1 indicates a lower risk with the treatment compared with placebo.

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

End point timeframe:

Week 12, Week 24

| End point values | Placebo | Losmapimod 7.5 mg BID | | |
|-----------------------------|----------------------|-----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 1758 ^[24] | 1731 ^[25] | | |
| Units: Participants | | | | |
| Week 12 | 122 | 134 | | |
| Week 24 | 157 | 170 | | |

Notes:

[24] - All Randomized (ITT) Population

[25] - All Randomized (ITT) Population

Statistical analyses

| | |
|----------------------------|------------------------|
| Statistical analysis title | Statistical Analysis 1 |
|----------------------------|------------------------|

Statistical analysis description:

Week 12 estimates

| | |
|---|---------------------------------|
| Comparison groups | Losmapimod 7.5 mg BID v Placebo |
| Number of subjects included in analysis | 3489 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.356 ^[26] |
| Method | Regression, Cox |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 1.12 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.88 |
| upper limit | 1.43 |

Notes:

[26] - Log rank test

Secondary: Number of participants with first occurrence of the expanded composite of CV death, MI, SRI-UR, stroke or hospitalization for HF through to Week 12 and Week 24

| | |
|-----------------|---|
| End point title | Number of participants with first occurrence of the expanded composite of CV death, MI, SRI-UR, stroke or hospitalization |
|-----------------|---|

End point description:

Number of participants with first occurrence of the expanded composite of CV death, MI, SRI-UR, stroke or hospitalization for HF through to Week 12 and Week 24 are presented. Time to first occurrence at Week 12 analyzed by cox model with log-rank test. Hazard ratio and CI were estimated using a cox proportional hazard regression model stratified by Baseline STEMI/ NSTEMI status with treatment as the only covariate. A hazard ratio <1 indicates a lower risk with the treatment compared with placebo.

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

End point timeframe:

| |
|------------------|
| Week 12, Week 24 |
|------------------|

| End point values | Placebo | Losmapimod 7.5 mg BID | | |
|-----------------------------|----------------------|-----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 1758 ^[27] | 1731 ^[28] | | |
| Units: Participants | | | | |
| Week 12 | 155 | 169 | | |
| Week 24 | 197 | 212 | | |

Notes:

[27] - All Randomized (ITT) Population

[28] - All Randomized (ITT) Population

Statistical analyses

| | |
|----------------------------|------------------------|
| Statistical analysis title | Statistical Analysis 1 |
|----------------------------|------------------------|

Statistical analysis description:

Week 12 estimates

| | |
|---|---------------------------------|
| Comparison groups | Placebo v Losmapimod 7.5 mg BID |
| Number of subjects included in analysis | 3489 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.329 ^[29] |
| Method | Regression, Cox |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 1.11 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.9 |
| upper limit | 1.39 |

Notes:

[29] - Log rank test

Secondary: Number of participants with first occurrence of the composite of CHD death, MI or SRI-UR through to Week 12 and Week 24

| | |
|-----------------|---|
| End point title | Number of participants with first occurrence of the composite of CHD death, MI or SRI-UR through to Week 12 and Week 24 |
|-----------------|---|

End point description:

Number of participants with first occurrence of the composite of CHD death, MI or SRI-UR through to Week 12 and Week 24 are presented. Time to first occurrence at Week 12 analyzed by cox model with log-rank test. Hazard ratio and CI were estimated using a cox proportional hazard regression model

stratified by Baseline STEMI/ NSTEMI status with treatment as the only covariate. A hazard ratio <1 indicates a lower risk with the treatment compared with placebo.

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Week 12, Week 24 | |

| End point values | Placebo | Losmapimod 7.5 mg BID | | |
|-----------------------------|----------------------|--------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 1758 ^[30] | 1731 ^[31] | | |
| Units: Participants | | | | |
| Week 12 | 119 | 133 | | |
| Week 24 | 152 | 167 | | |

Notes:

[30] - All Randomized (ITT) Population

[31] - All Randomized (ITT) Population

Statistical analyses

| | |
|---|---------------------------------|
| Statistical analysis title | Statistical Analysis 1 |
| Statistical analysis description: | |
| Week 12 estimates | |
| Comparison groups | Placebo v Losmapimod 7.5 mg BID |
| Number of subjects included in analysis | 3489 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.285 ^[32] |
| Method | Regression, Cox |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 1.14 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.89 |
| upper limit | 1.47 |

Notes:

[32] - Log rank test

Secondary: Number of participants with first occurrence of the composite of CHD death or MI through to Week 12 and Week 24

| | |
|---|---|
| End point title | Number of participants with first occurrence of the composite of CHD death or MI through to Week 12 and Week 24 |
| End point description: | |
| Number of participants with first occurrence of the composite of CHD death or MI through to Week 12 and Week 24 are presented. Time to first occurrence at Week 12 analyzed by cox model with log-rank test. Hazard ratio and CI were estimated using a cox proportional hazard regression model stratified by Baseline STEMI/ NSTEMI status with treatment as the only covariate. A hazard ratio <1 indicates a lower risk with the treatment compared with placebo. | |
| End point type | Secondary |
| End point timeframe: | |
| Week 12, Week 24 | |

| End point values | Placebo | Losmapimod 7.5 mg BID | | |
|-----------------------------|----------------------|--------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 1758 ^[33] | 1731 ^[34] | | |
| Units: Participants | | | | |
| Week 12 | 106 | 116 | | |
| Week 24 | 135 | 147 | | |

Notes:

[33] - All Randomized (ITT) Population

[34] - All Randomized (ITT) Population

Statistical analyses

| Statistical analysis title | Statistical Analysis 1 |
|---|---------------------------------|
| Statistical analysis description: | |
| Week 12 estimates | |
| Comparison groups | Placebo v Losmapimod 7.5 mg BID |
| Number of subjects included in analysis | 3489 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.401 ^[35] |
| Method | Regression, Cox |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 1.12 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.86 |
| upper limit | 1.46 |

Notes:

[35] - Log rank test

Secondary: Number of participants with first occurrence of the composite of all-cause death, MI or SRI-UR through to Week 12 and Week 24

| | |
|---|---|
| End point title | Number of participants with first occurrence of the composite of all-cause death, MI or SRI-UR through to Week 12 and Week 24 |
| End point description: | |
| Number of participants with first occurrence of the composite of all-cause death, MI or SRI-UR through to Week 12 and Week 24 are presented. Time to first occurrence at Week 12 analyzed by cox model with log-rank test. Hazard ratio and CI were estimated using a cox proportional hazard regression model stratified by Baseline STEMI/ NSTEMI status with treatment as the only covariate. A hazard ratio <1 indicates a lower risk with the treatment compared with placebo. | |
| End point type | Secondary |
| End point timeframe: | |
| Week 12, Week 24 | |

| End point values | Placebo | Losmapimod 7.5 mg BID | | |
|-----------------------------|----------------------|--------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 1758 ^[36] | 1731 ^[37] | | |
| Units: Participants | | | | |
| Week 12 | 128 | 142 | | |
| Week 24 | 169 | 185 | | |

Notes:

[36] - All Randomized (ITT) Population

[37] - All Randomized (ITT) Population

Statistical analyses

| Statistical analysis title | Statistical Analysis 1 |
|---|---------------------------------|
| Statistical analysis description: | |
| Week 12 estimates | |
| Comparison groups | Placebo v Losmapimod 7.5 mg BID |
| Number of subjects included in analysis | 3489 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.295 ^[38] |
| Method | Regression, Cox |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 1.14 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.89 |
| upper limit | 1.44 |

Notes:

[38] - Log rank test

Secondary: Number of participants with first occurrence of the composite of all-cause death or MI through to Week 12 and Week 24

| | |
|---|---|
| End point title | Number of participants with first occurrence of the composite of all-cause death or MI through to Week 12 and Week 24 |
| End point description: | |
| Number of participants with first occurrence of the composite of all-cause death or MI through to Week 12 and Week 24 are presented. Time to first occurrence at Week 12 analyzed by cox model with log-rank test. Hazard ratio and CI were estimated using a cox proportional hazard regression model stratified by Baseline STEMI/ NSTEMI status with treatment as the only covariate. A hazard ratio <1 indicates a lower risk with the treatment compared with placebo. | |
| End point type | Secondary |
| End point timeframe: | |
| Week 12, Week 24 | |

| End point values | Placebo | Losmapimod 7.5 mg BID | | |
|-----------------------------|----------------------|--------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 1758 ^[39] | 1731 ^[40] | | |
| Units: Participants | | | | |
| Week 12 | 115 | 125 | | |
| Week 24 | 152 | 165 | | |

Notes:

[39] - All Randomized (ITT) Population

[40] - All Randomized (ITT) Population

Statistical analyses

| Statistical analysis title | Statistical Analysis 1 |
|---|---------------------------------|
| Statistical analysis description: | |
| Week 12 estimates | |
| Comparison groups | Placebo v Losmapimod 7.5 mg BID |
| Number of subjects included in analysis | 3489 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.412 ^[41] |
| Method | Regression, Cox |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 1.11 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.86 |
| upper limit | 1.43 |

Notes:

[41] - Log rank test

Secondary: Number of participants with first occurrence of the composite of CV death, type I (spontaneous) MI or SRI-UR through to Week 12 and Week 24

| | |
|-----------------|---|
| End point title | Number of participants with first occurrence of the composite of CV death, type I (spontaneous) MI or SRI-UR through to Week 12 and Week 24 |
|-----------------|---|

End point description:

Number of participants with first occurrence of the composite of CV death, type I (spontaneous) MI or SRI-UR through to Week 12 and Week 24 are presented. Time to first occurrence at Week 12 analyzed by cox model with log-rank test. Hazard ratio and CI were estimated using a cox proportional hazard regression model stratified by Baseline STEMI/ NSTEMI status with treatment as the only covariate. A hazard ratio <1 indicates a lower risk with the treatment compared with placebo.

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Week 12, Week 24 | |

| | | | | |
|-----------------------------|----------------------|--------------------------|--|--|
| End point values | Placebo | Losmapimod 7.5 mg BID | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 1758 ^[42] | 1731 ^[43] | | |
| Units: Participants | | | | |
| Week 12 | 86 | 94 | | |
| Week 24 | 122 | 127 | | |

Notes:

[42] - All Randomized (ITT) Population

[43] - All Randomized (ITT) Population

Statistical analyses

| | |
|---|---------------------------------|
| Statistical analysis title | Statistical Analysis 1 |
| Statistical analysis description: | |
| Week 12 estimates | |
| Comparison groups | Placebo v Losmapimod 7.5 mg BID |
| Number of subjects included in analysis | 3489 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.469 ^[44] |
| Method | Regression, Cox |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 1.11 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.83 |
| upper limit | 1.49 |

Notes:

[44] - Log rank test

Secondary: Number of participants with first occurrence of the composite of CV death or type I (spontaneous) MI through to Week 12 and Week 24

| | |
|---|---|
| End point title | Number of participants with first occurrence of the composite of CV death or type I (spontaneous) MI through to Week 12 and Week 24 |
| End point description: | |
| Number of participants with first occurrence of the composite of CV death or type I (spontaneous) MI through to Week 12 and Week 24 are presented. Time to first occurrence at Week 12 analyzed by cox model with log-rank test. Hazard ratio and CI were estimated using a cox proportional hazard regression model stratified by Baseline STEMI/ NSTEMI status with treatment as the only covariate. A hazard ratio <1 indicates a lower risk with the treatment compared with placebo. | |
| End point type | Secondary |
| End point timeframe: | |
| Week 12, Week 24 | |

| End point values | Placebo | Losmapimod 7.5 mg BID | | |
|-----------------------------|----------------------|-----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 1758 ^[45] | 1731 ^[46] | | |
| Units: Participants | | | | |
| Week 12 | 73 | 77 | | |
| Week 24 | 104 | 106 | | |

Notes:

[45] - All Randomized (ITT) Population

[46] - All Randomized (ITT) Population

Statistical analyses

| Statistical analysis title | Statistical Analysis 1 |
|---|---------------------------------|
| Statistical analysis description: | |
| Week 12 estimates | |
| Comparison groups | Placebo v Losmapimod 7.5 mg BID |
| Number of subjects included in analysis | 3489 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.664 ^[47] |
| Method | Regression, Cox |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 1.07 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.78 |
| upper limit | 1.48 |

Notes:

[47] - Log rank test

Secondary: Number of participants with first occurrence of definite or probable stent thrombosis through to Week 12 and Week 24

| | |
|--|--|
| End point title | Number of participants with first occurrence of definite or probable stent thrombosis through to Week 12 and Week 24 |
| End point description: | |
| <p>Number of participants with first occurrence of definite or probable stent thrombosis through to Week 12 and Week 24 are presented. Participants receiving stent prior to randomization or during the study prior to Week 12 were included. Only those participants available at the specified time points were analyzed (represented by n=X, X, in the category titles). Time to first occurrence at Week 12 analyzed by cox model with log-rank test. Hazard ratio and CI were estimated using a cox proportional hazard regression model stratified by Baseline STEMI/ NSTEMI status with treatment as the only covariate. A hazard ratio <1 indicates a lower risk with the treatment compared with placebo.</p> | |
| End point type | Secondary |
| End point timeframe: | |
| Week 12, Week 24 | |

| End point values | Placebo | Losmapimod 7.5 mg BID | | |
|-----------------------------|----------------------|--------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 1758 ^[48] | 1731 ^[49] | | |
| Units: Participants | | | | |
| Week 12, n=1281, 1306 | 19 | 11 | | |
| Week 24, n=1758, 1731 | 21 | 12 | | |

Notes:

[48] - All Randomized (ITT) Population

[49] - All Randomized (ITT) Population

Statistical analyses

| Statistical analysis title | Statistical Analysis 1 |
|---|---------------------------------|
| Statistical analysis description: | |
| Week 12 estimates | |
| Comparison groups | Placebo v Losmapimod 7.5 mg BID |
| Number of subjects included in analysis | 3489 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.13 ^[50] |
| Method | Regression, Cox |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.57 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.27 |
| upper limit | 1.19 |

Notes:

[50] - Log rank test

Secondary: Number of participants re-hospitalized within 30 days of discharge

| | |
|---|--|
| End point title | Number of participants re-hospitalized within 30 days of discharge |
| End point description: | |
| Participants who had a death or re-hospitalization within 30 days of discharge, plus participants who were never discharged from the initial hospitalization were included. Odds ratio was estimated using a logistic regression model stratified by Baseline STEMI/NSTEMI status with treatment as the only covariate. An odds ratio <1 indicated a lower risk with the treatment compared with placebo. | |
| End point type | Secondary |
| End point timeframe: | |
| Within up to 30 days of post discharge | |

| End point values | Placebo | Losmapimod 7.5 mg BID | | |
|-----------------------------|----------------------|-----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 1758 ^[51] | 1731 ^[52] | | |
| Units: Participants | 210 | 213 | | |

Notes:

[51] - All Randomized (ITT) Population

[52] - All Randomized (ITT) Population

Statistical analyses

| Statistical analysis title | Statistical Analysis 1 |
|---|---------------------------------|
| Comparison groups | Placebo v Losmapimod 7.5 mg BID |
| Number of subjects included in analysis | 3489 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.744 ^[53] |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 1.03 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.84 |
| upper limit | 1.27 |

Notes:

[53] - Wald chi-squared

Secondary: Number of participants with all-cause mortality through to Week 12 and Week 24

| | |
|------------------------|--|
| End point title | Number of participants with all-cause mortality through to Week 12 and Week 24 |
| End point description: | Number of participants with all-cause mortality through to Week 12 and Week 24 are presented. Time to first occurrence at Week 12 analyzed by cox model with log-rank test. Hazard ratio and CI were estimated using a cox proportional hazard regression model stratified by Baseline STEMI/ NSTEMI status with treatment as the only covariate. A hazard ratio <1 indicates a lower risk with the treatment compared with placebo. |
| End point type | Secondary |
| End point timeframe: | |
| Week 12, Week 24 | |

| End point values | Placebo | Losmapimod 7.5 mg BID | | |
|-----------------------------|----------------------|-----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 1758 ^[54] | 1731 ^[55] | | |
| Units: Participants | | | | |
| Week 12 | 49 | 39 | | |
| Week 24 | 68 | 57 | | |

Notes:

[54] - All Randomized (ITT) Population

[55] - All Randomized (ITT) Population

Statistical analyses

| | |
|---|---------------------------------|
| Statistical analysis title | Statistical Analysis 1 |
| Statistical analysis description: | |
| Week 12 estimates | |
| Comparison groups | Losmapimod 7.5 mg BID v Placebo |
| Number of subjects included in analysis | 3489 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.309 ^[56] |
| Method | Regression, Cox |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.8 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.53 |
| upper limit | 1.22 |

Notes:

[56] - Log rank test

Secondary: Number of participants with CV death events through to Week 12 and Week 24

| | |
|--|--|
| End point title | Number of participants with CV death events through to Week 12 and Week 24 |
| End point description: | |
| Number of participants with CV death events through to Week 12 and Week 24 are presented. Time to first occurrence at Week 12 analyzed by cox model with log-rank test. Hazard ratio and CI were estimated using a cox proportional hazard regression model stratified by Baseline STEMI/ NSTEMI status with treatment as the only covariate. A hazard ratio <1 indicates a lower risk with the treatment compared with placebo. | |
| End point type | Secondary |
| End point timeframe: | |
| Week 12, Week 24 | |

| | | | | |
|-----------------------------|----------------------|-----------------------|--|--|
| End point values | Placebo | Losmapimod 7.5 mg BID | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 1758 ^[57] | 1731 ^[58] | | |
| Units: Participants | | | | |
| Week 12 | 44 | 36 | | |
| Week 24 | 59 | 47 | | |

Notes:

[57] - All Randomized (ITT) Population

[58] - All Randomized (ITT) Population

Statistical analyses

| Statistical analysis title | Statistical Analysis 1 |
|---|---------------------------------|
| Statistical analysis description: | |
| Week 12 estimates | |
| Comparison groups | Placebo v Losmapimod 7.5 mg BID |
| Number of subjects included in analysis | 3489 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.398 ^[59] |
| Method | Regression, Cox |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.83 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.53 |
| upper limit | 1.28 |

Notes:

[59] - Log rank test

| Statistical analysis title | Statistical Analysis 2 |
|---|---------------------------------|
| Statistical analysis description: | |
| Week 24 estimates | |
| Comparison groups | Placebo v Losmapimod 7.5 mg BID |
| Number of subjects included in analysis | 3489 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.264 ^[60] |
| Method | Regression, Cox |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.8 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.55 |
| upper limit | 1.18 |

Notes:

[60] - Log rank test

Secondary: Number of participants with CHD death events through to Week 12 and Week 24

| | |
|-----------------|---|
| End point title | Number of participants with CHD death events through to Week 12 and Week 24 |
|-----------------|---|

End point description:

Number of participants with CHD death events through to Week 12 and Week 24 are presented. Time to first occurrence at Week 12 analyzed by cox model with log-rank test. Hazard ratio and CI were estimated using a cox proportional hazard regression model stratified by Baseline STEMI/ NSTEMI status with treatment as the only covariate. A hazard ratio <1 indicates a lower risk with the treatment compared with placebo.

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

End point timeframe:

Week 12, Week 24

| End point values | Placebo | Losmapimod 7.5 mg BID | | |
|-----------------------------|----------------------|-----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 1758 ^[61] | 1731 ^[62] | | |
| Units: Participants | | | | |
| Week 12 | 40 | 30 | | |
| Week 24 | 49 | 37 | | |

Notes:

[61] - All Randomized (ITT) Population

[62] - All Randomized (ITT) Population

Statistical analyses

| | |
|----------------------------|------------------------|
| Statistical analysis title | Statistical Analysis 1 |
|----------------------------|------------------------|

Statistical analysis description:

Week 12 estimates

| | |
|---|---------------------------------|
| Comparison groups | Placebo v Losmapimod 7.5 mg BID |
| Number of subjects included in analysis | 3489 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.251 ^[63] |
| Method | Regression, Cox |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.76 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.47 |
| upper limit | 1.22 |

Notes:

[63] - Log rank test

Secondary: Number of participants with first occurrence of myocardial infarction (fatal and non-fatal) events through to Week 12 and Week 24

| | |
|-----------------|---|
| End point title | Number of participants with first occurrence of myocardial infarction (fatal and non-fatal) events through to Week 12 and Week 24 |
|-----------------|---|

End point description:

Number of participants with first occurrence of myocardial infarction (fatal and non-fatal) events through to Week 12 and Week 24 are presented. Time to first occurrence at Week 12 analyzed by cox model with log-rank test. Hazard ratio and CI were estimated using a cox proportional hazard regression model stratified by Baseline STEMI/ NSTEMI status with treatment as the only covariate. A hazard ratio <1

indicates a lower risk with the treatment compared with placebo.

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Week 12, Week 24 | |

| End point values | Placebo | Losmapimod 7.5 mg BID | | |
|-----------------------------|----------------------|--------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 1758 ^[64] | 1731 ^[65] | | |
| Units: Participants | | | | |
| Week 12 | 75 | 90 | | |
| Week 24 | 99 | 117 | | |

Notes:

[64] - All Randomized (ITT) Population

[65] - All Randomized (ITT) Population

Statistical analyses

| Statistical analysis title | Statistical Analysis 1 |
|---|---------------------------------|
| Statistical analysis description: | |
| Week 12 estimates | |
| Comparison groups | Placebo v Losmapimod 7.5 mg BID |
| Number of subjects included in analysis | 3489 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.182 ^[66] |
| Method | Regression, Cox |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 1.23 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.91 |
| upper limit | 1.67 |

Notes:

[66] - Log rank test

| Statistical analysis title | Statistical Analysis 2 |
|---|---------------------------------|
| Statistical analysis description: | |
| Week 24 estimates | |
| Comparison groups | Placebo v Losmapimod 7.5 mg BID |
| Number of subjects included in analysis | 3489 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.158 ^[67] |
| Method | Regression, Cox |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 1.21 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.93 |
| upper limit | 1.58 |

Notes:

[67] - Log rank test

Secondary: Number of participants with first occurrence of type I (spontaneous) MI events through to Week 12 and Week 24

| | |
|-----------------|---|
| End point title | Number of participants with first occurrence of type I (spontaneous) MI events through to Week 12 and Week 24 |
|-----------------|---|

End point description:

Number of participants with first occurrence of type I (spontaneous) MI events through to Week 12 and Week 24 are presented. Time to first occurrence at Week 12 analyzed by cox model with log-rank test. Hazard ratio and CI were estimated using a cox proportional hazard regression model stratified by Baseline STEMI/ NSTEMI status with treatment as the only covariate. A hazard ratio <1 indicates a lower risk with the treatment compared with placebo.

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Week 12, Week 24 | |

| End point values | Placebo | Losmapimod 7.5 mg BID | | |
|-----------------------------|----------------------|-----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 1758 ^[68] | 1731 ^[69] | | |
| Units: Participants | | | | |
| Week 12 | 32 | 42 | | |
| Week 24 | 51 | 62 | | |

Notes:

[68] - All Randomized (ITT) Population

[69] - All Randomized (ITT) Population

Statistical analyses

| | |
|---|---------------------------------|
| Statistical analysis title | Statistical Analysis 1 |
| Statistical analysis description: | |
| Week 12 estimates | |
| Comparison groups | Placebo v Losmapimod 7.5 mg BID |
| Number of subjects included in analysis | 3489 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.21 ^[70] |
| Method | Regression, Cox |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 1.34 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.85 |
| upper limit | 2.12 |

Notes:

[70] - Log rank st

Secondary: Number of participants with first occurrence of SRI-UR events through to Week 12 and Week 24

| | |
|-----------------|--|
| End point title | Number of participants with first occurrence of SRI-UR events through to Week 12 and Week 24 |
|-----------------|--|

End point description:

Number of participants with first occurrence of SRI-UR events through to Week 12 and Week 24 are presented. Time to first occurrence at Week 12 analyzed by cox model with log-rank test. Hazard ratio and CI were estimated using a cox proportional hazard regression model stratified by Baseline STEMI/NSTEMI status with treatment as the only covariate. A hazard ratio <1 indicates a lower risk with the treatment compared with placebo.

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

End point timeframe:

Week 12, Week 24

| End point values | Placebo | Losmapimod 7.5 mg BID | | |
|-----------------------------|----------------------|-----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 1758 ^[71] | 1731 ^[72] | | |
| Units: Participants | | | | |
| Week 12 | 16 | 18 | | |
| Week 24 | 22 | 22 | | |

Notes:

[71] - All Randomized (ITT) Population

[72] - All Randomized (ITT) Population

Statistical analyses

| | |
|----------------------------|------------------------|
| Statistical analysis title | Statistical Analysis 1 |
|----------------------------|------------------------|

Statistical analysis description:

Week 12 estimates

| | |
|---|---------------------------------|
| Comparison groups | Placebo v Losmapimod 7.5 mg BID |
| Number of subjects included in analysis | 3489 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.697 ^[73] |
| Method | Regression, Cox |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 1.14 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.58 |
| upper limit | 2.24 |

Notes:

[73] - Log rank test

Secondary: Number of participants with first occurrence of stroke (fatal and non-fatal) events through to Week 12 and Week 24

| | |
|-----------------|--|
| End point title | Number of participants with first occurrence of stroke (fatal and non-fatal) events through to Week 12 and Week 24 |
|-----------------|--|

End point description:

Number of participants with first occurrence of stroke (fatal and non-fatal) events through to Week 12 and Week 24 are presented. Time to first occurrence at Week 12 analyzed by cox model with log-rank test. Hazard ratio and CI were estimated using a cox proportional hazard regression model stratified by Baseline STEMI/ NSTEMI status with treatment as the only covariate. A hazard ratio <1 indicates a lower risk with the treatment compared with placebo.

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

End point timeframe:

Week 12, Week 24

| End point values | Placebo | Losmapimod 7.5 mg BID | | |
|-----------------------------|----------------------|-----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 1758 ^[74] | 1731 ^[75] | | |
| Units: Participants | | | | |
| Week 12 | 15 | 14 | | |
| Week 24 | 19 | 18 | | |

Notes:

[74] - All Randomized (ITT) Population

[75] - All Randomized (ITT) Population

Statistical analyses

| | |
|----------------------------|------------------------|
| Statistical analysis title | Statistical Analysis 1 |
|----------------------------|------------------------|

Statistical analysis description:

Week 12 estimates

| | |
|---|---------------------------------|
| Comparison groups | Placebo v Losmapimod 7.5 mg BID |
| Number of subjects included in analysis | 3489 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.883 ^[76] |
| Method | Regression, Cox |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.95 |

Confidence interval

| | |
|-------------|---------|
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.46 |
| upper limit | 1.96 |

Notes:

[76] - Log rank test

Secondary: Number of participants with first occurrence of hospitalization for HF through to Week 12 and Week 24

| | |
|-----------------|---|
| End point title | Number of participants with first occurrence of hospitalization for HF through to Week 12 and Week 24 |
|-----------------|---|

End point description:

Number of participants with first occurrence of hospitalization for HF through to Week 12 and Week 24 are presented. Time to first occurrence at Week 12 analyzed by cox model with log-rank test. Hazard ratio and CI were estimated using a cox proportional hazard regression model stratified by Baseline STEMI/ NSTEMI status with treatment as the only covariate. A hazard ratio <1 indicates a lower risk with the treatment compared with placebo.

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

End point timeframe:

Week 12, Week 24

| End point values | Placebo | Losmapimod 7.5 mg BID | | |
|-----------------------------|----------------------|-----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 1758 ^[77] | 1731 ^[78] | | |
| Units: Participants | | | | |
| Week 12 | 42 | 35 | | |
| Week 24 | 53 | 49 | | |

Notes:

[77] - All Randomized (ITT) Population

[78] - All Randomized (ITT) Population

Statistical analyses

| | |
|----------------------------|------------------------|
| Statistical analysis title | Statistical Analysis 1 |
|----------------------------|------------------------|

Statistical analysis description:

week 12 estimates

| | |
|-------------------|---------------------------------|
| Comparison groups | Placebo v Losmapimod 7.5 mg BID |
|-------------------|---------------------------------|

| | |
|---|------|
| Number of subjects included in analysis | 3489 |
|---|------|

| | |
|------------------------|---------------|
| Analysis specification | Pre-specified |
|------------------------|---------------|

| | |
|---------------|-------------|
| Analysis type | superiority |
|---------------|-------------|

| | |
|---------|-------------------------|
| P-value | = 0.457 ^[79] |
|---------|-------------------------|

| | |
|--------|-----------------|
| Method | Regression, Cox |
|--------|-----------------|

| | |
|--------------------|-------------------|
| Parameter estimate | Hazard ratio (HR) |
|--------------------|-------------------|

| | |
|----------------|------|
| Point estimate | 0.84 |
|----------------|------|

Confidence interval

| | |
|-------|------|
| level | 95 % |
|-------|------|

| | |
|-------|---------|
| sides | 2-sided |
|-------|---------|

| | |
|-------------|------|
| lower limit | 0.54 |
|-------------|------|

| | |
|-------------|------|
| upper limit | 1.32 |
|-------------|------|

Notes:

[79] - Log rank test

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

Statistical analysis description:

week 24 estimates

| | |
|---|---------------------------------|
| Comparison groups | Placebo v Losmapimod 7.5 mg BID |
| Number of subjects included in analysis | 3489 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.736 ^[80] |
| Method | Regression, Cox |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.94 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.63 |
| upper limit | 1.38 |

Notes:

[80] - Log rank test

Secondary: Number of participants with first occurrence of any unplanned coronary revascularization through to Week 12 and Week 24

| | |
|-----------------|---|
| End point title | Number of participants with first occurrence of any unplanned coronary revascularization through to Week 12 and Week 24 |
|-----------------|---|

End point description:

Number of participants with first occurrence of any unplanned coronary revascularization through to Week 12 and Week 24 are presented. Time to first occurrence at Week 12 analyzed by cox model with log-rank test. Hazard ratio and CI were estimated using a cox proportional hazard regression model stratified by Baseline STEMI/ NSTEMI status with treatment as the only covariate. A hazard ratio <1 indicates a lower risk with the treatment compared with placebo.

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

End point timeframe:

Week 12, Week 24

| End point values | Placebo | Losmapimod 7.5 mg BID | | |
|-----------------------------|----------------------|-----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 1758 ^[81] | 1731 ^[82] | | |
| Units: Participants | | | | |
| Week 12 | 57 | 62 | | |
| Week 24 | 75 | 87 | | |

Notes:

[81] - All Randomized (ITT) Population

[82] - All Randomized (ITT) Population

Statistical analyses

| | |
|-----------------------------------|------------------------|
| Statistical analysis title | Statistical Analysis 1 |
|-----------------------------------|------------------------|

Statistical analysis description:

Week 12 estimates

| | |
|-------------------|---------------------------------|
| Comparison groups | Placebo v Losmapimod 7.5 mg BID |
|-------------------|---------------------------------|

| | |
|---|-------------------------|
| Number of subjects included in analysis | 3489 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.581 ^[83] |
| Method | Regression, Cox |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 1.11 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.77 |
| upper limit | 1.59 |

Notes:

[83] - Log rank test

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Serious adverse events (SAEs) and non-serious adverse events (AEs) were collected from the start of study medication until follow-up (up to Week 26)

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 18.1 |
|--------------------|------|

Reporting groups

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

Reporting group description:

Participants received matching placebo BID according to the randomization schedule for 12 weeks in addition to standard of care, and were followed for an additional 12 weeks after completing treatment, for a total study duration of 24 weeks.

| | |
|-----------------------|-----------------------|
| Reporting group title | Losmapimod 7.5 mg BID |
|-----------------------|-----------------------|

Reporting group description:

Participants received oral losmapimod 7.5 mg BID according to the randomization schedule for 12 weeks in addition to standard of care, and were followed for an additional 12 weeks after completing treatment, for a total study duration of 24 weeks.

| Serious adverse events | Placebo | Losmapimod 7.5 mg BID | |
|---|---------------------|-----------------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 323 / 1752 (18.44%) | 363 / 1724 (21.06%) | |
| number of deaths (all causes) | 10 | 13 | |
| number of deaths resulting from adverse events | | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Adenocarcinoma of colon | | | |
| subjects affected / exposed | 3 / 1752 (0.17%) | 2 / 1724 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Adrenocortical carcinoma | | | |
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bone neoplasm | | | |
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|------------------|------------------|--|
| Breast cancer | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Colon adenoma | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Colon cancer | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Colon cancer metastatic | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Colorectal cancer | | | |
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastric cancer | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatocellular carcinoma | | | |
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Invasive ductal breast carcinoma | | | |
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lung cancer metastatic | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Malignant melanoma | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metastases to bone | | | |
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metastases to liver | | | |
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metastases to lymph nodes | | | |
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Non-small cell lung cancer | | | |
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pancreatic carcinoma metastatic | | | |
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Plasma cell myeloma | | | |
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Prostatic adenoma | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Small cell lung cancer | | | |
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Small cell lung cancer metastatic | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Transitional cell carcinoma | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vascular disorders | | | |
| Air embolism | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Aortic aneurysm | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Aortic dissection | | | |
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Arterial haemorrhage | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Arteriosclerosis | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Artery dissection | | | |
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Circulatory collapse | | | |
| subjects affected / exposed | 2 / 1752 (0.11%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Deep vein thrombosis | | | |
| subjects affected / exposed | 0 / 1752 (0.00%) | 2 / 1724 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Extremity necrosis | | | |
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haematoma | | | |
| subjects affected / exposed | 0 / 1752 (0.00%) | 4 / 1724 (0.23%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypertension | | | |
| subjects affected / exposed | 4 / 1752 (0.23%) | 2 / 1724 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypertensive crisis | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 2 / 1724 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypotension | | | |

| | | | |
|--|------------------|------------------|--|
| subjects affected / exposed | 5 / 1752 (0.29%) | 4 / 1724 (0.23%) | |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ischaemia | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Malignant hypertension | | | |
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Orthostatic hypotension | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Peripheral arterial occlusive disease | | | |
| subjects affected / exposed | 3 / 1752 (0.17%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Peripheral ischaemia | | | |
| subjects affected / exposed | 6 / 1752 (0.34%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 6 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Shock haemorrhagic | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Thrombophlebitis | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General disorders and administration site conditions | | | |
| Asthenia | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Catheter site haematoma | | | |
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Catheter site haemorrhage | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Chest discomfort | | | |
| subjects affected / exposed | 2 / 1752 (0.11%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Chest pain | | | |
| subjects affected / exposed | 5 / 1752 (0.29%) | 2 / 1724 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Death | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 3 / 1724 (0.17%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 3 | |
| Discomfort | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Drug intolerance | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Medical device complication | | | |

| | | | |
|---|-------------------|-------------------|--|
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Multi-organ failure | | | |
| subjects affected / exposed | 3 / 1752 (0.17%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Non-cardiac chest pain | | | |
| subjects affected / exposed | 19 / 1752 (1.08%) | 15 / 1724 (0.87%) | |
| occurrences causally related to treatment / all | 0 / 19 | 0 / 15 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Oedema peripheral | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pyrexia | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Systemic inflammatory response syndrome | | | |
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vascular stent restenosis | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Immune system disorders | | | |
| Drug hypersensitivity | | | |
| subjects affected / exposed | 2 / 1752 (0.11%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Reproductive system and breast disorders | | | |

| | | | |
|---|------------------|------------------|--|
| Benign prostatic hyperplasia | | | |
| subjects affected / exposed | 2 / 1752 (0.11%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Prostatism | | | |
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Prostatitis | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Acute pulmonary oedema | | | |
| subjects affected / exposed | 2 / 1752 (0.11%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Acute respiratory failure | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 3 / 1724 (0.17%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Asthma | | | |
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Atelectasis | | | |
| subjects affected / exposed | 0 / 1752 (0.00%) | 2 / 1724 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Chronic obstructive pulmonary disease | | | |
| subjects affected / exposed | 4 / 1752 (0.23%) | 7 / 1724 (0.41%) | |
| occurrences causally related to treatment / all | 1 / 5 | 1 / 10 | |
| deaths causally related to treatment / all | 0 / 2 | 0 / 0 | |

| | | | |
|---|------------------|------------------|--|
| Dyspnoea | | | |
| subjects affected / exposed | 2 / 1752 (0.11%) | 4 / 1724 (0.23%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dyspnoea exertional | | | |
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Epistaxis | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haemoptysis | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haemothorax | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 2 / 1724 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypoxia | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Laryngospasm | | | |
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lung infiltration | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Obstructive airways disorder | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Pharyngeal haematoma | | | |
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pleural effusion | | | |
| subjects affected / exposed | 6 / 1752 (0.34%) | 9 / 1724 (0.52%) | |
| occurrences causally related to treatment / all | 0 / 6 | 0 / 11 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pleurisy | | | |
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pleuritic pain | | | |
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia aspiration | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Pneumothorax | | | |
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pulmonary embolism | | | |
| subjects affected / exposed | 2 / 1752 (0.11%) | 4 / 1724 (0.23%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Pulmonary mass | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 0 / 1752 (0.00%) | 2 / 1724 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pulmonary oedema | | | |
| subjects affected / exposed | 2 / 1752 (0.11%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pulmonary hypertension | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory failure | | | |
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory depression | | | |
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Tracheomalacia | | | |
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Psychiatric disorders | | | |
| Acute psychosis | | | |
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Anxiety disorder due to a general medical condition | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Delirium | | | |

| | | | |
|--|------------------|------------------|--|
| subjects affected / exposed | 1 / 1752 (0.06%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Depression | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hallucination | | | |
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Mental disorder | | | |
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Mental disorder due to a general medical condition | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Suicide attempt | | | |
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Investigations | | | |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 2 / 1752 (0.11%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 1 / 2 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Blood creatinine increased | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Electrocardiogram QT prolonged | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Electrocardiogram change | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haemoglobin abnormal | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatic enzyme increased | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| International normalised ratio increased | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Laboratory test abnormal | | | |
| subjects affected / exposed | 3 / 1752 (0.17%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Liver function test abnormal | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Myocardial necrosis marker increased | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Transaminases increased | | | |

| | | | |
|---|-------------------|------------------|--|
| subjects affected / exposed | 1 / 1752 (0.06%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Troponin I increased | | | |
| subjects affected / exposed | 2 / 1752 (0.11%) | 2 / 1724 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Troponin T increased | | | |
| subjects affected / exposed | 2 / 1752 (0.11%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Troponin increased | | | |
| subjects affected / exposed | 11 / 1752 (0.63%) | 9 / 1724 (0.52%) | |
| occurrences causally related to treatment / all | 0 / 11 | 0 / 10 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Injury, poisoning and procedural complications | | | |
| Animal bite | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ankle fracture | | | |
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac procedure complication | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 7 / 1724 (0.41%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 7 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Contrast media reaction | | | |
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Contusion | | | |

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|---|------------------|------------------|--|
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Coronary vascular graft occlusion | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Facial bones fracture | | | |
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Failure to anastomose | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Fall | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Femoral neck fracture | | | |
| subjects affected / exposed | 2 / 1752 (0.11%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Femur fracture | | | |
| subjects affected / exposed | 2 / 1752 (0.11%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Fibula fracture | | | |
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Graft loss | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Head injury | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatic rupture | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Humerus fracture | | | |
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Injury | | | |
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Overdose | | | |
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Patella fracture | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Post procedural complication | | | |
| subjects affected / exposed | 2 / 1752 (0.11%) | 2 / 1724 (0.12%) | |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Post procedural haemorrhage | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 1 / 1752 (0.06%) | 3 / 1724 (0.17%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Post procedural myocardial infarction | | | |
| subjects affected / exposed | 2 / 1752 (0.11%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Postimplantation syndrome | | | |
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Postoperative renal failure | | | |
| subjects affected / exposed | 0 / 1752 (0.00%) | 2 / 1724 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Procedural haemorrhage | | | |
| subjects affected / exposed | 3 / 1752 (0.17%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Rib fracture | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Spinal compression fracture | | | |
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Splenic rupture | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Subdural haematoma | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Toxicity to various agents | | | |
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Upper limb fracture | | | |
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vascular pseudoaneurysm | | | |
| subjects affected / exposed | 0 / 1752 (0.00%) | 3 / 1724 (0.17%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Wrist fracture | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Postoperative thoracic procedure complication | | | |
| subjects affected / exposed | 0 / 1752 (0.00%) | 2 / 1724 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Congenital, familial and genetic disorders | | | |
| Gastrointestinal arteriovenous malformation | | | |
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac disorders | | | |
| Acute coronary syndrome | | | |

| | | | |
|---|-------------------|-------------------|--|
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Acute myocardial infarction | | | |
| subjects affected / exposed | 7 / 1752 (0.40%) | 13 / 1724 (0.75%) | |
| occurrences causally related to treatment / all | 0 / 7 | 1 / 13 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Angina pectoris | | | |
| subjects affected / exposed | 14 / 1752 (0.80%) | 24 / 1724 (1.39%) | |
| occurrences causally related to treatment / all | 0 / 14 | 0 / 24 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Angina unstable | | | |
| subjects affected / exposed | 24 / 1752 (1.37%) | 26 / 1724 (1.51%) | |
| occurrences causally related to treatment / all | 0 / 26 | 0 / 27 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Aortic valve disease | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Aortic valve incompetence | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Arrhythmia supraventricular | | | |
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Arteriospasm coronary | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 2 / 1724 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Atrial fibrillation | | | |

| | | | |
|---|-------------------|-------------------|--|
| subjects affected / exposed | 14 / 1752 (0.80%) | 19 / 1724 (1.10%) | |
| occurrences causally related to treatment / all | 0 / 16 | 0 / 21 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Atrial flutter | | | |
| subjects affected / exposed | 4 / 1752 (0.23%) | 4 / 1724 (0.23%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Atrioventricular block | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Atrioventricular block complete | | | |
| subjects affected / exposed | 4 / 1752 (0.23%) | 3 / 1724 (0.17%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Atrioventricular block second degree | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bradyarrhythmia | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bradycardia | | | |
| subjects affected / exposed | 0 / 1752 (0.00%) | 3 / 1724 (0.17%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac arrest | | | |
| subjects affected / exposed | 3 / 1752 (0.17%) | 5 / 1724 (0.29%) | |
| occurrences causally related to treatment / all | 1 / 4 | 0 / 5 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac failure | | | |

| | | | |
|---|------------------|-------------------|--|
| subjects affected / exposed | 6 / 1752 (0.34%) | 10 / 1724 (0.58%) | |
| occurrences causally related to treatment / all | 0 / 6 | 0 / 10 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac failure acute | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac failure congestive | | | |
| subjects affected / exposed | 5 / 1752 (0.29%) | 8 / 1724 (0.46%) | |
| occurrences causally related to treatment / all | 0 / 7 | 0 / 8 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac tamponade | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 2 / 1724 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac ventricular thrombosis | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiogenic shock | | | |
| subjects affected / exposed | 6 / 1752 (0.34%) | 5 / 1724 (0.29%) | |
| occurrences causally related to treatment / all | 0 / 6 | 0 / 5 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Coronary artery disease | | | |
| subjects affected / exposed | 0 / 1752 (0.00%) | 3 / 1724 (0.17%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Coronary artery dissection | | | |
| subjects affected / exposed | 3 / 1752 (0.17%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Coronary artery perforation | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 2 / 1752 (0.11%) | 2 / 1724 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Coronary artery thrombosis | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dressler's syndrome | | | |
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypertensive heart disease | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Left ventricular failure | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Mitral valve incompetence | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Myocardial ischaemia | | | |
| subjects affected / exposed | 3 / 1752 (0.17%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Myocardial rupture | | | |
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Myocardial infarction | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Myocarditis | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Palpitations | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pericardial effusion | | | |
| subjects affected / exposed | 2 / 1752 (0.11%) | 3 / 1724 (0.17%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pericarditis | | | |
| subjects affected / exposed | 3 / 1752 (0.17%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Pericarditis lupus | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Postinfarction angina | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Prinzmetal angina | | | |
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sinus node dysfunction | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 4 / 1752 (0.23%) | 3 / 1724 (0.17%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Supraventricular tachycardia | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Tachycardia | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Torsade de pointes | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ventricular flutter | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ventricular dyssynchrony | | | |
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ventricular extrasystoles | | | |
| subjects affected / exposed | 0 / 1752 (0.00%) | 2 / 1724 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ventricular fibrillation | | | |
| subjects affected / exposed | 5 / 1752 (0.29%) | 7 / 1724 (0.41%) | |
| occurrences causally related to treatment / all | 1 / 7 | 0 / 7 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ventricular tachyarrhythmia | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ventricular tachycardia | | | |
| subjects affected / exposed | 5 / 1752 (0.29%) | 7 / 1724 (0.41%) | |
| occurrences causally related to treatment / all | 1 / 5 | 0 / 7 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Nervous system disorders | | | |
| Brain stem haemorrhage | | | |
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Carotid artery disease | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Carotid artery stenosis | | | |
| subjects affected / exposed | 4 / 1752 (0.23%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cerebral ischaemia | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cerebrovascular accident | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dizziness | | | |
| subjects affected / exposed | 3 / 1752 (0.17%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Encephalopathy | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 2 / 1752 (0.11%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Epilepsy | | | |
| subjects affected / exposed | 0 / 1752 (0.00%) | 2 / 1724 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Headache | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypertensive encephalopathy | | | |
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypoaesthesia | | | |
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypoxic-ischaemic encephalopathy | | | |
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Motor dysfunction | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Paraesthesia | | | |
| subjects affected / exposed | 2 / 1752 (0.11%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Presyncope | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 0 / 1752 (0.00%) | 2 / 1724 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Psychomotor hyperactivity | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Quadrantanopia | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Somnolence | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Subarachnoid haemorrhage | | | |
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Syncope | | | |
| subjects affected / exposed | 5 / 1752 (0.29%) | 4 / 1724 (0.23%) | |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Transient ischaemic attack | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vertebral artery stenosis | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 1 / 1752 (0.06%) | 5 / 1724 (0.29%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 5 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Autoimmune haemolytic anaemia | | | |
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Coagulopathy | | | |
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Iron deficiency anaemia | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Neutropenia | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Normochromic normocytic anaemia | | | |
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Thrombocytopenia | | | |
| subjects affected / exposed | 2 / 1752 (0.11%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ear and labyrinth disorders | | | |
| Vertigo | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 3 / 1724 (0.17%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vestibular disorder | | | |

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|---|------------------|------------------|--|
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Eye disorders | | | |
| Blindness | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diplopia | | | |
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Eye haemorrhage | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Optic ischaemic neuropathy | | | |
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Retinal artery occlusion | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Retinal detachment | | | |
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Abdominal mass | | | |
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Abdominal pain | | | |

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|---|------------------|------------------|--|
| subjects affected / exposed | 0 / 1752 (0.00%) | 2 / 1724 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Abdominal pain upper | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Colitis | | | |
| subjects affected / exposed | 2 / 1752 (0.11%) | 2 / 1724 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Colitis ischaemic | | | |
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Crohn's disease | | | |
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diarrhoea | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 2 / 1724 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diverticulum | | | |
| subjects affected / exposed | 2 / 1752 (0.11%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Duodenal perforation | | | |
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Duodenal ulcer | | | |

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|---|------------------|------------------|--|
| subjects affected / exposed | 0 / 1752 (0.00%) | 2 / 1724 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Duodenal ulcer haemorrhage | | | |
| subjects affected / exposed | 0 / 1752 (0.00%) | 3 / 1724 (0.17%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Duodenitis | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dysphagia | | | |
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Enterocolitis | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Erosive oesophagitis | | | |
| subjects affected / exposed | 2 / 1752 (0.11%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Faecaloma | | | |
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Food poisoning | | | |
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastric ulcer haemorrhage | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastritis | | | |
| subjects affected / exposed | 3 / 1752 (0.17%) | 3 / 1724 (0.17%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastritis erosive | | | |
| subjects affected / exposed | 0 / 1752 (0.00%) | 2 / 1724 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastritis haemorrhagic | | | |
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorder | | | |
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 3 / 1752 (0.17%) | 6 / 1724 (0.35%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 6 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Gastrointestinal pain | | | |
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal polyp haemorrhage | | | |
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal ulcer | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal ulcer haemorrhage | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrooesophageal reflux disease | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haematemesis | | | |
| subjects affected / exposed | 3 / 1752 (0.17%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haemorrhagic erosive gastritis | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haemorrhoidal haemorrhage | | | |
| subjects affected / exposed | 0 / 1752 (0.00%) | 2 / 1724 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haemorrhoids | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Intestinal ulcer | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Intestinal haemorrhage | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 0 / 1752 (0.00%) | 2 / 1724 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Large intestinal haemorrhage | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Large intestine polyp | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lower gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nausea | | | |
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Oesophageal varices haemorrhage | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| pancreatitis | | | |
| subjects affected / exposed | 2 / 1752 (0.11%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pancreatitis acute | | | |
| subjects affected / exposed | 2 / 1752 (0.11%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Peptic ulcer | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 1 / 1752 (0.06%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Peptic ulcer haemorrhage | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Proctitis ulcerative | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Rectal haemorrhage | | | |
| subjects affected / exposed | 2 / 1752 (0.11%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Rectal polyp | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Small intestinal obstruction | | | |
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ulcerative gastritis | | | |
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Upper gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Volvulus | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 1 / 1752 (0.06%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vomiting | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 2 / 1724 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatobiliary disorders | | | |
| Cholangitis | | | |
| subjects affected / exposed | 2 / 1752 (0.11%) | 2 / 1724 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cholecystitis | | | |
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cholecystitis acute | | | |
| subjects affected / exposed | 4 / 1752 (0.23%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cholecystitis chronic | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cholelithiasis | | | |
| subjects affected / exposed | 0 / 1752 (0.00%) | 2 / 1724 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Drug-induced liver injury | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 3 / 1724 (0.17%) | |
| occurrences causally related to treatment / all | 1 / 1 | 3 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatic failure | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatic function abnormal | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatic ischaemia | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatic necrosis | | | |
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatotoxicity | | | |
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Liver disorder | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Skin and subcutaneous tissue disorders | | | |
| Angioedema | | | |
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Drug eruption | | | |
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypersensitivity vasculitis | | | |

| | | | |
|---|------------------|-------------------|--|
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Rash generalised | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Skin ulcer | | | |
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal and urinary disorders | | | |
| Acute kidney injury | | | |
| subjects affected / exposed | 9 / 1752 (0.51%) | 13 / 1724 (0.75%) | |
| occurrences causally related to treatment / all | 0 / 9 | 0 / 15 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bladder tamponade | | | |
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Calculus ureteric | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Chronic kidney disease | | | |
| subjects affected / exposed | 3 / 1752 (0.17%) | 6 / 1724 (0.35%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 6 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cystitis haemorrhagic | | | |
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haematuria | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 2 / 1752 (0.11%) | 2 / 1724 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haemorrhage urinary tract | | | |
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nephrolithiasis | | | |
| subjects affected / exposed | 0 / 1752 (0.00%) | 2 / 1724 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal failure | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 4 / 1724 (0.23%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal haematoma | | | |
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal impairment | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urinary retention | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urogenital haemorrhage | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Endocrine disorders | | | |
| Primary hyperaldosteronism | | | |

| | | | |
|---|------------------|-------------------|--|
| subjects affected / exposed | 1 / 1752 (0.06%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal and connective tissue disorders | | | |
| Back disorder | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Back pain | | | |
| subjects affected / exposed | 0 / 1752 (0.00%) | 2 / 1724 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Costochondritis | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Muscular weakness | | | |
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal pain | | | |
| subjects affected / exposed | 2 / 1752 (0.11%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal chest pain | | | |
| subjects affected / exposed | 4 / 1752 (0.23%) | 14 / 1724 (0.81%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 14 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Myalgia | | | |
| subjects affected / exposed | 0 / 1752 (0.00%) | 2 / 1724 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Myopathy | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Neck pain | | | |
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Osteoarthritis | | | |
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Osteochondritis | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pain in extremity | | | |
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Rhabdomyolysis | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Rheumatoid arthritis | | | |
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Rotator cuff syndrome | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Spinal pain | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 1 / 1752 (0.06%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Systemic lupus erythematosus | | | |
| subjects affected / exposed | 2 / 1752 (0.11%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Acute hepatitis B | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| American trypanosomiasis | | | |
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bacteraemia | | | |
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bronchitis | | | |
| subjects affected / exposed | 3 / 1752 (0.17%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Campylobacter gastroenteritis | | | |
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cellulitis | | | |
| subjects affected / exposed | 0 / 1752 (0.00%) | 3 / 1724 (0.17%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cholecystitis infective | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 1 / 1752 (0.06%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Clostridium difficile infection | | | |
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cystitis | | | |
| subjects affected / exposed | 2 / 1752 (0.11%) | 3 / 1724 (0.17%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diverticulitis | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ear infection | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Endocarditis | | | |
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Enterococcal infection | | | |
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Erysipelas | | | |
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Escherichia sepsis | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 1 / 1752 (0.06%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gangrene | | | |
| subjects affected / exposed | 3 / 1752 (0.17%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastroenteritis | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 4 / 1724 (0.23%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastroenteritis norovirus | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Graft infection | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatitis B | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatobiliary infection | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infection | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infectious colitis | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 1 / 1752 (0.06%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infectious pleural effusion | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Influenza | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 2 / 1724 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Intervertebral discitis | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Klebsiella bacteraemia | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lower respiratory tract infection | | | |
| subjects affected / exposed | 3 / 1752 (0.17%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 2 / 4 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Mediastinitis | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Osteomyelitis | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Peritonitis | | | |

| | | | |
|---|-------------------|-------------------|--|
| subjects affected / exposed | 1 / 1752 (0.06%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia | | | |
| subjects affected / exposed | 12 / 1752 (0.68%) | 16 / 1724 (0.93%) | |
| occurrences causally related to treatment / all | 0 / 13 | 0 / 18 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 1 | |
| Post procedural cellulitis | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 2 / 1724 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Post procedural infection | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Post procedural pneumonia | | | |
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Postoperative wound infection | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pseudomembranous colitis | | | |
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pulmonary sepsis | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Puncture site infection | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory tract infection | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sepsis | | | |
| subjects affected / exposed | 4 / 1752 (0.23%) | 4 / 1724 (0.23%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Septic shock | | | |
| subjects affected / exposed | 2 / 1752 (0.11%) | 2 / 1724 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 1 | |
| Soft tissue infection | | | |
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Staphylococcal infection | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Staphylococcal sepsis | | | |
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Subcutaneous abscess | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Tracheobronchitis | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urinary tract infection | | | |
| subjects affected / exposed | 3 / 1752 (0.17%) | 5 / 1724 (0.29%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 5 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urinary tract infection bacterial | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urosepsis | | | |
| subjects affected / exposed | 2 / 1752 (0.11%) | 3 / 1724 (0.17%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Viral infection | | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 0 / 1724 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metabolism and nutrition disorders | | | |
| Dehydration | | | |
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diabetes mellitus | | | |
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diabetes mellitus inadequate control | | | |

| | | |
|---|------------------|------------------|
| subjects affected / exposed | 1 / 1752 (0.06%) | 1 / 1724 (0.06%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 |
| Gout | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 0 / 1724 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 |
| Hyperglycaemia | | |
| subjects affected / exposed | 1 / 1752 (0.06%) | 1 / 1724 (0.06%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 |
| Hypoglycaemia | | |
| subjects affected / exposed | 2 / 1752 (0.11%) | 1 / 1724 (0.06%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 |
| Hypokalaemia | | |
| subjects affected / exposed | 2 / 1752 (0.11%) | 0 / 1724 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 |
| Hyponatraemia | | |
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 |
| Metabolic acidosis | | |
| subjects affected / exposed | 0 / 1752 (0.00%) | 1 / 1724 (0.06%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 |
| Type 2 diabetes mellitus | | |
| subjects affected / exposed | 2 / 1752 (0.11%) | 1 / 1724 (0.06%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 |

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

| Non-serious adverse events | Placebo | Losmapimod 7.5 mg BID | |
|---|------------------------|--------------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 370 / 1752 (21.12%) | 376 / 1724 (21.81%) | |
| Investigations | | | |
| Troponin increased | | | |
| subjects affected / exposed | 39 / 1752 (2.23%) | 23 / 1724 (1.33%) | |
| occurrences (all) | 39 | 23 | |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 49 / 1752 (2.80%) | 33 / 1724 (1.91%) | |
| occurrences (all) | 49 | 34 | |
| Hypotension | | | |
| subjects affected / exposed | 29 / 1752 (1.66%) | 36 / 1724 (2.09%) | |
| occurrences (all) | 32 | 36 | |
| Cardiac disorders | | | |
| Angina pectoris | | | |
| subjects affected / exposed | 32 / 1752 (1.83%) | 40 / 1724 (2.32%) | |
| occurrences (all) | 33 | 40 | |
| Atrial fibrillation | | | |
| subjects affected / exposed | 65 / 1752 (3.71%) | 72 / 1724 (4.18%) | |
| occurrences (all) | 66 | 86 | |
| Nervous system disorders | | | |
| Dizziness | | | |
| subjects affected / exposed | 37 / 1752 (2.11%) | 39 / 1724 (2.26%) | |
| occurrences (all) | 39 | 41 | |
| Blood and lymphatic system disorders | | | |
| Anemia | | | |
| subjects affected / exposed | 35 / 1752 (2.00%) | 39 / 1724 (2.26%) | |
| occurrences (all) | 36 | 41 | |
| General disorders and administration site conditions | | | |
| Non-cardiac chest pain | | | |
| subjects affected / exposed | 41 / 1752 (2.34%) | 44 / 1724 (2.55%) | |
| occurrences (all) | 46 | 48 | |
| Gastrointestinal disorders | | | |

| | | | |
|--|--|--|--|
| Diarrhoea subjects affected / exposed occurrences (all) | 41 / 1752 (2.34%) 41 | 49 / 1724 (2.84%) 56 | |
| Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) Dyspnoea subjects affected / exposed occurrences (all) | 38 / 1752 (2.17%) 38 61 / 1752 (3.48%) 64 | 47 / 1724 (2.73%) 47 48 / 1724 (2.78%) 48 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

| |
|------|
| None |
|------|

Notes: