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	66.5	66.7	
standard deviation	± 9.72	± 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 occurence 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

	for HF through to Week 12 and Week 24

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:

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.

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 hypersenstivity			
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			

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			

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			

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			

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 occurrences (all)	39 / 1752 (2.23%) 39	23 / 1724 (1.33%) 23	
Vascular disorders Hypertension subjects affected / exposed occurrences (all)	49 / 1752 (2.80%) 49	33 / 1724 (1.91%) 34	
Hypotension subjects affected / exposed occurrences (all)	29 / 1752 (1.66%) 32	36 / 1724 (2.09%) 36	
Cardiac disorders Angina pectoris subjects affected / exposed occurrences (all)	32 / 1752 (1.83%) 33	40 / 1724 (2.32%) 40	
Atrial fibrillation subjects affected / exposed occurrences (all)	65 / 1752 (3.71%) 66	72 / 1724 (4.18%) 86	
Nervous system disorders Dizziness subjects affected / exposed occurrences (all)	37 / 1752 (2.11%) 39	39 / 1724 (2.26%) 41	
Blood and lymphatic system disorders Anemia subjects affected / exposed occurrences (all)	35 / 1752 (2.00%) 36	39 / 1724 (2.26%) 41	
General disorders and administration site conditions Non-cardiac chest pain subjects affected / exposed occurrences (all)	41 / 1752 (2.34%) 46	44 / 1724 (2.55%) 48	
Gastrointestinal disorders			

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