Clinical trial results:
A 30 day international, randomized, parallel-group, double-blind, placebo-controlled phase IV study to evaluate efficacy and safety of pre-hospital vs. in-hospital initiation of ticagrelor therapy in STEMI patients planned for PCI

Summary

EudraCT number	2011-000214-19
Trial protocol	GB DE AT SE DK NL ES IT HU
Global end of trial date	14 November 2013

Results information

Result version number	v1 (current)
This version publication date	04 March 2016
First version publication date	04 March 2016

Trial information

Trial identification

Sponsor protocol code	D5130L00006

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01347580
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	AstraZeneca
Sponsor organisation address	KC449/07 Pepparedsleden, Mölndal, Sweden,
Public contact	Dr Tomas Andersson MD, AstraZeneca, 46 8 553 260 00,
Scientific contact	Dr Tomas Andersson MD, AstraZeneca, tomas.lg.andersson@astrazeneca.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	23 April 2014
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	14 November 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the efficacy of pre-hospital vs. in-hospital initiation of ticagrelor therapy by comparing the percentage of patients reaching the co-primary endpoint of TIMI flow grade 3 of MI culprit vessel at initial angiography or a ≥70% ST-segment elevation resolution pre-PCI.

Protection of trial subjects:

Data Safety Monitoring Board

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	12 September 2011
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: 43
Country: Number of subjects enrolled	Austria: 42
Country: Number of subjects enrolled	Algeria: 36
Country: Number of subjects enrolled	Canada: 112
Country: Number of subjects enrolled	Denmark: 75
Country: Number of subjects enrolled	France: 660
Country: Number of subjects enrolled	Germany: 98
Country: Number of subjects enrolled	Hungary: 52
Country: Number of subjects enrolled	Italy: 83
Country: Number of subjects enrolled	Netherlands: 148
Country: Number of subjects enrolled	Spain: 131
Country: Number of subjects enrolled	Sweden: 202
Country: Number of subjects enrolled	United Kingdom: 180
Worldwide total number of subjects	1862
EEA total number of subjects	1671

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)	1179
From 65 to 84 years	683
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients were randomized in pre-hospital settings at 102 Emergency Medical Services between September 2011 and October 2013. 1875 patients were recruited in the study, 1862 consented patients were randomized.

Pre-assignment

Screening details:

no screening period

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Pre-hospital Ticagrelor

Arm description:

Loading dose of Ticagrelor (180 mg) followed by matching placebo. After the loading dose the patient will receive Ticagrelor (90 mg bid) for 30 days.

Arm type	time administration strategy
Investigational medicinal product name	Ticagrelor
Investigational medicinal product code	AZD6140
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

loading dose of ticagrelor (180mg) followed by matching placebo. After the loading dose the patient will receive ticagrelor (90 mg bid) for 30 days

Arm title	In-hospital Ticagrelor

Arm description:

Placebo followed by a loading dose of Ticagrelor (180 mg). After the loading dose the patient will receive Ticagrelor (90 mg bid) for 30 days.

Arm type	time administration strategy
Investigational medicinal product name	Ticagrelor
Investigational medicinal product code	AZD6140
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

placebo followed by a loading dose of ticagrelor (180 mg).After the loading dose the patient will receive ticagrelor (90 mg bid) for 30 days.

Number of subjects in period 1	Pre-hospital Ticagrelor	In-hospital Ticagrelor
Started	909	953
Baseline period	909	953
Modified Intent to Treat population	906	952
Safety population	908	950
Completed	844	897
Not completed	65	56
Adverse event, serious fatal	30	19
Consent withdrawn by subject	13	23
Had other reason	9	6
Lost to follow-up	3	1
Protocol deviation	10	7

Baseline characteristics

Reporting groups	
Reporting group title	Pre-hospital Ticagrelor
Reporting group description:	
Loading dose of Ticagrelor (180 mg) followed by matching placebo. After the loading dose the patient will receive Ticagrelor (90 mg bid) for 30 days.	
Reporting group title	In-hospital Ticagrelor
Reporting group description:	
Placebo followed by a loading dose of Ticagrelor (180 mg). After the loading dose the patient will receive Ticagrelor (90 mg bid) for 30 days.	

Reporting group values	Pre-hospital Ticagrelor	In-hospital Ticagrelor	Total
Number of subjects	909	953	1862
Age categorical			
lessthan 65 years , 65 years and more			
Units: Subjects			
Adults (18-64 years)	583	596	1179
65 years and over	326	357	683
Age Continuous | Years			
Units: years			
arithmetic mean	60.6	61	
standard deviation	± 12.38	± 12.49	-
Gender, Male/Female			
Units: participants			
Female	173	196	369
Male	736	757	1493
Diabetes mellitus			
Units: Subjects			
yes	115	138	253
no/unknown	794	815	1609
Thrombolysis in Myocardial Infarction (TIMI) risk score			
TIMI risk is a score based on independant predictors of mortality such as age, diabetes mellitus, history of hypertension, history of angina, ST segment elevation.			
Units: Subjects			
0-2	552	573	1125
3-6	337	365	702
>6	20	15	35
KILLIP CLASS			
Killip class assesses the presence and severity of heart failure by physical examination. Class I :No rales, no 3rd heart sound. Class 2: Rales in <1/2 lung field or presence of a 3rd heart sound. Class 3: Rales in >1/2 lung field–pulmonary edema.Class 4 : Cardiogenic shock–determined clinically.			
Units: Subjects			
I	819	862	1681
II, III, IV	51	43	94
unknown	39	48	87
Location of 1st medical contact			
Units: Subjects			

in ambulance	689	723	1412
in emergency department	220	230	450
Percutaneous coronary intervention (PCI)			
PCI is a non-surgery intervention performed to open blocked coronary arteries and to restore arterial blood flow to the heart tissue.			
Units: Subjects			
yes	800	830	1630
no	109	123	232
Any stents during PCI			
on patients with PCI			
Units: Subjects			
with stent	760	776	1536
without stent	40	54	94
no PCI	109	123	232
Time between the 2 loading doses			
Units: minutes			
median	32	30	
inter-quartile range (Q1-Q3)	22 to 45	22 to 43	-

End points

End points reporting groups	
Reporting group title	Pre-hospital Ticagrelor
Reporting group description:	
Loading dose of Ticagrelor (180 mg) followed by matching placebo. After the loading dose the patient will receive Ticagrelor (90 mg bid) for 30 days.	
Reporting group title	In-hospital Ticagrelor
Reporting group description:	
Placebo followed by a loading dose of Ticagrelor (180 mg). After the loading dose the patient will receive Ticagrelor (90 mg bid) for 30 days.	

Primary: TIMI flow grade 3 of MI culprit vessel (co-primary endpoint)	
End point title	TIMI flow grade 3 of MI culprit vessel (co-primary endpoint)
End point description:	
Thrombolysis In Myocardial Infarction (TIMI) flow grade classification is used to assess coronary blood flow in acute coronary syndromes. grade 0:no reperfusion, grade 1: penetration without perfusion, grade 2: Partial reperfusion, grade 3: complete perfusion.	
End point type	Primary
End point timeframe:	
At initial angiography, pre PCI	

End point values	Pre-hospital Ticagrelor	In-hospital Ticagrelor		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	824	856		
Units: patients	143	145		

Statistical analyses

Statistical analysis title	TIMI Flow grade 3 pre PCI
Comparison groups	Pre-hospital Ticagrelor v In-hospital Ticagrelor
Number of subjects included in analysis	1680
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8214 [1]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.799
upper limit	1.327

Notes:

[1] - pvalue at 0.025 , adjusted for multiple comparisons

Primary: ST-segment elevation resolution pre PCI ≥70% (co-primary endpoint)

End point title	ST-segment elevation resolution pre PCI ≥70% (co-primary endpoint)

End point description:

ST segment elevation resolution is the mean ST elevation pre-hospital minus the mean STelevation pre-PCI divided by the mean ST elevation pre-hospital. It is expressed as a percentage and split in 2 categories , complete (≥70%) versus incomplete (<70%) resolution.

End point type	Primary

End point timeframe:

Between baseline and PCI

End point values	Pre-hospital Ticagrelor	In-hospital Ticagrelor		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	774	824		
Units: patients	102	102		

Statistical analyses

Statistical analysis title	ST segment Elevation Resolution pre-PCI >= 70%
Comparison groups	Pre-hospital Ticagrelor v In-hospital Ticagrelor
Number of subjects included in analysis	1598
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6322 [2]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.074
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.801
upper limit	1.441

Notes:

[2] - P value at 0.025 adjusted for multiple comparisons

Secondary: 1st Composite clinical endpoint

End point title	1st Composite clinical endpoint

End point description:

death/MI/stroke/urgent revascularization/stent thrombosis. Adjudicated events except death

End point type	Secondary

End point timeframe:

during the 30 days of treatment

End point values	Pre-hospital Ticagrelor	In-hospital Ticagrelor		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	906	952		
Units: patients	41	42		

Statistical analyses

Statistical analysis title	first composite endpoint
Statistical analysis description: death, MI, stroke, urgent revascularisation, stent thrombosis.	
Comparison groups	Pre-hospital Ticagrelor v In-hospital Ticagrelor
Number of subjects included in analysis	1858
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9056
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.027
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.661
upper limit	1.595

Secondary: 2nd composite clinical endpoint

End point title	2nd composite clinical endpoint
End point description: Death/MI/urgent revascularization. Adjudicated events except death	
End point type	Secondary
End point timeframe: within 30 days of study	

End point values	Pre-hospital Ticagrelor	In-hospital Ticagrelor		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	906	952		
Units: patients	39	34		

Statistical analyses

Statistical analysis title	second composite clinical endpoint
Statistical analysis description: death, MI, urgent revascularisation. adjudicated event except deaths	
Comparison groups	Pre-hospital Ticagrelor v In-hospital Ticagrelor
Number of subjects included in analysis	1858
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4168
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.215
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.76
upper limit	1.942

Secondary: Definite stent thrombosis	
End point title	Definite stent thrombosis
End point description: Definite stent thrombosis is considered to have occurred by either angiographic or pathologic confirmation. It is an adjudicated endpoint	
End point type	Secondary
End point timeframe: during 30 days of treatment	

End point values	Pre-hospital Ticagrelor	In-hospital Ticagrelor		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	906	952		
Units: patients	2	11		

Statistical analyses

Statistical analysis title	definite stent thrombosis

Statistical analysis description: adjudicated endpoint, within 30 days of study	
Comparison groups	Pre-hospital Ticagrelor v In-hospital Ticagrelor
Number of subjects included in analysis	1858
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0307
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.189
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.042
upper limit	0.856

Secondary: TIMI flow grade 3 post -PCI	
End point title	TIMI flow grade 3 post -PCI
End point description: TIMI) flow grade 3 is complete perfusion post-PCI.	
End point type	Secondary
End point timeframe: at coroangiography post-PCI	

End point values	Pre-hospital Ticagrelor	In-hospital Ticagrelor		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	760	784		
Units: patients	625	630		

Statistical analyses

Statistical analysis title	TIMI flow grade 3 post PCI
Comparison groups	Pre-hospital Ticagrelor v In-hospital Ticagrelor
Number of subjects included in analysis	1544
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.344
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.132

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.876
upper limit	1.462

Secondary: ST segment elevation resolution post-PCI >= 70%

End point title	ST segment elevation resolution post-PCI >= 70%
End point description:	
ST segment elevation resolution post PCI >=70% is defined as complete resolution	
End point type	Secondary
End point timeframe:	
Between baseline and ECG 60 mn post-PCI	

End point values	Pre-hospital Ticagrelor	In-hospital Ticagrelor		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	713	743		
Units: patients	410	390		

Statistical analyses

Statistical analysis title	ST segment elevation resolution post-PCI >= 70%
Comparison groups	Pre-hospital Ticagrelor v In-hospital Ticagrelor
Number of subjects included in analysis	1456
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0547
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.225
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.996
upper limit	1.506

Secondary: Thrombotic bail-out with GPIIb/IIIa inhibitors at initial PCI

End point title	Thrombotic bail-out with GPIIb/IIIa inhibitors at initial PCI
End point description:	
Glycoprotein (GP) IIb/IIIa inhibitors are often used as a rescue or bailout therapy to manage complications arising during percutaneous coronary intervention.	

End point type	Secondary
End point timeframe: during PCI	

End point values	Pre-hospital Ticagrelor	In-hospital Ticagrelor		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	906	952		
Units: patients	78	100		

Statistical analyses

Statistical analysis title	Thrombotic bail-out
Statistical analysis description: with GPIIb/IIIa inhibitors at initial PCI	
Comparison groups	Pre-hospital Ticagrelor v In-hospital Ticagrelor
Number of subjects included in analysis	1858
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.166
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.803
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.588
upper limit	1.096

Secondary: Major Bleeds within 48 hours	
End point title	Major Bleeds within 48 hours
End point description: non CABG related bleeds, (PLATO definition) include Life threatening and other major bleeds	
End point type	Secondary
End point timeframe: within 48 hours of first dose	

End point values	Pre-hospital Ticagrelor	In-hospital Ticagrelor		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	908	950		
Units: patients	16	15		

Statistical analyses

No statistical analyses for this end point

Secondary: Minor and Major bleedings within 48 hours

End point title	Minor and Major bleedings within 48 hours

End point description:

non CABG related bleeds (PLATO definition)

End point type	Secondary

End point timeframe:

within 48 hours of first dose

End point values	Pre-hospital Ticagrelor	In-hospital Ticagrelor		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	908	950		
Units: patients	24	24		

Statistical analyses

No statistical analyses for this end point

Secondary: Major Bleeds after 48 hours

End point title	Major Bleeds after 48 hours

End point description:

non CABG related bleeds (PLATO definition) include life threatening and other major bleedings

End point type	Secondary

End point timeframe:

after 48hours post-first dose

End point values	Pre-hospital Ticagrelor	In-hospital Ticagrelor		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	908	950		
Units: patients	11	11		

Statistical analyses

No statistical analyses for this end point

Secondary: Minor and Major bleeds after 48 hours

End point title	Minor and Major bleeds after 48 hours

End point description:

non CABG related bleeds (PLATO definition)

End point type	Secondary

End point timeframe:

after 48 hours post first dose

End point values	Pre-hospital Ticagrelor	In-hospital Ticagrelor		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	908	950		
Units: patients	18	16		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
within 30 days of study	
Adverse event reporting additional description:	
Actual Treatment Safety analysis set concerns 1858 patients - Ticagrelor pre-hosp:908 and Ticagrelor in-hosp: 950. 4 patients receiveived study medication not according to randomization assignment	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	16.1

Reporting groups	
Reporting group title	Ticagrelor Pre-Hosp
Reporting group description:	
Loading dose of Ticagrelor (180 mg) followed by matching placebo. After the loading dose the patient will receive Ticagrelor (90 mg bid) for 30 days.	
Reporting group title	Ticagrelor In-Hosp
Reporting group description:	
Placebo followed by a loading dose of Ticagrelor (180 mg). After the loading dose the patient will receive Ticagrelor (90 mg bid) for 30 days.	

Serious adverse events	Ticagrelor Pre-Hosp	Ticagrelor In-Hosp	
Total subjects affected by serious adverse events			
subjects affected / exposed	140 / 908 (15.42%)	143 / 950 (15.05%)	
number of deaths (all causes)	30	19	
number of deaths resulting from adverse events	1	3	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
ADRENAL ADENOMA			
subjects affected / exposed	0 / 908 (0.00%)	1 / 950 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
BLADDER NEOPLASM			
subjects affected / exposed	0 / 908 (0.00%)	1 / 950 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
CARDIAC MYXOMA			

subjects affected / exposed	1 / 908 (0.11%)	0 / 950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
EXTRANODAL MARGINAL ZONE B-CELL LYMPHOMA (MALT TYPE)			
subjects affected / exposed	0 / 908 (0.00%)	1 / 950 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
RECTAL NEOPLASM			
subjects affected / exposed	1 / 908 (0.11%)	0 / 950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
RENAL CANCER METASTATIC			
subjects affected / exposed	1 / 908 (0.11%)	0 / 950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
AORTIC DISSECTION			
subjects affected / exposed	2 / 908 (0.22%)	1 / 950 (0.11%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
ARTERY DISSECTION			
subjects affected / exposed	0 / 908 (0.00%)	2 / 950 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
HAEMATOMA			
subjects affected / exposed	1 / 908 (0.11%)	0 / 950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
HAEMODYNAMIC INSTABILITY			
subjects affected / exposed	1 / 908 (0.11%)	0 / 950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
HYPERTENSION			

subjects affected / exposed	1 / 908 (0.11%)	0 / 950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
HYPOTENSION			
subjects affected / exposed	1 / 908 (0.11%)	1 / 950 (0.11%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
THROMBOPHLEBITIS			
subjects affected / exposed	1 / 908 (0.11%)	0 / 950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ORTHOSTATIC HYPOTENSION			
subjects affected / exposed	0 / 908 (0.00%)	1 / 950 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
ASTHENIA			
subjects affected / exposed	1 / 908 (0.11%)	0 / 950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
CARDIAC DEATH			
subjects affected / exposed	1 / 908 (0.11%)	0 / 950 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
CHEST PAIN			
subjects affected / exposed	1 / 908 (0.11%)	4 / 950 (0.42%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
DEVICE MALFUNCTION			
subjects affected / exposed	1 / 908 (0.11%)	0 / 950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
MULTI-ORGAN FAILURE			

subjects affected / exposed	2 / 908 (0.22%)	1 / 950 (0.11%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 2	0 / 1	
NON-CARDIAC CHEST PAIN			
subjects affected / exposed	4 / 908 (0.44%)	5 / 950 (0.53%)	
occurrences causally related to treatment / all	0 / 4	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
SUDDEN CARDIAC DEATH			
subjects affected / exposed	0 / 908 (0.00%)	1 / 950 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
SUDDEN DEATH			
subjects affected / exposed	2 / 908 (0.22%)	1 / 950 (0.11%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 2	0 / 1	
THROMBOSIS IN DEVICE			
subjects affected / exposed	0 / 908 (0.00%)	1 / 950 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
VESSEL PUNCTURE SITE HAEMATOMA			
subjects affected / exposed	1 / 908 (0.11%)	0 / 950 (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	3 / 908 (0.33%)	3 / 950 (0.32%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 1	0 / 0	
ACUTE RESPIRATORY DISTRESS SYNDROME			
subjects affected / exposed	1 / 908 (0.11%)	0 / 950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

ATELECTASIS			
subjects affected / exposed	0 / 908 (0.00%)	1 / 950 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
CHRONIC OBSTRUCTIVE PULMONARY DISEASE			
subjects affected / exposed	0 / 908 (0.00%)	1 / 950 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
DIAPHRAGMATIC PARALYSIS			
subjects affected / exposed	0 / 908 (0.00%)	1 / 950 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
DYSPNOEA			
subjects affected / exposed	2 / 908 (0.22%)	1 / 950 (0.11%)	
occurrences causally related to treatment / all	1 / 2	1 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
HAEMOTHORAX			
subjects affected / exposed	0 / 908 (0.00%)	2 / 950 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
LUNG DISORDER			
subjects affected / exposed	1 / 908 (0.11%)	0 / 950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PLEURAL EFFUSION			
subjects affected / exposed	1 / 908 (0.11%)	0 / 950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PULMONARY EMBOLISM			
subjects affected / exposed	1 / 908 (0.11%)	1 / 950 (0.11%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
PULMONARY OEDEMA			

subjects affected / exposed	4 / 908 (0.44%)	1 / 950 (0.11%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
RESPIRATORY DISTRESS			
subjects affected / exposed	0 / 908 (0.00%)	1 / 950 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
RESPIRATORY FAILURE			
subjects affected / exposed	0 / 908 (0.00%)	1 / 950 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
ANXIETY			
subjects affected / exposed	0 / 908 (0.00%)	1 / 950 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
CONFUSIONAL STATE			
subjects affected / exposed	0 / 908 (0.00%)	1 / 950 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
SUICIDE ATTEMPT			
subjects affected / exposed	1 / 908 (0.11%)	0 / 950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
HAEMOGLOBIN DECREASED			
subjects affected / exposed	0 / 908 (0.00%)	1 / 950 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
HEPATIC ENZYME INCREASED			
subjects affected / exposed	1 / 908 (0.11%)	0 / 950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
NUTRITIONAL CONDITION			

ABNORMAL			
subjects affected / exposed	1 / 908 (0.11%)	0 / 950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PLATELET COUNT DECREASED			
subjects affected / exposed	1 / 908 (0.11%)	0 / 950 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
TROPONIN INCREASED			
subjects affected / exposed	2 / 908 (0.22%)	0 / 950 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
FEMORAL NECK FRACTURE			
subjects affected / exposed	1 / 908 (0.11%)	0 / 950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
POST PROCEDURAL HAEMATOMA			
subjects affected / exposed	1 / 908 (0.11%)	1 / 950 (0.11%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
POST PROCEDURAL HAEMORRHAGE			
subjects affected / exposed	1 / 908 (0.11%)	2 / 950 (0.21%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
PROCEDURAL HAEMORRHAGE			
subjects affected / exposed	3 / 908 (0.33%)	0 / 950 (0.00%)	
occurrences causally related to treatment / all	2 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
SUBDURAL HAEMATOMA			
subjects affected / exposed	1 / 908 (0.11%)	0 / 950 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

TRAUMATIC HAEMATOMA			
subjects affected / exposed	1 / 908 (0.11%)	0 / 950 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
UPPER LIMB FRACTURE			
subjects affected / exposed	1 / 908 (0.11%)	0 / 950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
VASCULAR PSEUDOANEURYSM			
subjects affected / exposed	0 / 908 (0.00%)	1 / 950 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congenital, familial and genetic disorders			
VENTRICULAR SEPTAL DEFECT			
subjects affected / exposed	0 / 908 (0.00%)	1 / 950 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cardiac disorders			
ACUTE MYOCARDIAL INFARCTION			
subjects affected / exposed	1 / 908 (0.11%)	1 / 950 (0.11%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
ANGINA PECTORIS			
subjects affected / exposed	3 / 908 (0.33%)	2 / 950 (0.21%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
ANGINA UNSTABLE			
subjects affected / exposed	1 / 908 (0.11%)	1 / 950 (0.11%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
AORTIC VALVE INCOMPETENCE			
subjects affected / exposed	0 / 908 (0.00%)	1 / 950 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

ARRHYTHMIA			
subjects affected / exposed	1 / 908 (0.11%)	1 / 950 (0.11%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
ARTERIOSPASM CORONARY			
subjects affected / exposed	0 / 908 (0.00%)	2 / 950 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
ATRIAL FIBRILLATION			
subjects affected / exposed	4 / 908 (0.44%)	2 / 950 (0.21%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
ATRIOVENTRICULAR BLOCK COMPLETE			
subjects affected / exposed	1 / 908 (0.11%)	3 / 950 (0.32%)	
occurrences causally related to treatment / all	1 / 1	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
BRADYCARDIA			
subjects affected / exposed	1 / 908 (0.11%)	2 / 950 (0.21%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
CARDIAC ARREST			
subjects affected / exposed	11 / 908 (1.21%)	7 / 950 (0.74%)	
occurrences causally related to treatment / all	0 / 11	0 / 7	
deaths causally related to treatment / all	0 / 5	0 / 1	
CARDIAC ASTHMA			
subjects affected / exposed	0 / 908 (0.00%)	1 / 950 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
CARDIAC FAILURE			
subjects affected / exposed	7 / 908 (0.77%)	7 / 950 (0.74%)	
occurrences causally related to treatment / all	0 / 7	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
CARDIAC FAILURE ACUTE			

subjects affected / exposed	2 / 908 (0.22%)	0 / 950 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
CARDIAC TAMPONADE			
subjects affected / exposed	1 / 908 (0.11%)	0 / 950 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
CARDIOGENIC SHOCK			
subjects affected / exposed	17 / 908 (1.87%)	16 / 950 (1.68%)	
occurrences causally related to treatment / all	1 / 17	0 / 16	
deaths causally related to treatment / all	0 / 5	0 / 2	
CARDIOPULMONARY FAILURE			
subjects affected / exposed	1 / 908 (0.11%)	0 / 950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
CONGESTIVE CARDIOMYOPATHY			
subjects affected / exposed	0 / 908 (0.00%)	1 / 950 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
CORONARY ARTERY OCCLUSION			
subjects affected / exposed	1 / 908 (0.11%)	0 / 950 (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	2 / 908 (0.22%)	1 / 950 (0.11%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
INTERVENTRICULAR SEPTUM RUPTURE			
subjects affected / exposed	0 / 908 (0.00%)	1 / 950 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
INTRACARDIAC THROMBUS			

subjects affected / exposed	2 / 908 (0.22%)	4 / 950 (0.42%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
LEFT VENTRICULAR DYSFUNCTION			
subjects affected / exposed	0 / 908 (0.00%)	1 / 950 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
LEFT VENTRICULAR FAILURE			
subjects affected / exposed	2 / 908 (0.22%)	0 / 950 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
MYOCARDIAL RUPTURE			
subjects affected / exposed	1 / 908 (0.11%)	1 / 950 (0.11%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
PALPITATIONS			
subjects affected / exposed	0 / 908 (0.00%)	2 / 950 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
PERICARDIAL EFFUSION			
subjects affected / exposed	0 / 908 (0.00%)	4 / 950 (0.42%)	
occurrences causally related to treatment / all	0 / 0	1 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
PERICARDITIS			
subjects affected / exposed	0 / 908 (0.00%)	1 / 950 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
TORSADE DE POINTES			
subjects affected / exposed	1 / 908 (0.11%)	0 / 950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
VENTRICLE RUPTURE			

subjects affected / exposed	1 / 908 (0.11%)	1 / 950 (0.11%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 1	1 / 1	
VENTRICULAR EXTRASYSTOLES			
subjects affected / exposed	0 / 908 (0.00%)	1 / 950 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
VENTRICULAR FIBRILLATION			
subjects affected / exposed	23 / 908 (2.53%)	30 / 950 (3.16%)	
occurrences causally related to treatment / all	0 / 23	0 / 30	
deaths causally related to treatment / all	0 / 1	0 / 2	
VENTRICULAR SEPTAL DEFECT ACQUIRED			
subjects affected / exposed	1 / 908 (0.11%)	0 / 950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
VENTRICULAR TACHYCARDIA			
subjects affected / exposed	6 / 908 (0.66%)	7 / 950 (0.74%)	
occurrences causally related to treatment / all	0 / 6	2 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
CEREBRAL HAEMORRHAGE			
subjects affected / exposed	0 / 908 (0.00%)	2 / 950 (0.21%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	2 / 2	
CEREBROVASCULAR ACCIDENT			
subjects affected / exposed	1 / 908 (0.11%)	0 / 950 (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	0 / 908 (0.00%)	1 / 950 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
DYSARTHRIA			

subjects affected / exposed	0 / 908 (0.00%)	1 / 950 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
HAEMORRHAGE INTRACRANIAL			
subjects affected / exposed	1 / 908 (0.11%)	0 / 950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
HEMIPARESIS			
subjects affected / exposed	1 / 908 (0.11%)	0 / 950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
LACUNAR INFARCTION			
subjects affected / exposed	1 / 908 (0.11%)	0 / 950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PRESYNCOPE			
subjects affected / exposed	1 / 908 (0.11%)	0 / 950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
SYNCOPE			
subjects affected / exposed	1 / 908 (0.11%)	0 / 950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
TRANSIENT ISCHAEMIC ATTACK			
subjects affected / exposed	1 / 908 (0.11%)	3 / 950 (0.32%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	1 / 908 (0.11%)	2 / 950 (0.21%)	
occurrences causally related to treatment / all	0 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
LEUKOCYTOSIS			

subjects affected / exposed	1 / 908 (0.11%)	0 / 950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
VERTIGO			
subjects affected / exposed	1 / 908 (0.11%)	0 / 950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
ABDOMINAL PAIN UPPER			
subjects affected / exposed	0 / 908 (0.00%)	1 / 950 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
COLITIS			
subjects affected / exposed	0 / 908 (0.00%)	1 / 950 (0.11%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
COLITIS ISCHAEMIC			
subjects affected / exposed	1 / 908 (0.11%)	0 / 950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
DIARRHOEA			
subjects affected / exposed	1 / 908 (0.11%)	1 / 950 (0.11%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
GASTRIC ULCER			
subjects affected / exposed	0 / 908 (0.00%)	1 / 950 (0.11%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
GASTRIC ULCER HAEMORRHAGE			
subjects affected / exposed	0 / 908 (0.00%)	1 / 950 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
GASTRITIS			

subjects affected / exposed	0 / 908 (0.00%)	1 / 950 (0.11%)	
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	2 / 908 (0.22%)	0 / 950 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
GASTROINTESTINAL TELANGIECTASIA			
subjects affected / exposed	1 / 908 (0.11%)	0 / 950 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
HAEMATEMESIS			
subjects affected / exposed	1 / 908 (0.11%)	0 / 950 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
HAEMATOCHEZIA			
subjects affected / exposed	1 / 908 (0.11%)	0 / 950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
INTESTINAL ISCHAEMIA			
subjects affected / exposed	1 / 908 (0.11%)	0 / 950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
MELAENA			
subjects affected / exposed	1 / 908 (0.11%)	1 / 950 (0.11%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
RECTAL HAEMORRHAGE			
subjects affected / exposed	0 / 908 (0.00%)	1 / 950 (0.11%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
RETROPERITONEAL HAEMATOMA			

subjects affected / exposed	2 / 908 (0.22%)	0 / 950 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
BILIARY COLIC			
subjects affected / exposed	0 / 908 (0.00%)	1 / 950 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
CHOLECYSTITIS			
subjects affected / exposed	0 / 908 (0.00%)	1 / 950 (0.11%)	
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	2 / 908 (0.22%)	1 / 950 (0.11%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
RASH PRURITIC			
subjects affected / exposed	0 / 908 (0.00%)	1 / 950 (0.11%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
HAEMATURIA			
subjects affected / exposed	1 / 908 (0.11%)	0 / 950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
RENAL COLIC			
subjects affected / exposed	0 / 908 (0.00%)	1 / 950 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
RENAL FAILURE			
subjects affected / exposed	2 / 908 (0.22%)	2 / 950 (0.21%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

RENAL FAILURE ACUTE			
subjects affected / exposed	2 / 908 (0.22%)	0 / 950 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
MUSCULOSKELETAL CHEST PAIN			
subjects affected / exposed	1 / 908 (0.11%)	0 / 950 (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 / 908 (0.00%)	1 / 950 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
PAIN IN JAW			
subjects affected / exposed	0 / 908 (0.00%)	1 / 950 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
PATHOLOGICAL FRACTURE			
subjects affected / exposed	1 / 908 (0.11%)	0 / 950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
BILIARY SEPSIS			
subjects affected / exposed	1 / 908 (0.11%)	0 / 950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
BRONCHITIS			
subjects affected / exposed	1 / 908 (0.11%)	0 / 950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
GASTROENTERITIS VIRAL			
subjects affected / exposed	0 / 908 (0.00%)	1 / 950 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

GROIN INFECTION			
subjects affected / exposed	1 / 908 (0.11%)	0 / 950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
LUNG INFECTION			
subjects affected / exposed	0 / 908 (0.00%)	1 / 950 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
PNEUMONIA			
subjects affected / exposed	2 / 908 (0.22%)	1 / 950 (0.11%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
RELAPSING FEVER			
subjects affected / exposed	1 / 908 (0.11%)	0 / 950 (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	1 / 908 (0.11%)	0 / 950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
SEPTIC SHOCK			
subjects affected / exposed	1 / 908 (0.11%)	0 / 950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
SKIN INFECTION			
subjects affected / exposed	1 / 908 (0.11%)	0 / 950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
URINARY TRACT INFECTION			
subjects affected / exposed	0 / 908 (0.00%)	1 / 950 (0.11%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
UROSEPSIS			

subjects affected / exposed	1 / 908 (0.11%)	0 / 950 (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	1 / 908 (0.11%)	0 / 950 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
DIABETES MELLITUS			
subjects affected / exposed	1 / 908 (0.11%)	0 / 950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 3 %

Non-serious adverse events	Ticagrelor Pre-Hosp	Ticagrelor In-Hosp	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	469 / 908 (51.65%)	529 / 950 (55.68%)	
Vascular disorders			
Hypotension			
subjects affected / exposed	44 / 908 (4.85%)	30 / 950 (3.16%)	
occurrences (all)	45	32	
Cardiac disorders			
Ventricular tachycardia			
subjects affected / exposed	79 / 908 (8.70%)	81 / 950 (8.53%)	
occurrences (all)	85	81	
Atrial fibrillation			
subjects affected / exposed	30 / 908 (3.30%)	38 / 950 (4.00%)	
occurrences (all)	32	39	
Ventricular fibrillation			
subjects affected / exposed	32 / 908 (3.52%)	37 / 950 (3.89%)	
occurrences (all)	33	39	
Cardiac failure			
subjects affected / exposed	30 / 908 (3.30%)	33 / 950 (3.47%)	
occurrences (all)	30	35	
Bradycardia			

subjects affected / exposed	28 / 908 (3.08%)	26 / 950 (2.74%)	
occurrences (all)	31	28	
Nervous system disorders			
Headache			
subjects affected / exposed	19 / 908 (2.09%)	31 / 950 (3.26%)	
occurrences (all)	20	33	
General disorders and administration site conditions			
Non cardiac chest pain			
subjects affected / exposed	42 / 908 (4.63%)	52 / 950 (5.47%)	
occurrences (all)	47	55	
Gastrointestinal disorders			
Dyspnoea			
subjects affected / exposed	62 / 908 (6.83%)	86 / 950 (9.05%)	
occurrences (all)	63	87	
Nausea			
subjects affected / exposed	41 / 908 (4.52%)	49 / 950 (5.16%)	
occurrences (all)	42	49	
Vomiting			
subjects affected / exposed	34 / 908 (3.74%)	40 / 950 (4.21%)	
occurrences (all)	36	40	
Metabolism and nutrition disorders			
Hypokalaemia			
subjects affected / exposed	28 / 908 (3.08%)	26 / 950 (2.74%)	
occurrences (all)	28	26	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
22 June 2011	To introduce an ECG sub-study to the ATLANTIC main study. This amendment was never implemented.
19 December 2011	To introduce the PRIVATE ATLANTIC sub-study to the main study. This was implemented in France and UK only.

Notes:

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.

This urgent setting study included 8.6% of patients with symptoms of MI in ambulance but having finally not a STEMI diagnosis in cathlab.
No prespecified hypothesis and procedure for adjustment was made on secondary endpoints.

Notes:

Online references

http://www.ncbi.nlm.nih.gov/pubmed/25175921