Clinical trial results:
Multicenter, randomized, active comparator-controlled, double-blind, double-dummy, parallel group, dose-finding Phase 2 study to compare the safety of the oral FXIa inhibitor BAY 2433334 to apixaban in patients with atrial fibrillation

Summary

EudraCT number	2019-002365-35
Trial protocol	CZ SE NL FR GB HU BE LV AT ES IT
Global end of trial date	08 October 2021

Results information

Result version number	v1 (current)
This version publication date	11 October 2022
First version publication date	11 October 2022

Trial information

Trial identification

Sponsor protocol code	BAY2433334/19765

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04218266
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Bayer AG
Sponsor organisation address	Kaiser-Wilhelm-Allee, Leverkusen, Germany, D-51368
Public contact	Therapeutic Area Head, Bayer AG, clinical-trials-contact@bayer.com
Scientific contact	Therapeutic Area Head, Bayer AG, clinical-trials-contact@bayer.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	05 November 2021
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	08 October 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate that the oral FXIa inhibitor BAY 2433334 (asundexian) when compared to apixaban leads to a lower incidence of bleeding in participants with atrial fibrillation

Protection of trial subjects:

The conduct of this clinical study met all local legal and regulatory requirements. The study was conducted in accordance with ethical principles that have their origin in the Declaration of Helsinki and the International Council for Harmonization guideline E6: Good Clinical Practice. Before entering the study, the informed consent was read by and explained to all the subjects. Participating subjects signed informed consent form and could withdraw from the study at any time without any disadvantage and without having to provide a reason for this decision. Only investigators qualified by training and experience were selected as appropriate experts to investigate the study drug.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	30 January 2020
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	Japan: 119
Country: Number of subjects enrolled	Czechia: 64
Country: Number of subjects enrolled	Hungary: 105
Country: Number of subjects enrolled	Latvia: 95
Country: Number of subjects enrolled	Canada: 21
Country: Number of subjects enrolled	Austria: 52
Country: Number of subjects enrolled	Belgium: 41
Country: Number of subjects enrolled	Switzerland: 20
Country: Number of subjects enrolled	Spain: 32
Country: Number of subjects enrolled	France: 49
Country: Number of subjects enrolled	United Kingdom: 37
Country: Number of subjects enrolled	Italy: 47
Country: Number of subjects enrolled	Netherlands: 49
Country: Number of subjects enrolled	Sweden: 24
Worldwide total number of subjects	755
EEA total number of subjects	558

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)	110
From 65 to 84 years	582
85 years and over	63

Subject disposition

Recruitment

Recruitment details:

Study was conducted at 94 centers in 14 countries or regions, between 30-Jan-2020 (first subject first visit) and 08-Oct-2021 (last subject last visit)

Pre-assignment

Screening details:

862 subjects were enrolled. 107 subjects were screening failures. 755 subjects were randomized in a 1:1:1 ratio to 3 treatment groups: 251 subjects to the asundexian 20 mg group, 254 subjects to the asundexian 50 mg group and 250 subjects to the apixaban group. 2 subjects of asundexian 20 mg group never administered drug.

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Asundexian 20 mg

Arm description:

Subjects received Asundexian (BAY2433334) 20 mg and Apixaban placebo for 12 weeks

Arm type	Experimental
Investigational medicinal product name	Asundexian
Investigational medicinal product code	BAY2433334
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received Asundexian (BAY2433334) 20 mg (5 mg and 15 mg tablets) orally once daily in the morning, and Apixaban placebo capsule orally twice daily for 12 weeks

Arm title	Asundexian 50 mg

Arm description:

Subjects received Asundexian (BAY2433334) 50 mg and Apixaban placebo for 12 weeks

Arm type	Experimental
Investigational medicinal product name	Asundexian
Investigational medicinal product code	BAY2433334
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received Asundexian (BAY2433334) 50 mg (two 25 mg tablets) orally once daily in the morning, and Apixaban placebo capsule orally twice daily for 12 weeks

Arm title	Apixaban

Arm description:

Subjects received Asundexian (BAY2433334) placebo and Apixaban for 12 weeks

Arm type	Active comparator

Investigational medicinal product name	Apixaban
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Subjects received Asundexian (BAY2433334) placebo tablet orally once daily in the morning, and Apixaban 2.5 mg or 5 mg capsule orally twice daily for 12 weeks

Number of subjects in period 1[1]	Asundexian 20 mg	Asundexian 50 mg	Apixaban
Started	249	254	250
Completed	226	227	218
Not completed	23	27	32
Consent withdrawn by subject	1	3	1
Physician decision	1	3	2
Adverse event, non-fatal	13	14	11
Death	1	2	3
Non-compliance with study drug	-	-	1
Unspecified	7	5	14

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: The worldwide number of subjects enrolled was 755, however, the baseline data is presented for the 753 subjects treated.

Baseline characteristics

Reporting groups	
Reporting group title	Asundexian 20 mg
Reporting group description:	
Subjects received Asundexian (BAY2433334) 20 mg and Apixaban placebo for 12 weeks	
Reporting group title	Asundexian 50 mg
Reporting group description:	
Subjects received Asundexian (BAY2433334) 50 mg and Apixaban placebo for 12 weeks	
Reporting group title	Apixaban
Reporting group description:	
Subjects received Asundexian (BAY2433334) placebo and Apixaban for 12 weeks	

Reporting group values	Asundexian 20 mg	Asundexian 50 mg	Apixaban
Number of subjects	249	254	250
Age Categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	33	43	34
From 65-84 years	198	191	191
85 years and over	18	20	25
Gender Categorical Units: Subjects			
Female	102	97	109
Male	147	157	141
Race Units: Subjects			
Asian	39	40	40
Black or African American	1	1	1
White	209	212	209
Not reported	0	1	0

Reporting group values	Total		
Number of subjects	753		
Age Categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	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)	110		
From 65-84 years	580		
85 years and over	63		
Gender Categorical Units: Subjects			
Female	308		
Male	445		
Race Units: Subjects			
Asian	119		
Black or African American	3		
White	630		
Not reported	1		

End points

End points reporting groups

Reporting group title	Asundexian 20 mg
Reporting group description:	
Subjects received Asundexian (BAY2433334) 20 mg and Apixaban placebo for 12 weeks	
Reporting group title	Asundexian 50 mg
Reporting group description:	
Subjects received Asundexian (BAY2433334) 50 mg and Apixaban placebo for 12 weeks	
Reporting group title	Apixaban
Reporting group description:	
Subjects received Asundexian (BAY2433334) placebo and Apixaban for 12 weeks	
Subject analysis set title	Safety analysis set (SAF)
Subject analysis set type	Safety analysis
Subject analysis set description:	
A subject was included in the SAF if he/she was randomized to a treatment group and had taken at least one unit of the study medication.	
Subject analysis set title	Asundexian pooled
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Asundexian 20 mg group and Asundexian 50 mg group	

Primary: Number of subjects with composite of International Society on Thrombosis and Hemostasis (ISTH) major bleeding or clinically relevant non-major (CRNM) bleeding

End point title	Number of subjects with composite of International Society on Thrombosis and Hemostasis (ISTH) major bleeding or clinically relevant non-major (CRNM) bleeding

End point description:

ISTH Major Bleeding criteria: 1. Fatal bleeding, and/or 2. Symptomatic bleeding in a critical area or organ (intracranial, intraocular, intraspinal, pericardial, retroperitoneal, intraarticular, or intramuscular with compartment syndrome), and/or 3. Clinically overt bleeding associated with a recent decrease in the hemoglobin level of ≥ 2 g/dL (20 g/L; 1.24 mmol/L) compared to the most recent hemoglobin value available before the event, and/or 4. Clinically overt bleeding leading to transfusion of 2 or more units of packed red blood cells or whole blood.
ISTH Clinically Relevant Non-Major Bleeding is considered any sign or symptom of hemorrhage that does not fit the criteria for the ISTH definition of major bleeding, but does meet at least one of the following criteria 1. requiring medical intervention by a healthcare professional. 2. leading to hospitalization or increased level of care. 3. prompting a face to face (i.e. not just a telephone or electronic communication) evaluation.

End point type	Primary

End point timeframe:

After the first administration of study intervention with an average administration of 12 weeks (but not starting after more than 2 days after the last administration)

End point values	Asundexian 20 mg	Asundexian 50 mg	Apixaban	Asundexian pooled
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	249	254	250	503
Units: Subjects				
ISTH major bleeding or CRNM bleeding	3	1	6	4

Statistical analyses

Statistical analysis title	Pooled ratio of the incidence proportions
Statistical analysis description:	
Comparison of the Asundexian pooled group versus Apixaban group in ISTH major bleeding or CRNM bleeding	
Comparison groups	Apixaban v Asundexian pooled
Number of subjects included in analysis	753
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Crude incidence ratio
Point estimate	0.33
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.09
upper limit	0.97

Secondary: Number of subjects with all bleeding

End point title	Number of subjects with all bleeding
End point description:	
Adjudication of all bleeding events was performed by members of the Clinical events committee (CEC) who reviewed events in a blinded fashion and adjudicated and classified the following events in a consistent and unbiased manner according to the following classifications: ISTH (major, clinically relevant non-major and minor); Thrombolysis in myocardial infarction (TIMI major, minor, requiring medical attention, minimal); Bleeding Academic Research Consortium (BARC type 1, 2, 3, 5).	
End point type	Secondary
End point timeframe:	
After the first administration of study intervention with an average administration of 12 weeks (but not starting after more than 2 days after the last administration)	

End point values	Asundexian 20 mg	Asundexian 50 mg	Apixaban	Asundexian pooled
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	249	254	250	503
Units: Subjects	12	10	26	22

Statistical analyses

Statistical analysis title	Pooled ratio of the incidence proportions
Statistical analysis description:	
Comparison of the Asundexian pooled group versus Apixaban group in all bleeding	
Comparison groups	Apixaban v Asundexian pooled
Number of subjects included in analysis	753
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Crude incidence ratio
Point estimate	0.42
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.26
upper limit	0.67

Secondary: Number of subjects with ISTH major bleeding

End point title	Number of subjects with ISTH major bleeding

End point description:

ISTH Major Bleeding criteria: 1. Fatal bleeding, and/or 2. Symptomatic bleeding in a critical area or organ (intracranial, intraocular, intraspinal, pericardial, retroperitoneal, intraarticular, or intramuscular with compartment syndrome), and/or 3. Clinically overt bleeding associated with a recent decrease in the hemoglobin level of ≥ 2 g/dL (20 g/L; 1.24 mmol/L) compared to the most recent hemoglobin value available before the event, and/or 4. Clinically overt bleeding leading to transfusion of 2 or more units of packed red blood cells or whole blood.

End point type	Secondary

End point timeframe:

After the first administration of study intervention with an average administration of 12 weeks (but not starting after more than 2 days after the last administration)

End point values	Asundexian 20 mg	Asundexian 50 mg	Apixaban	Asundexian pooled
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	249	254	250	503
Units: Subjects	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects of ISTH clinically relevant non-major (CRNM) bleeding

End point title	Number of subjects of ISTH clinically relevant non-major (CRNM) bleeding

End point description:

ISTH Clinically Relevant Non-Major Bleeding is considered any sign or symptom of hemorrhage that does not fit the criteria for the ISTH definition of major bleeding, but does meet at least one of the

following criteria 1. requiring medical intervention by a healthcare professional. 2. leading to hospitalization or increased level of care. 3. prompting a face to face (i.e. not just a telephone or electronic communication) evaluation.

End point type	Secondary

End point timeframe:

After the first administration of study intervention with an average administration of 12 weeks (but not starting after more than 2 days after the last administration)

End point values	Asundexian 20 mg	Asundexian 50 mg	Apixaban	Asundexian pooled
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	249	254	250	503
Units: Subjects	3	1	6	4

Statistical analyses

Statistical analysis title	Pooled ratio of the incidence proportions

Statistical analysis description:

Comparison of the Asundexian pooled group versus Apixaban group in ISTH CRNM bleeding

Comparison groups	Apixaban v Asundexian pooled
Number of subjects included in analysis	753
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Crude incidence ratio
Point estimate	0.33
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.09
upper limit	0.97

Secondary: Number of subjects with ISTH minor bleeding

End point title	Number of subjects with ISTH minor bleeding

End point description:

All other overt bleeding episodes not meeting ISTH Major Bleeding criteria or clinically relevant non major bleeding were classified as minor bleeding.

End point type	Secondary

End point timeframe:

After the first administration of study intervention with an average administration of 12 weeks (but not starting after more than 2 days after the last administration)

End point values	Asundexian 20 mg	Asundexian 50 mg	Apixaban	Asundexian pooled
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	249	254	250	503
Units: Subjects	10	9	20	19

Statistical analyses

Statistical analysis title	Pooled ratio of the incidence proportions
Statistical analysis description: Comparison of the Asundexian pooled group versus Apixaban group in ISTH minor bleeding	
Comparison groups	Apixaban v Asundexian pooled
Number of subjects included in analysis	753
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Crude incidence ratio
Point estimate	0.47
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.28
upper limit	0.83

Adverse events

Adverse events information

Timeframe for reporting adverse events:

After the first administration of study intervention with an average administration of 12 weeks (but not starting after more than 2 days after the last administration).

Adverse event reporting additional description:

Adverse event reporting for the deaths (all causes) considers all deaths that occurred at any time during the study before the last contact, with an average of 14 weeks.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.0

Reporting groups

Reporting group title	Asundexian 50 mg

Reporting group description:

Subjects received Asundexian (BAY2433334) 50 mg and Apixaban placebo for 12 weeks

Reporting group title	Asundexian 20 mg

Reporting group description:

Subjects received Asundexian (BAY2433334) 20 mg and Apixaban placebo for 12 weeks

Reporting group title	Apixaban

Reporting group description:

Subjects received Asundexian (BAY2433334) placebo and Apixaban for 12 weeks

Serious adverse events	Asundexian 50 mg	Asundexian 20 mg	Apixaban
Total subjects affected by serious adverse events			
subjects affected / exposed	20 / 254 (7.87%)	22 / 249 (8.84%)	20 / 250 (8.00%)
number of deaths (all causes)	4	2	5
number of deaths resulting from adverse events	3	1	2
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Bladder neoplasm			
subjects affected / exposed	0 / 254 (0.00%)	0 / 249 (0.00%)	1 / 250 (0.40%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung adenocarcinoma			
subjects affected / exposed	0 / 254 (0.00%)	1 / 249 (0.40%)	0 / 250 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colon neoplasm			

subjects affected / exposed	0 / 254 (0.00%)	0 / 249 (0.00%)	1 / 250 (0.40%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Cardiac ablation			
subjects affected / exposed	0 / 254 (0.00%)	1 / 249 (0.40%)	0 / 250 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Percutaneous coronary intervention			
subjects affected / exposed	0 / 254 (0.00%)	1 / 249 (0.40%)	0 / 250 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	1 / 254 (0.39%)	0 / 249 (0.00%)	1 / 250 (0.40%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Face oedema			
subjects affected / exposed	0 / 254 (0.00%)	1 / 249 (0.40%)	0 / 250 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sudden cardiac death			
subjects affected / exposed	0 / 254 (0.00%)	0 / 249 (0.00%)	1 / 250 (0.40%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	1 / 254 (0.39%)	1 / 249 (0.40%)	0 / 250 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchial haemorrhage			

subjects affected / exposed	0 / 254 (0.00%)	1 / 249 (0.40%)	0 / 250 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 254 (0.39%)	0 / 249 (0.00%)	0 / 250 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Completed suicide			
subjects affected / exposed	1 / 254 (0.39%)	0 / 249 (0.00%)	0 / 250 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Investigations			
Ejection fraction decreased			
subjects affected / exposed	0 / 254 (0.00%)	1 / 249 (0.40%)	0 / 250 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Humerus fracture			
subjects affected / exposed	0 / 254 (0.00%)	0 / 249 (0.00%)	1 / 250 (0.40%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	3 / 254 (1.18%)	3 / 249 (1.20%)	2 / 250 (0.80%)
occurrences causally related to treatment / all	0 / 4	0 / 3	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial flutter			
subjects affected / exposed	0 / 254 (0.00%)	0 / 249 (0.00%)	1 / 250 (0.40%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure			

subjects affected / exposed	4 / 254 (1.57%)	3 / 249 (1.20%)	3 / 250 (1.20%)
occurrences causally related to treatment / all	0 / 4	0 / 4	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Cardiac failure acute			
subjects affected / exposed	1 / 254 (0.39%)	0 / 249 (0.00%)	0 / 250 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure chronic			
subjects affected / exposed	0 / 254 (0.00%)	0 / 249 (0.00%)	1 / 250 (0.40%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery disease			
subjects affected / exposed	1 / 254 (0.39%)	0 / 249 (0.00%)	0 / 250 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	1 / 254 (0.39%)	0 / 249 (0.00%)	0 / 250 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Palpitations			
subjects affected / exposed	0 / 254 (0.00%)	1 / 249 (0.40%)	0 / 250 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinus arrest			
subjects affected / exposed	0 / 254 (0.00%)	1 / 249 (0.40%)	0 / 250 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ventricular tachycardia			
subjects affected / exposed	1 / 254 (0.39%)	0 / 249 (0.00%)	0 / 250 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial thrombosis			

subjects affected / exposed	1 / 254 (0.39%)	0 / 249 (0.00%)	0 / 250 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tachyarrhythmia			
subjects affected / exposed	0 / 254 (0.00%)	0 / 249 (0.00%)	1 / 250 (0.40%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Congestive cardiomyopathy			
subjects affected / exposed	0 / 254 (0.00%)	1 / 249 (0.40%)	0 / 250 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinus node dysfunction			
subjects affected / exposed	0 / 254 (0.00%)	1 / 249 (0.40%)	1 / 250 (0.40%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	1 / 254 (0.39%)	2 / 249 (0.80%)	0 / 250 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0
Presyncope			
subjects affected / exposed	0 / 254 (0.00%)	0 / 249 (0.00%)	1 / 250 (0.40%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seizure			
subjects affected / exposed	1 / 254 (0.39%)	0 / 249 (0.00%)	0 / 250 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral sensorimotor neuropathy			
subjects affected / exposed	1 / 254 (0.39%)	0 / 249 (0.00%)	0 / 250 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			

Colitis			
subjects affected / exposed	0 / 254 (0.00%)	0 / 249 (0.00%)	1 / 250 (0.40%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dysphagia			
subjects affected / exposed	1 / 254 (0.39%)	0 / 249 (0.00%)	0 / 250 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Inguinal hernia			
subjects affected / exposed	0 / 254 (0.00%)	1 / 249 (0.40%)	0 / 250 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	0 / 254 (0.00%)	1 / 249 (0.40%)	0 / 250 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal haemorrhage			
subjects affected / exposed	0 / 254 (0.00%)	1 / 249 (0.40%)	0 / 250 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Drug-induced liver injury			
subjects affected / exposed	1 / 254 (0.39%)	0 / 249 (0.00%)	0 / 250 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	0 / 254 (0.00%)	0 / 249 (0.00%)	1 / 250 (0.40%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal failure			
subjects affected / exposed	0 / 254 (0.00%)	0 / 249 (0.00%)	1 / 250 (0.40%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Renal impairment			
subjects affected / exposed	1 / 254 (0.39%)	0 / 249 (0.00%)	0 / 250 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute kidney injury			
subjects affected / exposed	0 / 254 (0.00%)	1 / 249 (0.40%)	0 / 250 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Pain in extremity			
subjects affected / exposed	0 / 254 (0.00%)	0 / 249 (0.00%)	1 / 250 (0.40%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Campylobacter gastroenteritis			
subjects affected / exposed	0 / 254 (0.00%)	1 / 249 (0.40%)	0 / 250 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	0 / 254 (0.00%)	1 / 249 (0.40%)	0 / 250 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Erysipelas			
subjects affected / exposed	0 / 254 (0.00%)	0 / 249 (0.00%)	1 / 250 (0.40%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes zoster			
subjects affected / exposed	1 / 254 (0.39%)	0 / 249 (0.00%)	0 / 250 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis acute			
subjects affected / exposed	0 / 254 (0.00%)	0 / 249 (0.00%)	1 / 250 (0.40%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Sepsis			
subjects affected / exposed	0 / 254 (0.00%)	0 / 249 (0.00%)	1 / 250 (0.40%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 254 (0.00%)	1 / 249 (0.40%)	1 / 250 (0.40%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19 pneumonia			
subjects affected / exposed	0 / 254 (0.00%)	0 / 249 (0.00%)	1 / 250 (0.40%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hyperglycaemia			
subjects affected / exposed	0 / 254 (0.00%)	1 / 249 (0.40%)	0 / 250 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Asundexian 50 mg	Asundexian 20 mg	Apixaban
Total subjects affected by non-serious adverse events			
subjects affected / exposed	116 / 254 (45.67%)	110 / 249 (44.18%)	113 / 250 (45.20%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Lung neoplasm malignant			
subjects affected / exposed	0 / 254 (0.00%)	1 / 249 (0.40%)	0 / 250 (0.00%)
occurrences (all)	0	1	0
Prostate cancer			
subjects affected / exposed	0 / 254 (0.00%)	0 / 249 (0.00%)	1 / 250 (0.40%)
occurrences (all)	0	0	1
Vascular disorders			
Circulatory collapse			
subjects affected / exposed	0 / 254 (0.00%)	1 / 249 (0.40%)	0 / 250 (0.00%)
occurrences (all)	0	1	0
Haematoma			

subjects affected / exposed	0 / 254 (0.00%)	0 / 249 (0.00%)	3 / 250 (1.20%)
occurrences (all)	0	0	3
Hypertension			
subjects affected / exposed	5 / 254 (1.97%)	6 / 249 (2.41%)	7 / 250 (2.80%)
occurrences (all)	6	6	7
Hypotension			
subjects affected / exposed	1 / 254 (0.39%)	2 / 249 (0.80%)	3 / 250 (1.20%)
occurrences (all)	1	2	3
Orthostatic hypotension			
subjects affected / exposed	0 / 254 (0.00%)	1 / 249 (0.40%)	0 / 250 (0.00%)
occurrences (all)	0	1	0
Peripheral coldness			
subjects affected / exposed	0 / 254 (0.00%)	2 / 249 (0.80%)	0 / 250 (0.00%)
occurrences (all)	0	2	0
Phlebitis superficial			
subjects affected / exposed	0 / 254 (0.00%)	0 / 249 (0.00%)	1 / 250 (0.40%)
occurrences (all)	0	0	1
Subclavian artery thrombosis			
subjects affected / exposed	1 / 254 (0.39%)	0 / 249 (0.00%)	0 / 250 (0.00%)
occurrences (all)	1	0	0
Hypertensive urgency			
subjects affected / exposed	1 / 254 (0.39%)	0 / 249 (0.00%)	0 / 250 (0.00%)
occurrences (all)	1	0	0
Hot flush			
subjects affected / exposed	1 / 254 (0.39%)	0 / 249 (0.00%)	0 / 250 (0.00%)
occurrences (all)	1	0	0
Surgical and medical procedures			
Cardiac pacemaker insertion			
subjects affected / exposed	0 / 254 (0.00%)	1 / 249 (0.40%)	0 / 250 (0.00%)
occurrences (all)	0	1	0
Cardioversion			
subjects affected / exposed	0 / 254 (0.00%)	0 / 249 (0.00%)	1 / 250 (0.40%)
occurrences (all)	0	0	1
Tooth extraction			
subjects affected / exposed	0 / 254 (0.00%)	1 / 249 (0.40%)	0 / 250 (0.00%)
occurrences (all)	0	1	0

Cataract operation			
subjects affected / exposed	0 / 254 (0.00%)	1 / 249 (0.40%)	1 / 250 (0.40%)
occurrences (all)	0	1	1
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 254 (0.39%)	3 / 249 (1.20%)	4 / 250 (1.60%)
occurrences (all)	1	3	4
Chest discomfort			
subjects affected / exposed	1 / 254 (0.39%)	0 / 249 (0.00%)	0 / 250 (0.00%)
occurrences (all)	1	0	0
Discomfort			
subjects affected / exposed	0 / 254 (0.00%)	1 / 249 (0.40%)	0 / 250 (0.00%)
occurrences (all)	0	1	0
Chest pain			
subjects affected / exposed	2 / 254 (0.79%)	3 / 249 (1.20%)	0 / 250 (0.00%)
occurrences (all)	2	3	0
Fatigue			
subjects affected / exposed	10 / 254 (3.94%)	5 / 249 (2.01%)	2 / 250 (0.80%)
occurrences (all)	10	5	2
Feeling abnormal			
subjects affected / exposed	1 / 254 (0.39%)	1 / 249 (0.40%)	0 / 250 (0.00%)
occurrences (all)	1	1	0
Feeling cold			
subjects affected / exposed	3 / 254 (1.18%)	0 / 249 (0.00%)	0 / 250 (0.00%)
occurrences (all)	3	0	0
Malaise			
subjects affected / exposed	0 / 254 (0.00%)	1 / 249 (0.40%)	1 / 250 (0.40%)
occurrences (all)	0	1	1
Feeling hot			
subjects affected / exposed	1 / 254 (0.39%)	0 / 249 (0.00%)	0 / 250 (0.00%)
occurrences (all)	1	0	0
Oedema			
subjects affected / exposed	1 / 254 (0.39%)	1 / 249 (0.40%)	0 / 250 (0.00%)
occurrences (all)	1	1	0
Oedema peripheral			

subjects affected / exposed	3 / 254 (1.18%)	2 / 249 (0.80%)	3 / 250 (1.20%)
occurrences (all)	3	2	3
Pyrexia			
subjects affected / exposed	0 / 254 (0.00%)	0 / 249 (0.00%)	1 / 250 (0.40%)
occurrences (all)	0	0	1
Pain			
subjects affected / exposed	2 / 254 (0.79%)	0 / 249 (0.00%)	0 / 250 (0.00%)
occurrences (all)	2	0	0
Thirst			
subjects affected / exposed	0 / 254 (0.00%)	0 / 249 (0.00%)	1 / 250 (0.40%)
occurrences (all)	0	0	1
Peripheral swelling			
subjects affected / exposed	0 / 254 (0.00%)	1 / 249 (0.40%)	1 / 250 (0.40%)
occurrences (all)	0	1	1
Hernia pain			
subjects affected / exposed	1 / 254 (0.39%)	0 / 249 (0.00%)	0 / 250 (0.00%)
occurrences (all)	1	0	0
General physical health deterioration			
subjects affected / exposed	0 / 254 (0.00%)	1 / 249 (0.40%)	0 / 250 (0.00%)
occurrences (all)	0	1	0
Inflammation			
subjects affected / exposed	1 / 254 (0.39%)	0 / 249 (0.00%)	0 / 250 (0.00%)
occurrences (all)	1	0	0
Adverse drug reaction			
subjects affected / exposed	0 / 254 (0.00%)	1 / 249 (0.40%)	0 / 250 (0.00%)
occurrences (all)	0	1	0
Non-cardiac chest pain			
subjects affected / exposed	1 / 254 (0.39%)	0 / 249 (0.00%)	0 / 250 (0.00%)
occurrences (all)	1	0	0
Vessel puncture site haematoma			
subjects affected / exposed	0 / 254 (0.00%)	1 / 249 (0.40%)	0 / 250 (0.00%)
occurrences (all)	0	1	0
Medical device site inflammation			
subjects affected / exposed	0 / 254 (0.00%)	1 / 249 (0.40%)	0 / 250 (0.00%)
occurrences (all)	0	1	0
Immune system disorders			

Amyloidosis			
subjects affected / exposed	1 / 254 (0.39%)	0 / 249 (0.00%)	0 / 250 (0.00%)
occurrences (all)	1	0	0
Reproductive system and breast disorders			
Prostatitis			
subjects affected / exposed	0 / 254 (0.00%)	0 / 249 (0.00%)	1 / 250 (0.40%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 254 (0.00%)	1 / 249 (0.40%)	0 / 250 (0.00%)
occurrences (all)	0	1	0
Cough			
subjects affected / exposed	1 / 254 (0.39%)	2 / 249 (0.80%)	0 / 250 (0.00%)
occurrences (all)	1	2	0
Dyspnoea			
subjects affected / exposed	5 / 254 (1.97%)	3 / 249 (1.20%)	3 / 250 (1.20%)
occurrences (all)	6	3	3
Dyspnoea exertional			
subjects affected / exposed	0 / 254 (0.00%)	0 / 249 (0.00%)	1 / 250 (0.40%)
occurrences (all)	0	0	1
Emphysema			
subjects affected / exposed	1 / 254 (0.39%)	0 / 249 (0.00%)	0 / 250 (0.00%)
occurrences (all)	1	0	0
Epistaxis			
subjects affected / exposed	5 / 254 (1.97%)	3 / 249 (1.20%)	11 / 250 (4.40%)
occurrences (all)	8	3	12
Hiccups			
subjects affected / exposed	1 / 254 (0.39%)	0 / 249 (0.00%)	0 / 250 (0.00%)
occurrences (all)	1	0	0
Productive cough			
subjects affected / exposed	1 / 254 (0.39%)	0 / 249 (0.00%)	0 / 250 (0.00%)
occurrences (all)	2	0	0
Pulmonary embolism			
subjects affected / exposed	1 / 254 (0.39%)	0 / 249 (0.00%)	0 / 250 (0.00%)
occurrences (all)	1	0	0

Pulmonary haemorrhage			
subjects affected / exposed	0 / 254 (0.00%)	1 / 249 (0.40%)	0 / 250 (0.00%)
occurrences (all)	0	1	0
Rhinorrhoea			
subjects affected / exposed	0 / 254 (0.00%)	0 / 249 (0.00%)	1 / 250 (0.40%)
occurrences (all)	0	0	1
Sleep apnoea syndrome			
subjects affected / exposed	0 / 254 (0.00%)	1 / 249 (0.40%)	0 / 250 (0.00%)
occurrences (all)	0	1	0
Sputum discoloured			
subjects affected / exposed	0 / 254 (0.00%)	1 / 249 (0.40%)	0 / 250 (0.00%)
occurrences (all)	0	1	0
Hydrothorax			
subjects affected / exposed	1 / 254 (0.39%)	0 / 249 (0.00%)	0 / 250 (0.00%)
occurrences (all)	1	0	0
Oropharyngeal pain			
subjects affected / exposed	0 / 254 (0.00%)	1 / 249 (0.40%)	0 / 250 (0.00%)
occurrences (all)	0	1	0
Pharyngeal paraesthesia			
subjects affected / exposed	1 / 254 (0.39%)	0 / 249 (0.00%)	0 / 250 (0.00%)
occurrences (all)	1	0	0
Pharyngeal swelling			
subjects affected / exposed	1 / 254 (0.39%)	0 / 249 (0.00%)	0 / 250 (0.00%)
occurrences (all)	1	0	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 254 (0.39%)	0 / 249 (0.00%)	1 / 250 (0.40%)
occurrences (all)	1	0	1
Confusional state			
subjects affected / exposed	0 / 254 (0.00%)	1 / 249 (0.40%)	0 / 250 (0.00%)
occurrences (all)	0	1	0
Delirium			
subjects affected / exposed	1 / 254 (0.39%)	0 / 249 (0.00%)	0 / 250 (0.00%)
occurrences (all)	1	0	0
Depression			

subjects affected / exposed	0 / 254 (0.00%)	0 / 249 (0.00%)	1 / 250 (0.40%)
occurrences (all)	0	0	1
Insomnia			
subjects affected / exposed	2 / 254 (0.79%)	1 / 249 (0.40%)	1 / 250 (0.40%)
occurrences (all)	3	1	1
Nightmare			
subjects affected / exposed	0 / 254 (0.00%)	0 / 249 (0.00%)	1 / 250 (0.40%)
occurrences (all)	0	0	1
Investigations			
Amylase increased			
subjects affected / exposed	1 / 254 (0.39%)	0 / 249 (0.00%)	0 / 250 (0.00%)
occurrences (all)	1	0	0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 254 (0.00%)	1 / 249 (0.40%)	0 / 250 (0.00%)
occurrences (all)	0	1	0
Blood creatinine increased			
subjects affected / exposed	0 / 254 (0.00%)	0 / 249 (0.00%)	1 / 250 (0.40%)
occurrences (all)	0	0	1
Blood glucose increased			
subjects affected / exposed	2 / 254 (0.79%)	0 / 249 (0.00%)	0 / 250 (0.00%)
occurrences (all)	2	0	0
Blood potassium increased			
subjects affected / exposed	0 / 254 (0.00%)	0 / 249 (0.00%)	1 / 250 (0.40%)
occurrences (all)	0	0	1
Blood pressure increased			
subjects affected / exposed	0 / 254 (0.00%)	1 / 249 (0.40%)	0 / 250 (0.00%)
occurrences (all)	0	1	0
Blood thyroid stimulating hormone decreased			
subjects affected / exposed	0 / 254 (0.00%)	1 / 249 (0.40%)	0 / 250 (0.00%)
occurrences (all)	0	1	0
Blood thyroid stimulating hormone increased			
subjects affected / exposed	1 / 254 (0.39%)	0 / 249 (0.00%)	1 / 250 (0.40%)
occurrences (all)	1	0	1
Blood urea increased			

subjects affected / exposed	0 / 254 (0.00%)	0 / 249 (0.00%)	1 / 250 (0.40%)
occurrences (all)	0	0	1
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 254 (0.00%)	1 / 249 (0.40%)	3 / 250 (1.20%)
occurrences (all)	0	1	3
Haemoglobin decreased			
subjects affected / exposed	0 / 254 (0.00%)	0 / 249 (0.00%)	1 / 250 (0.40%)
occurrences (all)	0	0	1
Heart rate decreased			
subjects affected / exposed	0 / 254 (0.00%)	0 / 249 (0.00%)	1 / 250 (0.40%)
occurrences (all)	0	0	1
Lipase increased			
subjects affected / exposed	0 / 254 (0.00%)	1 / 249 (0.40%)	0 / 250 (0.00%)
occurrences (all)	0	1	0
Lymphocyte count decreased			
subjects affected / exposed	0 / 254 (0.00%)	0 / 249 (0.00%)	1 / 250 (0.40%)
occurrences (all)	0	0	2
Neutrophil count increased			
subjects affected / exposed	0 / 254 (0.00%)	0 / 249 (0.00%)	1 / 250 (0.40%)
occurrences (all)	0	0	2
Reticulocyte count decreased			
subjects affected / exposed	0 / 254 (0.00%)	0 / 249 (0.00%)	1 / 250 (0.40%)
occurrences (all)	0	0	1
Weight increased			
subjects affected / exposed	0 / 254 (0.00%)	2 / 249 (0.80%)	1 / 250 (0.40%)
occurrences (all)	0	2	1
Urinary occult blood positive			
subjects affected / exposed	1 / 254 (0.39%)	0 / 249 (0.00%)	0 / 250 (0.00%)
occurrences (all)	1	0	0
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 254 (0.00%)	0 / 249 (0.00%)	2 / 250 (0.80%)
occurrences (all)	0	0	2
Angiocardiogram			
subjects affected / exposed	1 / 254 (0.39%)	0 / 249 (0.00%)	0 / 250 (0.00%)
occurrences (all)	1	0	0

SARS-CoV-2 test positive			
subjects affected / exposed	1 / 254 (0.39%)	0 / 249 (0.00%)	0 / 250 (0.00%)
occurrences (all)	1	0	0
Injury, poisoning and procedural complications			
Accident			
subjects affected / exposed	0 / 254 (0.00%)	1 / 249 (0.40%)	0 / 250 (0.00%)
occurrences (all)	0	1	0
Facial bones fracture			
subjects affected / exposed	0 / 254 (0.00%)	1 / 249 (0.40%)	0 / 250 (0.00%)
occurrences (all)	0	1	0
Haematuria traumatic			
subjects affected / exposed	0 / 254 (0.00%)	0 / 249 (0.00%)	1 / 250 (0.40%)
occurrences (all)	0	0	1
Ligament sprain			
subjects affected / exposed	0 / 254 (0.00%)	0 / 249 (0.00%)	1 / 250 (0.40%)
occurrences (all)	0	0	1
Humerus fracture			
subjects affected / exposed	0 / 254 (0.00%)	0 / 249 (0.00%)	1 / 250 (0.40%)
occurrences (all)	0	0	2
Sunburn			
subjects affected / exposed	1 / 254 (0.39%)	0 / 249 (0.00%)	0 / 250 (0.00%)
occurrences (all)	1	0	0
Wrist fracture			
subjects affected / exposed	1 / 254 (0.39%)	0 / 249 (0.00%)	0 / 250 (0.00%)
occurrences (all)	1	0	0
Lumbar vertebral fracture			
subjects affected / exposed	0 / 254 (0.00%)	1 / 249 (0.40%)	0 / 250 (0.00%)
occurrences (all)	0	1	0
Contusion			
subjects affected / exposed	1 / 254 (0.39%)	1 / 249 (0.40%)	3 / 250 (1.20%)
occurrences (all)	1	1	3
Inflammation of wound			
subjects affected / exposed	1 / 254 (0.39%)	0 / 249 (0.00%)	0 / 250 (0.00%)
occurrences (all)	1	0	0
Lip injury			

subjects affected / exposed	0 / 254 (0.00%)	1 / 249 (0.40%)	0 / 250 (0.00%)
occurrences (all)	0	1	0
Joint injury			
subjects affected / exposed	1 / 254 (0.39%)	0 / 249 (0.00%)	0 / 250 (0.00%)
occurrences (all)	1	0	0
Tooth fracture			
subjects affected / exposed	1 / 254 (0.39%)	0 / 249 (0.00%)	0 / 250 (0.00%)
occurrences (all)	1	0	0
Skin abrasion			
subjects affected / exposed	0 / 254 (0.00%)	0 / 249 (0.00%)	1 / 250 (0.40%)
occurrences (all)	0	0	1
Post-traumatic pain			
subjects affected / exposed	0 / 254 (0.00%)	1 / 249 (0.40%)	0 / 250 (0.00%)
occurrences (all)	0	1	0
Craniocerebral injury			
subjects affected / exposed	0 / 254 (0.00%)	1 / 249 (0.40%)	0 / 250 (0.00%)
occurrences (all)	0	1	0
Skin wound			
subjects affected / exposed	0 / 254 (0.00%)	1 / 249 (0.40%)	0 / 250 (0.00%)
occurrences (all)	0	1	0
Congenital, familial and genetic disorders			
Accessory spleen			
subjects affected / exposed	1 / 254 (0.39%)	0 / 249 (0.00%)	0 / 250 (0.00%)
occurrences (all)	1	0	0
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	2 / 254 (0.79%)	2 / 249 (0.80%)	1 / 250 (0.40%)
occurrences (all)	2	2	1
Aortic valve stenosis			
subjects affected / exposed	0 / 254 (0.00%)	1 / 249 (0.40%)	0 / 250 (0.00%)
occurrences (all)	0	1	0
Arrhythmia supraventricular			
subjects affected / exposed	1 / 254 (0.39%)	0 / 249 (0.00%)	0 / 250 (0.00%)
occurrences (all)	1	0	0
Atrial fibrillation			

subjects affected / exposed	8 / 254 (3.15%)	7 / 249 (2.81%)	7 / 250 (2.80%)
occurrences (all)	9	7	7
Atrial flutter			
subjects affected / exposed	0 / 254 (0.00%)	1 / 249 (0.40%)	1 / 250 (0.40%)
occurrences (all)	0	1	2
Atrial tachycardia			
subjects affected / exposed	0 / 254 (0.00%)	1 / 249 (0.40%)	0 / 250 (0.00%)
occurrences (all)	0	1	0
Atrioventricular block first degree			
subjects affected / exposed	1 / 254 (0.39%)	0 / 249 (0.00%)	0 / 250 (0.00%)
occurrences (all)	1	0	0
Bradycardia			
subjects affected / exposed	1 / 254 (0.39%)	1 / 249 (0.40%)	2 / 250 (0.80%)
occurrences (all)	1	1	2
Cardiac failure			
subjects affected / exposed	0 / 254 (0.00%)	2 / 249 (0.80%)	5 / 250 (2.00%)
occurrences (all)	0	2	5
Cardiac failure acute			
subjects affected / exposed	0 / 254 (0.00%)	1 / 249 (0.40%)	0 / 250 (0.00%)
occurrences (all)	0	1	0
Cardiac failure chronic			
subjects affected / exposed	0 / 254 (0.00%)	1 / 249 (0.40%)	2 / 250 (0.80%)
occurrences (all)	0	1	2
Cardiomegaly			
subjects affected / exposed	1 / 254 (0.39%)	0 / 249 (0.00%)	0 / 250 (0.00%)
occurrences (all)	1	0	0
Coronary artery disease			
subjects affected / exposed	0 / 254 (0.00%)	1 / 249 (0.40%)	0 / 250 (0.00%)
occurrences (all)	0	1	0
Coronary artery stenosis			
subjects affected / exposed	0 / 254 (0.00%)	0 / 249 (0.00%)	1 / 250 (0.40%)
occurrences (all)	0	0	2
Myocardial ischaemia			
subjects affected / exposed	0 / 254 (0.00%)	0 / 249 (0.00%)	1 / 250 (0.40%)
occurrences (all)	0	0	1
Palpitations			

subjects affected / exposed	4 / 254 (1.57%)	3 / 249 (1.20%)	1 / 250 (0.40%)
occurrences (all)	4	3	2
Sinus bradycardia			
subjects affected / exposed	3 / 254 (1.18%)	0 / 249 (0.00%)	1 / 250 (0.40%)
occurrences (all)	3	0	1
Sinus tachycardia			
subjects affected / exposed	0 / 254 (0.00%)	1 / 249 (0.40%)	0 / 250 (0.00%)
occurrences (all)	0	1	0
Tachycardia			
subjects affected / exposed	2 / 254 (0.79%)	0 / 249 (0.00%)	2 / 250 (0.80%)
occurrences (all)	2	0	2
Ventricular tachycardia			
subjects affected / exposed	1 / 254 (0.39%)	0 / 249 (0.00%)	0 / 250 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
Ageusia			
subjects affected / exposed	0 / 254 (0.00%)	0 / 249 (0.00%)	1 / 250 (0.40%)
occurrences (all)	0	0	1
Dizziness			
subjects affected / exposed	8 / 254 (3.15%)	9 / 249 (3.61%)	7 / 250 (2.80%)
occurrences (all)	8	9	10
Dysgeusia			
subjects affected / exposed	0 / 254 (0.00%)	1 / 249 (0.40%)	1 / 250 (0.40%)
occurrences (all)	0	1	1
Essential tremor			
subjects affected / exposed	1 / 254 (0.39%)	0 / 249 (0.00%)	0 / 250 (0.00%)
occurrences (all)	1	0	0
Head discomfort			
subjects affected / exposed	1 / 254 (0.39%)	0 / 249 (0.00%)	0 / 250 (0.00%)
occurrences (all)	1	0	0
Headache			
subjects affected / exposed	7 / 254 (2.76%)	4 / 249 (1.61%)	5 / 250 (2.00%)
occurrences (all)	7	4	5
Hypertonia			
subjects affected / exposed	0 / 254 (0.00%)	1 / 249 (0.40%)	0 / 250 (0.00%)
occurrences (all)	0	1	0

Hypoaesthesia			
subjects affected / exposed	0 / 254 (0.00%)	2 / 249 (0.80%)	0 / 250 (0.00%)
occurrences (all)	0	2	0
Neuritis			
subjects affected / exposed	0 / 254 (0.00%)	1 / 249 (0.40%)	0 / 250 (0.00%)
occurrences (all)	0	1	0
Paraesthesia			
subjects affected / exposed	1 / 254 (0.39%)	3 / 249 (1.20%)	0 / 250 (0.00%)
occurrences (all)	1	3	0
Parkinsonism			
subjects affected / exposed	0 / 254 (0.00%)	0 / 249 (0.00%)	1 / 250 (0.40%)
occurrences (all)	0	0	1
Presyncope			
subjects affected / exposed	1 / 254 (0.39%)	0 / 249 (0.00%)	0 / 250 (0.00%)
occurrences (all)	1	0	0
Sciatica			
subjects affected / exposed	0 / 254 (0.00%)	1 / 249 (0.40%)	0 / 250 (0.00%)
occurrences (all)	0	1	0
Somnolence			
subjects affected / exposed	0 / 254 (0.00%)	0 / 249 (0.00%)	1 / 250 (0.40%)
occurrences (all)	0	0	1
Syncope			
subjects affected / exposed	2 / 254 (0.79%)	2 / 249 (0.80%)	0 / 250 (0.00%)
occurrences (all)	2	2	0
Orthostatic intolerance			
subjects affected / exposed	0 / 254 (0.00%)	2 / 249 (0.80%)	0 / 250 (0.00%)
occurrences (all)	0	2	0
Tremor			
subjects affected / exposed	0 / 254 (0.00%)	1 / 249 (0.40%)	0 / 250 (0.00%)
occurrences (all)	0	1	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 254 (0.39%)	2 / 249 (0.80%)	0 / 250 (0.00%)
occurrences (all)	1	2	0
Polycythaemia			

subjects affected / exposed	0 / 254 (0.00%)	0 / 249 (0.00%)	1 / 250 (0.40%)
occurrences (all)	0	0	1
Spontaneous haematoma			
subjects affected / exposed	1 / 254 (0.39%)	0 / 249 (0.00%)	0 / 250 (0.00%)
occurrences (all)	1	0	0
Ear and labyrinth disorders			
Tinnitus			
subjects affected / exposed	1 / 254 (0.39%)	1 / 249 (0.40%)	0 / 250 (0.00%)
occurrences (all)	1	1	0
Vertigo			
subjects affected / exposed	4 / 254 (1.57%)	2 / 249 (0.80%)	3 / 250 (1.20%)
occurrences (all)	4	2	3
Vertigo labyrinthine			
subjects affected / exposed	1 / 254 (0.39%)	0 / 249 (0.00%)	0 / 250 (0.00%)
occurrences (all)	1	0	0
Eye disorders			
Conjunctival haemorrhage			
subjects affected / exposed	0 / 254 (0.00%)	2 / 249 (0.80%)	2 / 250 (0.80%)
occurrences (all)	0	2	2
Dry eye			
subjects affected / exposed	0 / 254 (0.00%)	0 / 249 (0.00%)	1 / 250 (0.40%)
occurrences (all)	0	0	1
Myopia			
subjects affected / exposed	0 / 254 (0.00%)	0 / 249 (0.00%)	1 / 250 (0.40%)
occurrences (all)	0	0	1
Eye irritation			
subjects affected / exposed	0 / 254 (0.00%)	1 / 249 (0.40%)	0 / 250 (0.00%)
occurrences (all)	0	1	0
Photophobia			
subjects affected / exposed	0 / 254 (0.00%)	1 / 249 (0.40%)	0 / 250 (0.00%)
occurrences (all)	0	1	0
Swelling of eyelid			
subjects affected / exposed	0 / 254 (0.00%)	1 / 249 (0.40%)	0 / 250 (0.00%)
occurrences (all)	0	1	0
Vision blurred			

subjects affected / exposed	0 / 254 (0.00%)	1 / 249 (0.40%)	2 / 250 (0.80%)
occurrences (all)	0	1	2
Visual acuity reduced			
subjects affected / exposed	1 / 254 (0.39%)	0 / 249 (0.00%)	0 / 250 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	1 / 254 (0.39%)	2 / 249 (0.80%)	0 / 250 (0.00%)
occurrences (all)	1	2	0
Abdominal distension			
subjects affected / exposed	1 / 254 (0.39%)	1 / 249 (0.40%)	0 / 250 (0.00%)
occurrences (all)	1	1	0
Abdominal pain			
subjects affected / exposed	0 / 254 (0.00%)	1 / 249 (0.40%)	0 / 250 (0.00%)
occurrences (all)	0	1	0
Abdominal pain upper			
subjects affected / exposed	3 / 254 (1.18%)	2 / 249 (0.80%)	6 / 250 (2.40%)
occurrences (all)	3	2	6
Change of bowel habit			
subjects affected / exposed	0 / 254 (0.00%)	0 / 249 (0.00%)	1 / 250 (0.40%)
occurrences (all)	0	0	1
Constipation			
subjects affected / exposed	2 / 254 (0.79%)	1 / 249 (0.40%)	0 / 250 (0.00%)
occurrences (all)	2	1	0
Dental caries			
subjects affected / exposed	0 / 254 (0.00%)	1 / 249 (0.40%)	0 / 250 (0.00%)
occurrences (all)	0	1	0
Dry mouth			
subjects affected / exposed	3 / 254 (1.18%)	3 / 249 (1.20%)	1 / 250 (0.40%)
occurrences (all)	3	3	1
Diarrhoea			
subjects affected / exposed	11 / 254 (4.33%)	4 / 249 (1.61%)	5 / 250 (2.00%)
occurrences (all)	11	5	5
Dyspepsia			
subjects affected / exposed	1 / 254 (0.39%)	1 / 249 (0.40%)	1 / 250 (0.40%)
occurrences (all)	1	1	1

Eructation			
subjects affected / exposed	1 / 254 (0.39%)	0 / 249 (0.00%)	0 / 250 (0.00%)
occurrences (all)	1	0	0
Flatulence			
subjects affected / exposed	0 / 254 (0.00%)	1 / 249 (0.40%)	0 / 250 (0.00%)
occurrences (all)	0	1	0
Food poisoning			
subjects affected / exposed	0 / 254 (0.00%)	1 / 249 (0.40%)	0 / 250 (0.00%)
occurrences (all)	0	1	0
Gastritis			
subjects affected / exposed	0 / 254 (0.00%)	0 / 249 (0.00%)	1 / 250 (0.40%)
occurrences (all)	0	0	1
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 254 (0.39%)	1 / 249 (0.40%)	0 / 250 (0.00%)
occurrences (all)	1	1	0
Gastrointestinal disorder			
subjects affected / exposed	0 / 254 (0.00%)	1 / 249 (0.40%)	0 / 250 (0.00%)
occurrences (all)	0	1	0
Gingival bleeding			
subjects affected / exposed	1 / 254 (0.39%)	0 / 249 (0.00%)	1 / 250 (0.40%)
occurrences (all)	1	0	1
Haematochezia			
subjects affected / exposed	0 / 254 (0.00%)	0 / 249 (0.00%)	1 / 250 (0.40%)
occurrences (all)	0	0	1
Nausea			
subjects affected / exposed	8 / 254 (3.15%)	6 / 249 (2.41%)	9 / 250 (3.60%)
occurrences (all)	8	7	10
Melaena			
subjects affected / exposed	0 / 254 (0.00%)	0 / 249 (0.00%)	1 / 250 (0.40%)
occurrences (all)	0	0	1
Oesophagitis			
subjects affected / exposed	0 / 254 (0.00%)	1 / 249 (0.40%)	0 / 250 (0.00%)
occurrences (all)	0	1	0
Oral discomfort			
subjects affected / exposed	1 / 254 (0.39%)	0 / 249 (0.00%)	0 / 250 (0.00%)
occurrences (all)	1	0	0

Saliva altered			
subjects affected / exposed	1 / 254 (0.39%)	0 / 249 (0.00%)	0 / 250 (0.00%)
occurrences (all)	1	0	0
Rectal haemorrhage			
subjects affected / exposed	0 / 254 (0.00%)	0 / 249 (0.00%)	1 / 250 (0.40%)
occurrences (all)	0	0	1
Stomatitis			
subjects affected / exposed	1 / 254 (0.39%)	1 / 249 (0.40%)	0 / 250 (0.00%)
occurrences (all)	1	1	0
Vomiting			
subjects affected / exposed	2 / 254 (0.79%)	2 / 249 (0.80%)	1 / 250 (0.40%)
occurrences (all)	2	2	1
Large intestinal haemorrhage			
subjects affected / exposed	1 / 254 (0.39%)	0 / 249 (0.00%)	0 / 250 (0.00%)
occurrences (all)	1	0	0
Toothache			
subjects affected / exposed	1 / 254 (0.39%)	1 / 249 (0.40%)	1 / 250 (0.40%)
occurrences (all)	1	1	1
Haemorrhoidal haemorrhage			
subjects affected / exposed	1 / 254 (0.39%)	0 / 249 (0.00%)	0 / 250 (0.00%)
occurrences (all)	1	0	0
Abdominal symptom			
subjects affected / exposed	0 / 254 (0.00%)	0 / 249 (0.00%)	1 / 250 (0.40%)
occurrences (all)	0	0	1
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 254 (0.00%)	0 / 249 (0.00%)	1 / 250 (0.40%)
occurrences (all)	0	0	1
Cholestasis			
subjects affected / exposed	1 / 254 (0.39%)	0 / 249 (0.00%)	0 / 250 (0.00%)
occurrences (all)	1	0	0
Hepatic fibrosis			
subjects affected / exposed	1 / 254 (0.39%)	0 / 249 (0.00%)	0 / 250 (0.00%)
occurrences (all)	1	0	0
Hepatomegaly			

subjects affected / exposed	1 / 254 (0.39%)	0 / 249 (0.00%)	0 / 250 (0.00%)
occurrences (all)	1	0	0
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	0 / 254 (0.00%)	2 / 249 (0.80%)	1 / 250 (0.40%)
occurrences (all)	0	2	1
Blister			
subjects affected / exposed	1 / 254 (0.39%)	0 / 249 (0.00%)	0 / 250 (0.00%)
occurrences (all)	1	0	0
Dermatitis			
subjects affected / exposed	0 / 254 (0.00%)	1 / 249 (0.40%)	0 / 250 (0.00%)
occurrences (all)	0	1	0
Dermatitis contact			
subjects affected / exposed	0 / 254 (0.00%)	1 / 249 (0.40%)	0 / 250 (0.00%)
occurrences (all)	0	1	0
Hyperhidrosis			
subjects affected / exposed	0 / 254 (0.00%)	1 / 249 (0.40%)	1 / 250 (0.40%)
occurrences (all)	0	1	1
Intertrigo			
subjects affected / exposed	1 / 254 (0.39%)	0 / 249 (0.00%)	0 / 250 (0.00%)
occurrences (all)	1	0	0
Papule			
subjects affected / exposed	0 / 254 (0.00%)	0 / 249 (0.00%)	1 / 250 (0.40%)
occurrences (all)	0	0	1
Pruritus			
subjects affected / exposed	3 / 254 (1.18%)	5 / 249 (2.01%)	3 / 250 (1.20%)
occurrences (all)	3	5	3
Rash			
subjects affected / exposed	2 / 254 (0.79%)	0 / 249 (0.00%)	0 / 250 (0.00%)
occurrences (all)	2	0	0
Rash papular			
subjects affected / exposed	1 / 254 (0.39%)	0 / 249 (0.00%)	0 / 250 (0.00%)
occurrences (all)	1	0	0
Rash pruritic			
subjects affected / exposed	0 / 254 (0.00%)	1 / 249 (0.40%)	0 / 250 (0.00%)
occurrences (all)	0	2	0

Skin disorder			
subjects affected / exposed	0 / 254 (0.00%)	0 / 249 (0.00%)	1 / 250 (0.40%)
occurrences (all)	0	0	1
Skin fissures			
subjects affected / exposed	0 / 254 (0.00%)	1 / 249 (0.40%)	0 / 250 (0.00%)
occurrences (all)	0	1	0
Skin ulcer			
subjects affected / exposed	0 / 254 (0.00%)	0 / 249 (0.00%)	1 / 250 (0.40%)
occurrences (all)	0	0	1
Skin reaction			
subjects affected / exposed	0 / 254 (0.00%)	1 / 249 (0.40%)	0 / 250 (0.00%)
occurrences (all)	0	1	0
Urticaria			
subjects affected / exposed	0 / 254 (0.00%)	1 / 249 (0.40%)	0 / 250 (0.00%)
occurrences (all)	0	1	0
Skin haemorrhage			
subjects affected / exposed	0 / 254 (0.00%)	1 / 249 (0.40%)	1 / 250 (0.40%)
occurrences (all)	0	1	1
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	1 / 254 (0.39%)	0 / 249 (0.00%)	1 / 250 (0.40%)
occurrences (all)	1	0	1
Haematuria			
subjects affected / exposed	0 / 254 (0.00%)	2 / 249 (0.80%)	6 / 250 (2.40%)
occurrences (all)	0	2	6
Hydronephrosis			
subjects affected / exposed	0 / 254 (0.00%)	1 / 249 (0.40%)	0 / 250 (0.00%)
occurrences (all)	0	1	0
Nocturia			
subjects affected / exposed	1 / 254 (0.39%)	0 / 249 (0.00%)	0 / 250 (0.00%)
occurrences (all)	1	0	0
Pollakiuria			
subjects affected / exposed	0 / 254 (0.00%)	2 / 249 (0.80%)	0 / 250 (0.00%)
occurrences (all)	0	2	0
Renal colic			

subjects affected / exposed	0 / 254 (0.00%)	0 / 249 (0.00%)	1 / 250 (0.40%)
occurrences (all)	0	0	1
Renal cyst			
subjects affected / exposed	1 / 254 (0.39%)	0 / 249 (0.00%)	1 / 250 (0.40%)
occurrences (all)	1	0	1
Renal failure			
subjects affected / exposed	1 / 254 (0.39%)	0 / 249 (0.00%)	1 / 250 (0.40%)
occurrences (all)	1	0	1
Urinary retention			
subjects affected / exposed	0 / 254 (0.00%)	0 / 249 (0.00%)	1 / 250 (0.40%)
occurrences (all)	0	0	1
Renal impairment			
subjects affected / exposed	3 / 254 (1.18%)	2 / 249 (0.80%)	0 / 250 (0.00%)
occurrences (all)	3	2	0
Chronic kidney disease			
subjects affected / exposed	0 / 254 (0.00%)	0 / 249 (0.00%)	2 / 250 (0.80%)
occurrences (all)	0	0	2
Acute kidney injury			
subjects affected / exposed	1 / 254 (0.39%)	0 / 249 (0.00%)	0 / 250 (0.00%)
occurrences (all)	1	0	0
Endocrine disorders			
Hyperthyroidism			
subjects affected / exposed	2 / 254 (0.79%)	0 / 249 (0.00%)	0 / 250 (0.00%)
occurrences (all)	2	0	0
Hypothyroidism			
subjects affected / exposed	0 / 254 (0.00%)	1 / 249 (0.40%)	2 / 250 (0.80%)
occurrences (all)	0	1	2
Autoimmune thyroiditis			
subjects affected / exposed	0 / 254 (0.00%)	1 / 249 (0.40%)	0 / 250 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	4 / 254 (1.57%)	0 / 249 (0.00%)	2 / 250 (0.80%)
occurrences (all)	4	0	2
Back pain			

subjects affected / exposed	1 / 254 (0.39%)	4 / 249 (1.61%)	1 / 250 (0.40%)
occurrences (all)	1	5	1
Bursitis			
subjects affected / exposed	0 / 254 (0.00%)	0 / 249 (0.00%)	1 / 250 (0.40%)
occurrences (all)	0	0	1
Joint swelling			
subjects affected / exposed	1 / 254 (0.39%)	1 / 249 (0.40%)	0 / 250 (0.00%)
occurrences (all)	1	1	0
Lumbar spinal stenosis			
subjects affected / exposed	1 / 254 (0.39%)	1 / 249 (0.40%)	0 / 250 (0.00%)
occurrences (all)	1	1	0
Muscle spasms			
subjects affected / exposed	2 / 254 (0.79%)	1 / 249 (0.40%)	0 / 250 (0.00%)
occurrences (all)	2	1	0
Muscular weakness			
subjects affected / exposed	0 / 254 (0.00%)	2 / 249 (0.80%)	0 / 250 (0.00%)
occurrences (all)	0	3	0
Musculoskeletal pain			
subjects affected / exposed	0 / 254 (0.00%)	0 / 249 (0.00%)	1 / 250 (0.40%)
occurrences (all)	0	0	1
Myalgia			
subjects affected / exposed	1 / 254 (0.39%)	0 / 249 (0.00%)	1 / 250 (0.40%)
occurrences (all)	1	0	1
Pain in extremity			
subjects affected / exposed	2 / 254 (0.79%)	2 / 249 (0.80%)	0 / 250 (0.00%)
occurrences (all)	2	2	0
Spinal osteoarthritis			
subjects affected / exposed	0 / 254 (0.00%)	0 / 249 (0.00%)	1 / 250 (0.40%)
occurrences (all)	0	0	1
Intervertebral disc protrusion			
subjects affected / exposed	0 / 254 (0.00%)	0 / 249 (0.00%)	1 / 250 (0.40%)
occurrences (all)	0	0	1
Musculoskeletal chest pain			
subjects affected / exposed	0 / 254 (0.00%)	0 / 249 (0.00%)	1 / 250 (0.40%)
occurrences (all)	0	0	1
Musculoskeletal stiffness			

subjects affected / exposed	1 / 254 (0.39%)	0 / 249 (0.00%)	1 / 250 (0.40%)
occurrences (all)	1	0	1
Musculoskeletal discomfort			
subjects affected / exposed	1 / 254 (0.39%)	0 / 249 (0.00%)	0 / 250 (0.00%)
occurrences (all)	1	0	0
Limb discomfort			
subjects affected / exposed	0 / 254 (0.00%)	1 / 249 (0.40%)	0 / 250 (0.00%)
occurrences (all)	0	1	0
Spinal stenosis			
subjects affected / exposed	1 / 254 (0.39%)	0 / 249 (0.00%)	0 / 250 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			
Bronchitis			
subjects affected / exposed	1 / 254 (0.39%)	0 / 249 (0.00%)	0 / 250 (0.00%)
occurrences (all)	1	0	0
Cellulitis			
subjects affected / exposed	0 / 254 (0.00%)	1 / 249 (0.40%)	0 / 250 (0.00%)
occurrences (all)	0	1	0
Cystitis			
subjects affected / exposed	0 / 254 (0.00%)	1 / 249 (0.40%)	1 / 250 (0.40%)
occurrences (all)	0	1	1
Gastroenteritis			
subjects affected / exposed	0 / 254 (0.00%)	1 / 249 (0.40%)	1 / 250 (0.40%)
occurrences (all)	0	1	1
Erysipelas			
subjects affected / exposed	0 / 254 (0.00%)	0 / 249 (0.00%)	1 / 250 (0.40%)
occurrences (all)	0	0	1
Gastroenteritis viral			
subjects affected / exposed	0 / 254 (0.00%)	0 / 249 (0.00%)	1 / 250 (0.40%)
occurrences (all)	0	0	1
Gingivitis			
subjects affected / exposed	0 / 254 (0.00%)	1 / 249 (0.40%)	0 / 250 (0.00%)
occurrences (all)	0	1	0
Herpes zoster			
subjects affected / exposed	0 / 254 (0.00%)	3 / 249 (1.20%)	0 / 250 (0.00%)
occurrences (all)	0	3	0

Localised infection			
subjects affected / exposed	1 / 254 (0.39%)	0 / 249 (0.00%)	0 / 250 (0.00%)
occurrences (all)	1	0	0
Lower respiratory tract infection			
subjects affected / exposed	0 / 254 (0.00%)	0 / 249 (0.00%)	1 / 250 (0.40%)
occurrences (all)	0	0	1
Nasopharyngitis			
subjects affected / exposed	3 / 254 (1.18%)	1 / 249 (0.40%)	2 / 250 (0.80%)
occurrences (all)	3	1	3
Pharyngitis			
subjects affected / exposed	0 / 254 (0.00%)	1 / 249 (0.40%)	0 / 250 (0.00%)
occurrences (all)	0	1	0
Periodontitis			
subjects affected / exposed	0 / 254 (0.00%)	1 / 249 (0.40%)	0 / 250 (0.00%)
occurrences (all)	0	1	0
Pneumonia			
subjects affected / exposed	2 / 254 (0.79%)	0 / 249 (0.00%)	0 / 250 (0.00%)
occurrences (all)	2	0	0
Pulpitis dental			
subjects affected / exposed	1 / 254 (0.39%)	0 / 249 (0.00%)	0 / 250 (0.00%)
occurrences (all)	1	0	0
Sinusitis			
subjects affected / exposed	0 / 254 (0.00%)	1 / 249 (0.40%)	0 / 250 (0.00%)
occurrences (all)	0	1	0
Tinea cruris			
subjects affected / exposed	1 / 254 (0.39%)	0 / 249 (0.00%)	0 / 250 (0.00%)
occurrences (all)	1	0	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 254 (0.00%)	1 / 249 (0.40%)	0 / 250 (0.00%)
occurrences (all)	0	1	0
Urinary tract infection			
subjects affected / exposed	0 / 254 (0.00%)	2 / 249 (0.80%)	3 / 250 (1.20%)
occurrences (all)	0	2	3
Viral infection			
subjects affected / exposed	1 / 254 (0.39%)	0 / 249 (0.00%)	0 / 250 (0.00%)
occurrences (all)	1	0	0

Gingival abscess			
subjects affected / exposed	1 / 254 (0.39%)	0 / 249 (0.00%)	0 / 250 (0.00%)
occurrences (all)	1	0	0
Infective exacerbation of chronic obstructive airways disease			
subjects affected / exposed	1 / 254 (0.39%)	0 / 249 (0.00%)	0 / 250 (0.00%)
occurrences (all)	1	0	0
Oral fungal infection			
subjects affected / exposed	0 / 254 (0.00%)	1 / 249 (0.40%)	0 / 250 (0.00%)
occurrences (all)	0	1	0
Respiratory tract infection viral			
subjects affected / exposed	0 / 254 (0.00%)	1 / 249 (0.40%)	0 / 250 (0.00%)
occurrences (all)	0	1	0
COVID-19			
subjects affected / exposed	2 / 254 (0.79%)	0 / 249 (0.00%)	0 / 250 (0.00%)
occurrences (all)	2	0	0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 254 (0.00%)	0 / 249 (0.00%)	1 / 250 (0.40%)
occurrences (all)	0	0	1
Diabetes mellitus			
subjects affected / exposed	2 / 254 (0.79%)	0 / 249 (0.00%)	0 / 250 (0.00%)
occurrences (all)	2	0	0
Diabetes mellitus inadequate control			
subjects affected / exposed	0 / 254 (0.00%)	0 / 249 (0.00%)	1 / 250 (0.40%)
occurrences (all)	0	0	1
Fluid overload			
subjects affected / exposed	0 / 254 (0.00%)	0 / 249 (0.00%)	1 / 250 (0.40%)
occurrences (all)	0	0	1
Gout			
subjects affected / exposed	1 / 254 (0.39%)	4 / 249 (1.61%)	1 / 250 (0.40%)
occurrences (all)	1	4	1
Folate deficiency			
subjects affected / exposed	0 / 254 (0.00%)	0 / 249 (0.00%)	1 / 250 (0.40%)
occurrences (all)	0	0	1
Hypercholesterolaemia			

subjects affected / exposed	0 / 254 (0.00%)	0 / 249 (0.00%)	1 / 250 (0.40%)
occurrences (all)	0	0	1
Hyperglycaemia			
subjects affected / exposed	1 / 254 (0.39%)	1 / 249 (0.40%)	2 / 250 (0.80%)
occurrences (all)	1	1	2
Hyperkalaemia			
subjects affected / exposed	1 / 254 (0.39%)	1 / 249 (0.40%)	1 / 250 (0.40%)
occurrences (all)	1	1	1
Hyperuricaemia			
subjects affected / exposed	2 / 254 (0.79%)	1 / 249 (0.40%)	1 / 250 (0.40%)
occurrences (all)	2	1	1
Hypoglycaemia			
subjects affected / exposed	1 / 254 (0.39%)	1 / 249 (0.40%)	0 / 250 (0.00%)
occurrences (all)	1	1	0
Hypokalaemia			
subjects affected / exposed	0 / 254 (0.00%)	1 / 249 (0.40%)	1 / 250 (0.40%)
occurrences (all)	0	1	1
Hyponatraemia			
subjects affected / exposed	0 / 254 (0.00%)	1 / 249 (0.40%)	0 / 250 (0.00%)
occurrences (all)	0	1	0
Decreased appetite			
subjects affected / exposed	0 / 254 (0.00%)	0 / 249 (0.00%)	1 / 250 (0.40%)
occurrences (all)	0	0	1
Hyperlipidaemia			
subjects affected / exposed	1 / 254 (0.39%)	0 / 249 (0.00%)	0 / 250 (0.00%)
occurrences (all)	1	0	0

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

None reported