Clinical trial results:
Multicenter, randomized, placebo controlled, double-blind, parallel group, dose-finding Phase 2 study to evaluate the efficacy and safety of BAY 2433334 in patients following an acute myocardial infarction

Summary

EudraCT number	2019-003244-79
Trial protocol	CZ BE HU NL DE AT ES SE PL GB IT
Global end of trial date	21 February 2022

Results information

Result version number	v1 (current)
This version publication date	07 March 2023
First version publication date	07 March 2023

Trial information

Trial identification

Sponsor protocol code	BAY2433334/20603

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04304534
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	11 March 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	21 February 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate whether the oral activated Factor XI (FXIa) inhibitor asundexian compared to placebo leads to a lower incidence of Cardiovascular (CV) death, Myocardial infarction (MI), stroke and stent thrombosis in participants with an acute myocardial infarction and who are treated with dual antiplatelet therapy

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:

Asundexian or placebo was administered on top of standard of care treatment for post-MI patients, consisting of DAPT. The choice of P2Y12 inhibitor therapy (ticagrelor, clopidogrel or prasugrel) and duration of treatment with DAPT after hospital discharge for the index AMI, was left to the discretion of the treating physician and had to follow local standard of care guidelines. The use of the antiplatelet background therapy (ASA and P2Y12 inhibitors) was documented on the eCRF

Evidence for comparator: -

Actual start date of recruitment	17 June 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	Czechia: 103
Country: Number of subjects enrolled	Hungary: 218
Country: Number of subjects enrolled	Poland: 122
Country: Number of subjects enrolled	Austria: 82
Country: Number of subjects enrolled	Belgium: 70
Country: Number of subjects enrolled	Germany: 73
Country: Number of subjects enrolled	Spain: 206
Country: Number of subjects enrolled	United Kingdom: 33
Country: Number of subjects enrolled	Italy: 139
Country: Number of subjects enrolled	Netherlands: 212
Country: Number of subjects enrolled	Sweden: 42
Country: Number of subjects enrolled	Japan: 194

Country: Number of subjects enrolled	United States: 59
Country: Number of subjects enrolled	Switzerland: 48
Worldwide total number of subjects	1601
EEA total number of subjects	1267

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)	499
From 65 to 84 years	1089
85 years and over	13

Subject disposition

Recruitment

Recruitment details:

Study was conducted at 157 centers in 14 countries or regions, between 17-Jun-2020 (first subject first visit) and 21-Feb-2022 (last subject last visit)

Pre-assignment

Screening details:

1664 subjects were screened, 63 subjects were screening failures. 1601 subjects were randomized in a 1:1:1:1 ratio to 4 treatment groups: 397, 401, and 402 subjects to the asundexian 10 mg, 20 mg and 50 mg groups and 401 participants to the placebo group.

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 10 mg

Arm description:

Subjects received Asundexian (BAY2433334) 10 mg

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) 10 mg (5 mg tablets) orally once daily in the morning

Arm title	Asundexian 20 mg

Arm description:

Subjects received Asundexian (BAY2433334) 20 mg

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

Arm title	Asundexian 50 mg

Arm description:

Subjects received Asundexian (BAY2433334) 50 mg

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 (25 mg tablets) orally once daily in the morning

Arm title	Placebo

Arm description:

Subjects received placebo

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

Dosage and administration details:

Subjects received placebo orally once daily in the morning.

Number of subjects in period 1	Asundexian 10 mg	Asundexian 20 mg	Asundexian 50 mg
Started	397	401	402
Treated	395	397	402
Completed	303	317	309
Not completed	94	84	93
Consent withdrawn by subject	7	2	7
Physician decision	4	9	9
Subject Decision	34	25	25
Adverse event, non-fatal	35	40	39
Other	4	2	2
Death	7	2	4
Technical Problems	2	2	3
Subject decision COVID-19 pandemic related	1	-	1
Non-Compliance with study drug	-	1	1
Lost to follow-up	-	1	2

Number of subjects in period 1	Placebo
Started	401
Treated	399
Completed	309
Not completed	92
Consent withdrawn by subject	4
Physician decision	5

Subject Decision	26
Adverse event, non-fatal	44
Other	2
Death	3
Technical Problems	4
Subject decision COVID-19 pandemic related	-
Non-Compliance with study drug	1
Lost to follow-up	3

Baseline characteristics

Reporting groups	
Reporting group title	Asundexian 10 mg
Reporting group description: Subjects received Asundexian (BAY2433334) 10 mg	
Reporting group title	Asundexian 20 mg
Reporting group description: Subjects received Asundexian (BAY2433334) 20 mg	
Reporting group title	Asundexian 50 mg
Reporting group description: Subjects received Asundexian (BAY2433334) 50 mg	
Reporting group title	Placebo
Reporting group description: Subjects received placebo	

Reporting group values	Asundexian 10 mg	Asundexian 20 mg	Asundexian 50 mg
Number of subjects	397	401	402
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)	122	123	118
From 65-84 years	275	275	280
85 years and over	0	3	4
Gender Categorical Units: Subjects			
Female	93	87	100
Male	304	314	302
Race Units: Subjects			
American Indian or Alaska Native	1	2	0
Asian	53	50	50
Black or African American	3	2	2
Multiple	1	0	2
Not Reported	5	2	1
White	334	345	347

Reporting group values	Placebo	Total	
Number of subjects	401	1601	
Age Categorical Units: Subjects			
In utero	0	0	

Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	136	499	
From 65-84 years	259	1089	
85 years and over	6	13	
Gender Categorical Units: Subjects			
Female	90	370	
Male	311	1231	
Race Units: Subjects			
American Indian or Alaska Native	0	3	
Asian	50	203	
Black or African American	1	8	
Multiple	2	5	
Not Reported	9	17	
White	339	1365	

End points

End points reporting groups

Reporting group title	Asundexian 10 mg
Reporting group description:	
Subjects received Asundexian (BAY2433334) 10 mg	
Reporting group title	Asundexian 20 mg
Reporting group description:	
Subjects received Asundexian (BAY2433334) 20 mg	
Reporting group title	Asundexian 50 mg
Reporting group description:	
Subjects received Asundexian (BAY2433334) 50 mg	
Reporting group title	Placebo
Reporting group description:	
Subjects received placebo	
Subject analysis set title	Full analysis set (FAS)
Subject analysis set type	Full analysis
Subject analysis set description:	
A subject was included in the FAS if he/she was randomized to study intervention.	
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 study intervention and had taken at least one dose of the study intervention.	
Subject analysis set title	Asundexian 20+50 mg
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Asundexian 20 mg group and Asundexian 50 mg group	
Subject analysis set title	Pooled Asundexian
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Asundexian 10 mg group and Asundexian 20 mg group and Asundexian 50 mg group	

Primary: Efficacy - Number of subjects with composite of CV death, MI, stroke and stent thrombosis (ST)

End point title	Efficacy - Number of subjects with composite of CV death, MI, stroke and stent thrombosis (ST)
End point description:	
CV death included death due to stroke, MI, heart failure or cardiogenic shock, sudden death or any other death due to other cardiovascular causes. Death due to non-traumatic hemorrhage was included. Acute MI was used when there was evidence of myocardial necrosis in a clinical setting consistent with acute myocardial ischemia. Stroke was defined as an acute episode of focal or global neurological dysfunction caused by an injury of the brain, spinal cord, or retina as a result of hemorrhage or infarction. ST was defined incorporating diagnostic certainty as well as timing: “Definite” ST: The highest level of certainty. Either angiographic or pathological confirmation of stent thrombosis. “Probable” ST: Regardless of the time after the index procedure, any MI that is related to documented acute ischemia in the territory of the implanted stent without angiographic confirmation of stent thrombosis and in the absence of any other obvious cause	
End point type	Primary
End point timeframe:	
From baseline up to 52 weeks	

End point values	Asundexian 10 mg	Asundexian 20 mg	Asundexian 50 mg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	397	401	402	401
Units: Subjects	27	24	22	22

End point values	Asundexian 20+50 mg			
Subject group type	Subject analysis set			
Number of subjects analysed	803			
Units: Subjects	46			

Statistical analyses

Statistical analysis title	Hazard ratio (HR)
Statistical analysis description:	
Comparison of the Asundexian Asundexian 20+50 mg group versus Placebo group	
Comparison groups	Placebo v Asundexian 20+50 mg
Number of subjects included in analysis	1204
Analysis specification	Pre-specified
Analysis type	other[1]
P-value	= 0.8439
Method	Logrank
Parameter estimate	Cox proportional hazard
Point estimate	1.052
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.687
upper limit	1.612

Notes:

[1] - HRs were only calculated if at least three events occurred in one of the compared groups and at least one event in each of the compared treatment groups. The competing event was non-CV death for events that include CV death.

Statistical analysis title	Hazard Ratio (HR)
Statistical analysis description:	
Comparison of the Asundexian 50 mg group versus Placebo group	
Comparison groups	Placebo v Asundexian 50 mg

Number of subjects included in analysis	803
Analysis specification	Pre-specified
Analysis type	other[2]
P-value	= 0.978
Method	Logrank
Parameter estimate	Cox proportional hazard
Point estimate	1.008
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.614
upper limit	1.656

Notes:

[2] - HRs were only calculated if at least three events occurred in one of the compared groups and at least one event in each of the compared treatment groups. The competing event was non-CV death for events that include CV death.

Statistical analysis title	Hazard ratio (HR)

Statistical analysis description:

Comparison of the Asundexian 20 mg group versus Placebo group

Comparison groups	Placebo v Asundexian 20 mg
Number of subjects included in analysis	802
Analysis specification	Pre-specified
Analysis type	other[3]
P-value	= 0.7562
Method	Logrank
Parameter estimate	Cox proportional hazard
Point estimate	1.096
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.674
upper limit	1.781

Notes:

[3] - HRs were only calculated if at least three events occurred in one of the compared groups and at least one event in each of the compared treatment groups. The competing event was non-CV death for events that include CV death.

Primary: Safety - Number of subjects with BARC bleeding definition type 2, 3 and 5

End point title	Safety - Number of subjects with BARC bleeding definition type 2, 3 and 5

End point description:

Type 2: any overt, actionable sign of hemorrhage that doesn't fit the criteria for type 3 or 5 but meets at least one of the following criteria: 1) requires nonsurgical, med intervention by a HCP, 2) leads to hospital or rise in level of care, or 3) prompt eval. Type 3a: 1) overt bleed + Hg drop of 3 to <5 g/dl (provided Hg drop is related to bleed); 2 any transfusion with overt bleed. Type 3b: 1) overt bleed + Hg drop ≥5 g/dL (provided Hg drop is related to bleed); 2) cardiac tamponade; 3) bleed requiring surgical intervention for control (exclude dental/nasal /skin/hemorrhoid); 4) bleed requiring IV vasoactive agents. Type 3c: 1) ICH hemorrhage (doesn't include microbleeds or HT, does include intraspinal); subcategories confirmed by autopsy or imaging or LP; 2) intraocular bleed compromising vision. Type 5: fatal bleed. Type 5a: probable fatal bleed; no autopsy or image confirmation but clinical suspicion. Type 5b: definite fatal bleed; overt bleed or autopsy or image confirmation.

End point type	Primary

End point timeframe:

From baseline up to 52 weeks

End point values	Asundexian 10 mg	Asundexian 20 mg	Asundexian 50 mg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	395	397	402	399
Units: Subjects	30	32	42	36

End point values	Pooled Asundexian			
Subject group type	Subject analysis set			
Number of subjects analysed	1194			
Units: Subjects	104			

Statistical analyses

Statistical analysis title	Hazard Ratio (HR)
Statistical analysis description:	
Comparison of the Pooled Asundexian group versus Placebo group	
Comparison groups	Placebo v Pooled Asundexian
Number of subjects included in analysis	1593
Analysis specification	Pre-specified
Analysis type	other[4]
P-value	= 0.9158
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.98
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.713
upper limit	1.347

Notes:

[4] - HR was only calculated if at least three events occurred in one of the compared groups and at least one event in each of the compared treatment groups.

Statistical analysis title	Hazard Ratio (HR)
Statistical analysis description:	
Comparison of the Asundexian 50 mg group versus Placebo group	
Comparison groups	Placebo v Asundexian 50 mg

Number of subjects included in analysis	801
Analysis specification	Pre-specified
Analysis type	other[5]
P-value	= 0.417
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.202
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.828
upper limit	1.747

Notes:

[5] - HR was only calculated if at least three events occurred in one of the compared groups and at least one event in each of the compared treatment groups.

Statistical analysis title	Hazard Ratio (HR)
Statistical analysis description:	
Comparison of the Asundexian 20 mg group versus Placebo group	
Comparison groups	Placebo v Asundexian 20 mg
Number of subjects included in analysis	796
Analysis specification	Pre-specified
Analysis type	other[6]
P-value	= 0.584
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.875
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.587
upper limit	1.306

Notes:

[6] - HR was only calculated if at least three events occurred in one of the compared groups and at least one event in each of the compared treatment groups.

Statistical analysis title	Hazard Ratio (HR)
Statistical analysis description:	
Comparison of the Asundexian 10 mg group versus Placebo group	
Comparison groups	Placebo v Asundexian 10 mg
Number of subjects included in analysis	794
Analysis specification	Pre-specified
Analysis type	other[7]
P-value	= 0.5633
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.867
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.577
upper limit	1.302

Notes:

[7] - HR was only calculated if at least three events occurred in one of the compared groups and at least one event in each of the compared treatment groups.

Secondary: Efficacy - Number of subjects with CV death

End point title	Efficacy - Number of subjects with CV death

End point description:

CV death included death due to stroke, MI, heart failure or cardiogenic shock, sudden death or any other death due to other cardiovascular causes. Death due to non-traumatic hemorrhage was included.

End point type	Secondary

End point timeframe:

From baseline up to 52 weeks

End point values	Asundexian 10 mg	Asundexian 20 mg	Asundexian 50 mg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	397	401	402	401
Units: Subjects	7	4	5	2

End point values	Asundexian 20+50 mg			
Subject group type	Subject analysis set			
Number of subjects analysed	803			
Units: Subjects	9			

Statistical analyses

Statistical analysis title	Hazard Ratio (HR)

Statistical analysis description:

Comparison of the Asundexian 20+50 mg group versus Placebo group

Comparison groups	Placebo v Asundexian 20+50 mg
Number of subjects included in analysis	1204
Analysis specification	Pre-specified
Analysis type	other[8]
Parameter estimate	Cox proportional hazard
Point estimate	1.275
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.322
upper limit	5.05

Notes:

[8] - HRs were only calculated if at least three events occurred in one of the compared groups and at least one event in each of the compared treatment groups. The competing event was non-CV death for events that include CV death.

Statistical analysis title	Hazard Ratio (HR)
Statistical analysis description:	
Comparison of the Asundexian 50 mg group versus Placebo group	
Comparison groups	Asundexian 50 mg v Placebo
Number of subjects included in analysis	803
Analysis specification	Pre-specified
Analysis type	other[9]
Parameter estimate	Cox proportional hazard
Point estimate	1.991
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.479
upper limit	8.273

Notes:

[9] - HRs were only calculated if at least three events occurred in one of the compared groups and at least one event in each of the compared treatment groups. The competing event was non-CV death for events that include CV death.

Secondary: Efficacy - Number of subjects with MI

End point title	Efficacy - Number of subjects with MI

End point description:

Acute MI was used when there was evidence of myocardial necrosis in a clinical setting consistent with acute myocardial ischemia. According to MI Universal Definition from 2018 the diagnosis of MI requires combination of: 1. Presence of acute myocardial injury. 2. Evidence of acute myocardial ischemia derived from the clinical presentation, electrocardiographic changes, or the results of myocardial or coronary artery imaging, or in case of post-mortem pathological findings irrespective of biomarker values.

End point type	Secondary

End point timeframe:

From baseline up to 52 weeks

End point values	Asundexian 10 mg	Asundexian 20 mg	Asundexian 50 mg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	397	401	402	401
Units: Subjects	18	20	18	17

End point values	Asundexian 20+50 mg			
Subject group type	Subject analysis set			
Number of subjects analysed	803			
Units: Subjects	38			

Statistical analyses

Statistical analysis title	Hazard Ratio (HR)
Statistical analysis description:	
Comparison of the Asundexian 20+50 mg group versus Placebo group	
Comparison groups	Placebo v Asundexian 20+50 mg
Number of subjects included in analysis	1204
Analysis specification	Pre-specified
Analysis type	other[10]
Parameter estimate	Cox proportional hazard
Point estimate	1.125
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.696
upper limit	1.819

Notes:

[10] - HRs were only calculated if at least three events occurred in one of the compared groups and at least one event in each of the compared treatment groups. The competing event was non-CV death for events that include CV death.

Statistical analysis title	Hazard Ratio (HR)
Statistical analysis description:	
Comparison of the Asundexian 50 mg group versus Placebo group	
Comparison groups	Asundexian 50 mg v Placebo
Number of subjects included in analysis	803
Analysis specification	Pre-specified
Analysis type	other[11]
Parameter estimate	Cox proportional hazard
Point estimate	1.07
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.613
upper limit	1.866

Notes:

[11] - HRs were only calculated if at least three events occurred in one of the compared groups and at least one event in each of the compared treatment groups. The competing event was non-CV death for events that include CV death.

Statistical analysis title	Hazard Ratio (HR)
Statistical analysis description:	
Comparison of the Asundexian 20 mg group versus Placebo group	
Comparison groups	Asundexian 20 mg v Placebo
Number of subjects included in analysis	802
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Cox proportional hazard
Point estimate	1.181
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.686
upper limit	2.031

Secondary: Efficacy - Number of subjects with stroke

End point title	Efficacy - Number of subjects with stroke

End point description:

Stroke was defined as an acute episode of focal or global neurological dysfunction caused by an injury of the brain, spinal cord, or retina as a result of hemorrhage or infarction.

End point type	Secondary

End point timeframe:

From baseline up to 52 weeks

End point values	Asundexian 10 mg	Asundexian 20 mg	Asundexian 50 mg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	397	401	402	401
Units: Subjects	4	3	0	2

End point values	Asundexian 20+50 mg			
Subject group type	Subject analysis set			
Number of subjects analysed	803			
Units: Subjects	3			

Statistical analyses

No statistical analyses for this end point

Secondary: Efficacy - Number of subjects with stent thrombosis

End point title	Efficacy - Number of subjects with stent thrombosis

End point description:

ST was defined incorporating diagnostic certainty as well as timing: “Definite” ST: The highest level of certainty. Either angiographic or pathological confirmation of stent thrombosis. “Probable” ST: Regardless of the time after the index procedure, any MI that is related to documented acute ischemia in the territory of the implanted stent without angiographic confirmation of stent thrombosis and in the absence of any other obvious cause

End point type	Secondary

End point timeframe:

From baseline up to 52 weeks

End point values	Asundexian 10 mg	Asundexian 20 mg	Asundexian 50 mg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	397	401	402	401
Units: Subjects	4	5	4	4

End point values	Asundexian 20+50 mg			
Subject group type	Subject analysis set			
Number of subjects analysed	803			
Units: Subjects	9			

Statistical analyses

No statistical analyses for this end point

Secondary: Efficacy - Number of subjects with all cause mortality

End point title	Efficacy - Number of subjects with all cause mortality

End point description:

End point type	Secondary

End point timeframe:

From baseline up to 52 weeks

End point values	Asundexian 10 mg	Asundexian 20 mg	Asundexian 50 mg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	397	401	402	401
Units: Subjects	10	7	10	7

End point values	Asundexian 20+50 mg			
Subject group type	Subject analysis set			
Number of subjects analysed	803			
Units: Subjects	17			

Statistical analyses

Statistical analysis title	Hazard Ratio (HR)

Statistical analysis description:	
Comparison of the Asundexian 20+50 mg group versus Placebo group	
Comparison groups	Placebo v Asundexian 20+50 mg
Number of subjects included in analysis	1204
Analysis specification	Pre-specified
Analysis type	other[12]
P-value	= 0.6016
Method	Logrank
Parameter estimate	Cox proportional hazard
Point estimate	1.266
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.603
upper limit	2.658

Notes:

[12] - For all-cause mortality there is no competing event.

Statistical analysis title	Hazard Ratio (HR)
Statistical analysis description:	
Comparison of the Asundexian 20 mg group versus Placebo group	
Comparison groups	Asundexian 20 mg v Placebo
Number of subjects included in analysis	802
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.9945
Method	Logrank
Parameter estimate	Cox proportional hazard
Point estimate	0.996
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.414
upper limit	2.401

Statistical analysis title	Hazard Ratio (HR)
Statistical analysis description:	
Comparison of the Asundexian 50 mg group versus Placebo group	
Comparison groups	Asundexian 50 mg v Placebo
Number of subjects included in analysis	803
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.4085
Method	Logrank
Parameter estimate	Cox proportional hazard
Point estimate	1.506

Confidence interval	
level	90 %
sides	2-sided
lower limit	0.667
upper limit	3.405

Secondary: Safety - Number of subjects with all bleeding

End point title	Safety - Number of subjects with all bleeding

End point description:

All bleeding events occurred from first intake of study intervention until 2 days after the last intake of study intervention

End point type	Secondary

End point timeframe:

From baseline up to 52 weeks

End point values	Asundexian 10 mg	Asundexian 20 mg	Asundexian 50 mg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	395	397	402	399
Units: Subjects	70	75	82	85

Statistical analyses

No statistical analyses for this end point

Secondary: Safety - Number of subjects with BARC bleeding definition type 3, 5

End point title	Safety - Number of subjects with BARC bleeding definition type 3, 5

End point description:

BARC bleeding Type 3,5 definition, please refer to primary endpoint "Number of subjects with BARC bleeding definition type 2, 3 and 5".

End point type	Secondary

End point timeframe:

From baseline up to 52 weeks

End point values	Asundexian 10 mg	Asundexian 20 mg	Asundexian 50 mg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	395	397	402	399
Units: Subjects	5	3	3	5

Statistical analyses

No statistical analyses for this end point

Secondary: Safety - Number of subjects with BARC bleeding definition type 1,2,3,5

End point title	Safety - Number of subjects with BARC bleeding definition type 1,2,3,5

End point description:

Type 1: bleeding that is not actionable and does not cause the patient to seek unscheduled performance of studies, hospitalization, or treatment by a healthcare professional; may include episodes leading to self-discontinuation of medical therapy by the patient without consulting a healthcare professional.

BARC bleeding Type 2,3,5 definition, please refer to primary endpoint "Number of subjects with BARC bleeding definition type 2, 3 and 5".

End point type	Secondary

End point timeframe:

From baseline up to 52 weeks

End point values	Asundexian 10 mg	Asundexian 20 mg	Asundexian 50 mg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	395	397	402	399
Units: Subjects	70	75	82	85

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
After the first administration of study intervention for up to 52 weeks (but not starting after more than 2 days after the last administration).	
Adverse event reporting additional description:	
Reporting for the deaths (all causes) considers all deaths that occurred at any time during the study before the last contact, for up to 54 weeks.	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	24.1

Reporting groups	
Reporting group title	Asundexian 10 mg
Reporting group description:	
Subjects received Asundexian (BAY2433334) 10 mg	
Reporting group title	Placebo
Reporting group description:	
Subjects received placebo	
Reporting group title	Asundexian 50 mg
Reporting group description:	
Subjects received Asundexian (BAY2433334) 50 mg	
Reporting group title	Asundexian 20 mg
Reporting group description:	
Subjects received Asundexian (BAY2433334) 20 mg	

Serious adverse events	Asundexian 10 mg	Placebo	Asundexian 50 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	74 / 395 (18.73%)	82 / 399 (20.55%)	67 / 402 (16.67%)
number of deaths (all causes)	10	7	10
number of deaths resulting from adverse events	7	5	7
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma gastric			
subjects affected / exposed	0 / 395 (0.00%)	0 / 399 (0.00%)	0 / 402 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bladder neoplasm			
subjects affected / exposed	0 / 395 (0.00%)	1 / 399 (0.25%)	0 / 402 (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
Bronchial carcinoma			

subjects affected / exposed	0 / 395 (0.00%)	0 / 399 (0.00%)	0 / 402 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymphoma			
subjects affected / exposed	1 / 395 (0.25%)	0 / 399 (0.00%)	0 / 402 (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
Malignant melanoma			
subjects affected / exposed	0 / 395 (0.00%)	0 / 399 (0.00%)	1 / 402 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Non-Hodgkin's lymphoma			
subjects affected / exposed	0 / 395 (0.00%)	0 / 399 (0.00%)	0 / 402 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatic carcinoma			
subjects affected / exposed	2 / 395 (0.51%)	0 / 399 (0.00%)	0 / 402 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tongue neoplasm malignant stage unspecified			
subjects affected / exposed	0 / 395 (0.00%)	1 / 399 (0.25%)	0 / 402 (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
Transitional cell carcinoma			
subjects affected / exposed	0 / 395 (0.00%)	1 / 399 (0.25%)	0 / 402 (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
Tumour haemorrhage			
subjects affected / exposed	0 / 395 (0.00%)	0 / 399 (0.00%)	1 / 402 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prostate cancer			

subjects affected / exposed	1 / 395 (0.25%)	0 / 399 (0.00%)	0 / 402 (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
Pancreatic neoplasm			
subjects affected / exposed	0 / 395 (0.00%)	0 / 399 (0.00%)	0 / 402 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urethral cancer			
subjects affected / exposed	0 / 395 (0.00%)	0 / 399 (0.00%)	1 / 402 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Shock			
subjects affected / exposed	0 / 395 (0.00%)	0 / 399 (0.00%)	1 / 402 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular stenosis			
subjects affected / exposed	1 / 395 (0.25%)	0 / 399 (0.00%)	0 / 402 (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
Hypertensive urgency			
subjects affected / exposed	1 / 395 (0.25%)	0 / 399 (0.00%)	0 / 402 (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
Hypertension			
subjects affected / exposed	1 / 395 (0.25%)	1 / 399 (0.25%)	0 / 402 (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
Haematoma			
subjects affected / exposed	0 / 395 (0.00%)	1 / 399 (0.25%)	0 / 402 (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
Giant cell arteritis			

subjects affected / exposed	0 / 395 (0.00%)	0 / 399 (0.00%)	1 / 402 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arterial rupture			
subjects affected / exposed	0 / 395 (0.00%)	1 / 399 (0.25%)	0 / 402 (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
Aortic stenosis			
subjects affected / exposed	0 / 395 (0.00%)	0 / 399 (0.00%)	1 / 402 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral arterial occlusive disease			
subjects affected / exposed	0 / 395 (0.00%)	0 / 399 (0.00%)	1 / 402 (0.25%)
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			
Percutaneous coronary intervention			
subjects affected / exposed	1 / 395 (0.25%)	0 / 399 (0.00%)	0 / 402 (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 resynchronisation therapy			
subjects affected / exposed	1 / 395 (0.25%)	0 / 399 (0.00%)	0 / 402 (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
Sigmoidectomy			
subjects affected / exposed	0 / 395 (0.00%)	1 / 399 (0.25%)	0 / 402 (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
Polypectomy			
subjects affected / exposed	0 / 395 (0.00%)	0 / 399 (0.00%)	0 / 402 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transurethral bladder resection			

subjects affected / exposed	0 / 395 (0.00%)	0 / 399 (0.00%)	0 / 402 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary arterial stent insertion			
subjects affected / exposed	1 / 395 (0.25%)	0 / 399 (0.00%)	0 / 402 (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
Revascularisation procedure			
subjects affected / exposed	0 / 395 (0.00%)	1 / 399 (0.25%)	0 / 402 (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 discomfort			
subjects affected / exposed	0 / 395 (0.00%)	1 / 399 (0.25%)	0 / 402 (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
Asthenia			
subjects affected / exposed	0 / 395 (0.00%)	1 / 399 (0.25%)	0 / 402 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Inflammation			
subjects affected / exposed	0 / 395 (0.00%)	0 / 399 (0.00%)	0 / 402 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Death			
subjects affected / exposed	1 / 395 (0.25%)	0 / 399 (0.00%)	1 / 402 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Malaise			
subjects affected / exposed	0 / 395 (0.00%)	0 / 399 (0.00%)	0 / 402 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			

subjects affected / exposed	0 / 395 (0.00%)	0 / 399 (0.00%)	0 / 402 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chest pain			
subjects affected / exposed	4 / 395 (1.01%)	4 / 399 (1.00%)	4 / 402 (1.00%)
occurrences causally related to treatment / all	0 / 4	0 / 4	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular stent stenosis			
subjects affected / exposed	2 / 395 (0.51%)	2 / 399 (0.50%)	1 / 402 (0.25%)
occurrences causally related to treatment / all	0 / 2	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular stent thrombosis			
subjects affected / exposed	1 / 395 (0.25%)	2 / 399 (0.50%)	0 / 402 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Non-cardiac chest pain			
subjects affected / exposed	0 / 395 (0.00%)	0 / 399 (0.00%)	0 / 402 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Uterine polyp			
subjects affected / exposed	0 / 395 (0.00%)	0 / 399 (0.00%)	0 / 402 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prostatitis			
subjects affected / exposed	0 / 395 (0.00%)	0 / 399 (0.00%)	0 / 402 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	0 / 395 (0.00%)	2 / 399 (0.50%)	0 / 402 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0

Bronchitis chronic			
subjects affected / exposed	1 / 395 (0.25%)	0 / 399 (0.00%)	0 / 402 (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
Pleural effusion			
subjects affected / exposed	0 / 395 (0.00%)	0 / 399 (0.00%)	0 / 402 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperventilation			
subjects affected / exposed	0 / 395 (0.00%)	0 / 399 (0.00%)	0 / 402 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epistaxis			
subjects affected / exposed	1 / 395 (0.25%)	0 / 399 (0.00%)	0 / 402 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	1 / 395 (0.25%)	3 / 399 (0.75%)	1 / 402 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 395 (0.00%)	1 / 399 (0.25%)	1 / 402 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	0 / 395 (0.00%)	0 / 399 (0.00%)	1 / 402 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary oedema			
subjects affected / exposed	2 / 395 (0.51%)	0 / 399 (0.00%)	0 / 402 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary hypertension			

subjects affected / exposed	1 / 395 (0.25%)	0 / 399 (0.00%)	0 / 402 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary fibrosis			
subjects affected / exposed	0 / 395 (0.00%)	2 / 399 (0.50%)	0 / 402 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			
subjects affected / exposed	1 / 395 (0.25%)	0 / 399 (0.00%)	0 / 402 (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			
Haemoglobin decreased			
subjects affected / exposed	0 / 395 (0.00%)	0 / 399 (0.00%)	1 / 402 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coagulation factor VIII level increased			
subjects affected / exposed	0 / 395 (0.00%)	1 / 399 (0.25%)	0 / 402 (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
Hepatic enzyme increased			
subjects affected / exposed	1 / 395 (0.25%)	0 / 399 (0.00%)	0 / 402 (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
Von Willebrand's factor antigen increased			
subjects affected / exposed	0 / 395 (0.00%)	1 / 399 (0.25%)	0 / 402 (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
Von Willebrand's factor activity increased			
subjects affected / exposed	0 / 395 (0.00%)	1 / 399 (0.25%)	0 / 402 (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

Arterial bruit			
subjects affected / exposed	0 / 395 (0.00%)	0 / 399 (0.00%)	1 / 402 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Femoral neck fracture			
subjects affected / exposed	0 / 395 (0.00%)	0 / 399 (0.00%)	1 / 402 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Periprocedural myocardial infarction			
subjects affected / exposed	0 / 395 (0.00%)	1 / 399 (0.25%)	0 / 402 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary retention postoperative			
subjects affected / exposed	0 / 395 (0.00%)	0 / 399 (0.00%)	0 / 402 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Head injury			
subjects affected / exposed	0 / 395 (0.00%)	1 / 399 (0.25%)	0 / 402 (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
Vaccination complication			
subjects affected / exposed	0 / 395 (0.00%)	0 / 399 (0.00%)	0 / 402 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subdural haematoma			
subjects affected / exposed	0 / 395 (0.00%)	0 / 399 (0.00%)	1 / 402 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Road traffic accident			
subjects affected / exposed	1 / 395 (0.25%)	0 / 399 (0.00%)	0 / 402 (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

Contusion			
subjects affected / exposed	0 / 395 (0.00%)	0 / 399 (0.00%)	0 / 402 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	9 / 395 (2.28%)	8 / 399 (2.01%)	10 / 402 (2.49%)
occurrences causally related to treatment / all	0 / 9	0 / 8	0 / 11
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Angina pectoris			
subjects affected / exposed	5 / 395 (1.27%)	1 / 399 (0.25%)	6 / 402 (1.49%)
occurrences causally related to treatment / all	0 / 5	0 / 1	0 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina unstable			
subjects affected / exposed	4 / 395 (1.01%)	4 / 399 (1.00%)	2 / 402 (0.50%)
occurrences causally related to treatment / all	0 / 4	0 / 6	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			
subjects affected / exposed	1 / 395 (0.25%)	2 / 399 (0.50%)	1 / 402 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrioventricular block complete			
subjects affected / exposed	0 / 395 (0.00%)	1 / 399 (0.25%)	0 / 402 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrioventricular block second degree			
subjects affected / exposed	0 / 395 (0.00%)	1 / 399 (0.25%)	0 / 402 (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
Cardiac failure acute			
subjects affected / exposed	0 / 395 (0.00%)	0 / 399 (0.00%)	1 / 402 (0.25%)
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 failure			

subjects affected / exposed	3 / 395 (0.76%)	5 / 399 (1.25%)	2 / 402 (0.50%)
occurrences causally related to treatment / all	0 / 5	0 / 6	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac arrest			
subjects affected / exposed	3 / 395 (0.76%)	1 / 399 (0.25%)	1 / 402 (0.25%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 3	0 / 0	0 / 0
Cardiac failure chronic			
subjects affected / exposed	0 / 395 (0.00%)	1 / 399 (0.25%)	0 / 402 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery disease			
subjects affected / exposed	0 / 395 (0.00%)	0 / 399 (0.00%)	1 / 402 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiogenic shock			
subjects affected / exposed	0 / 395 (0.00%)	0 / 399 (0.00%)	1 / 402 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Cardiac tamponade			
subjects affected / exposed	0 / 395 (0.00%)	1 / 399 (0.25%)	0 / 402 (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
Cardiac failure congestive			
subjects affected / exposed	1 / 395 (0.25%)	0 / 399 (0.00%)	0 / 402 (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
Coronary artery embolism			
subjects affected / exposed	0 / 395 (0.00%)	0 / 399 (0.00%)	0 / 402 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery stenosis			

subjects affected / exposed	0 / 395 (0.00%)	1 / 399 (0.25%)	0 / 402 (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
Mitral valve incompetence			
subjects affected / exposed	0 / 395 (0.00%)	0 / 399 (0.00%)	1 / 402 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Interventricular septum rupture			
subjects affected / exposed	0 / 395 (0.00%)	1 / 399 (0.25%)	0 / 402 (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
Dressler's syndrome			
subjects affected / exposed	0 / 395 (0.00%)	0 / 399 (0.00%)	1 / 402 (0.25%)
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 thrombosis			
subjects affected / exposed	0 / 395 (0.00%)	0 / 399 (0.00%)	0 / 402 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	2 / 395 (0.51%)	3 / 399 (0.75%)	3 / 402 (0.75%)
occurrences causally related to treatment / all	0 / 2	0 / 3	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Supraventricular tachycardia			
subjects affected / exposed	0 / 395 (0.00%)	0 / 399 (0.00%)	0 / 402 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericardial effusion			
subjects affected / exposed	0 / 395 (0.00%)	1 / 399 (0.25%)	0 / 402 (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
Palpitations			

subjects affected / exposed	0 / 395 (0.00%)	1 / 399 (0.25%)	0 / 402 (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
Myocardial ischaemia			
subjects affected / exposed	1 / 395 (0.25%)	0 / 399 (0.00%)	1 / 402 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ventricular fibrillation			
subjects affected / exposed	0 / 395 (0.00%)	2 / 399 (0.50%)	1 / 402 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Coronary artery dissection			
subjects affected / exposed	0 / 395 (0.00%)	1 / 399 (0.25%)	0 / 402 (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
Intracardiac thrombus			
subjects affected / exposed	1 / 395 (0.25%)	0 / 399 (0.00%)	0 / 402 (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
Ventricular tachycardia			
subjects affected / exposed	1 / 395 (0.25%)	1 / 399 (0.25%)	0 / 402 (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
Stress cardiomyopathy			
subjects affected / exposed	0 / 395 (0.00%)	0 / 399 (0.00%)	1 / 402 (0.25%)
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 perforation			
subjects affected / exposed	0 / 395 (0.00%)	0 / 399 (0.00%)	1 / 402 (0.25%)
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 ventricular thrombosis			

subjects affected / exposed	0 / 395 (0.00%)	1 / 399 (0.25%)	1 / 402 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute coronary syndrome			
subjects affected / exposed	0 / 395 (0.00%)	3 / 399 (0.75%)	1 / 402 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiopulmonary failure			
subjects affected / exposed	0 / 395 (0.00%)	1 / 399 (0.25%)	0 / 402 (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	1 / 395 (0.25%)	0 / 399 (0.00%)	0 / 402 (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
Nervous system disorders			
Altered state of consciousness			
subjects affected / exposed	0 / 395 (0.00%)	0 / 399 (0.00%)	1 / 402 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ataxia			
subjects affected / exposed	1 / 395 (0.25%)	0 / 399 (0.00%)	0 / 402 (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
Cerebral haemorrhage			
subjects affected / exposed	0 / 395 (0.00%)	1 / 399 (0.25%)	0 / 402 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral infarction			
subjects affected / exposed	2 / 395 (0.51%)	1 / 399 (0.25%)	0 / 402 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrovascular accident			

subjects affected / exposed	1 / 395 (0.25%)	1 / 399 (0.25%)	1 / 402 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dizziness			
subjects affected / exposed	0 / 395 (0.00%)	1 / 399 (0.25%)	0 / 402 (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
Dizziness postural			
subjects affected / exposed	0 / 395 (0.00%)	0 / 399 (0.00%)	0 / 402 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myelitis transverse			
subjects affected / exposed	0 / 395 (0.00%)	1 / 399 (0.25%)	0 / 402 (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
Sciatica			
subjects affected / exposed	0 / 395 (0.00%)	0 / 399 (0.00%)	1 / 402 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	2 / 395 (0.51%)	0 / 399 (0.00%)	2 / 402 (0.50%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolic encephalopathy			
subjects affected / exposed	1 / 395 (0.25%)	0 / 399 (0.00%)	0 / 402 (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
Ischaemic stroke			
subjects affected / exposed	2 / 395 (0.51%)	0 / 399 (0.00%)	0 / 402 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoxic-ischaemic encephalopathy			

subjects affected / exposed	0 / 395 (0.00%)	0 / 399 (0.00%)	1 / 402 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Transient ischaemic attack			
subjects affected / exposed	1 / 395 (0.25%)	0 / 399 (0.00%)	0 / 402 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal epidural haematoma			
subjects affected / exposed	0 / 395 (0.00%)	0 / 399 (0.00%)	0 / 402 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic cerebral infarction			
subjects affected / exposed	1 / 395 (0.25%)	0 / 399 (0.00%)	0 / 402 (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
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 395 (0.00%)	0 / 399 (0.00%)	1 / 402 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 395 (0.00%)	0 / 399 (0.00%)	1 / 402 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 395 (0.00%)	0 / 399 (0.00%)	1 / 402 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis ulcerative			
subjects affected / exposed	0 / 395 (0.00%)	0 / 399 (0.00%)	1 / 402 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Colitis			
subjects affected / exposed	0 / 395 (0.00%)	0 / 399 (0.00%)	0 / 402 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain upper			
subjects affected / exposed	0 / 395 (0.00%)	0 / 399 (0.00%)	0 / 402 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastritis			
subjects affected / exposed	1 / 395 (0.25%)	0 / 399 (0.00%)	0 / 402 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal obstruction			
subjects affected / exposed	0 / 395 (0.00%)	0 / 399 (0.00%)	0 / 402 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematochezia			
subjects affected / exposed	0 / 395 (0.00%)	0 / 399 (0.00%)	0 / 402 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematemesis			
subjects affected / exposed	0 / 395 (0.00%)	0 / 399 (0.00%)	1 / 402 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Melaena			
subjects affected / exposed	0 / 395 (0.00%)	0 / 399 (0.00%)	1 / 402 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis			
subjects affected / exposed	1 / 395 (0.25%)	0 / 399 (0.00%)	0 / 402 (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
Pancreatitis chronic			

subjects affected / exposed	0 / 395 (0.00%)	0 / 399 (0.00%)	0 / 402 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Proctalgia			
subjects affected / exposed	1 / 395 (0.25%)	0 / 399 (0.00%)	0 / 402 (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
Mechanical ileus			
subjects affected / exposed	1 / 395 (0.25%)	0 / 399 (0.00%)	0 / 402 (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
Rectal ulcer haemorrhage			
subjects affected / exposed	0 / 395 (0.00%)	1 / 399 (0.25%)	0 / 402 (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
Upper gastrointestinal haemorrhage			
subjects affected / exposed	1 / 395 (0.25%)	0 / 399 (0.00%)	0 / 402 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 395 (0.00%)	0 / 399 (0.00%)	0 / 402 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal haemorrhage			
subjects affected / exposed	1 / 395 (0.25%)	1 / 399 (0.25%)	0 / 402 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestine polyp			
subjects affected / exposed	0 / 395 (0.00%)	1 / 399 (0.25%)	0 / 402 (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
Gastric antral vascular ectasia			

subjects affected / exposed	0 / 395 (0.00%)	1 / 399 (0.25%)	0 / 402 (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			
Bile duct stone			
subjects affected / exposed	0 / 395 (0.00%)	1 / 399 (0.25%)	0 / 402 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis			
subjects affected / exposed	0 / 395 (0.00%)	1 / 399 (0.25%)	0 / 402 (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
Ischaemic hepatitis			
subjects affected / exposed	0 / 395 (0.00%)	1 / 399 (0.25%)	0 / 402 (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
Hepatitis toxic			
subjects affected / exposed	0 / 395 (0.00%)	0 / 399 (0.00%)	0 / 402 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic function abnormal			
subjects affected / exposed	0 / 395 (0.00%)	1 / 399 (0.25%)	0 / 402 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis acute			
subjects affected / exposed	0 / 395 (0.00%)	0 / 399 (0.00%)	1 / 402 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Portal hypertension			
subjects affected / exposed	0 / 395 (0.00%)	1 / 399 (0.25%)	0 / 402 (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
Skin and subcutaneous tissue disorders			

Angioedema			
subjects affected / exposed	0 / 395 (0.00%)	0 / 399 (0.00%)	1 / 402 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetic foot			
subjects affected / exposed	2 / 395 (0.51%)	0 / 399 (0.00%)	0 / 402 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Henoch-Schonlein purpura			
subjects affected / exposed	1 / 395 (0.25%)	0 / 399 (0.00%)	0 / 402 (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			
Renal artery stenosis			
subjects affected / exposed	1 / 395 (0.25%)	0 / 399 (0.00%)	0 / 402 (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
Nephrolithiasis			
subjects affected / exposed	0 / 395 (0.00%)	0 / 399 (0.00%)	0 / 402 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematuria			
subjects affected / exposed	0 / 395 (0.00%)	0 / 399 (0.00%)	1 / 402 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal colic			
subjects affected / exposed	0 / 395 (0.00%)	0 / 399 (0.00%)	1 / 402 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute kidney injury			
subjects affected / exposed	2 / 395 (0.51%)	0 / 399 (0.00%)	2 / 402 (0.50%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal impairment			

subjects affected / exposed	0 / 395 (0.00%)	1 / 399 (0.25%)	2 / 402 (0.50%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary retention			
subjects affected / exposed	0 / 395 (0.00%)	1 / 399 (0.25%)	0 / 402 (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
Ureterolithiasis			
subjects affected / exposed	0 / 395 (0.00%)	1 / 399 (0.25%)	0 / 402 (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
Musculoskeletal and connective tissue disorders			
Lumbar spinal stenosis			
subjects affected / exposed	0 / 395 (0.00%)	0 / 399 (0.00%)	1 / 402 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoarthritis			
subjects affected / exposed	0 / 395 (0.00%)	0 / 399 (0.00%)	0 / 402 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rhabdomyolysis			
subjects affected / exposed	0 / 395 (0.00%)	1 / 399 (0.25%)	0 / 402 (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
Tenosynovitis			
subjects affected / exposed	1 / 395 (0.25%)	0 / 399 (0.00%)	0 / 402 (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
Intervertebral disc protrusion			
subjects affected / exposed	0 / 395 (0.00%)	0 / 399 (0.00%)	0 / 402 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			

Appendicitis			
subjects affected / exposed	3 / 395 (0.76%)	0 / 399 (0.00%)	0 / 402 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cystitis			
subjects affected / exposed	1 / 395 (0.25%)	0 / 399 (0.00%)	0 / 402 (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
Diverticulitis			
subjects affected / exposed	0 / 395 (0.00%)	1 / 399 (0.25%)	0 / 402 (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
Pneumonia aspiration			
subjects affected / exposed	1 / 395 (0.25%)	0 / 399 (0.00%)	0 / 402 (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
Gastroenteritis			
subjects affected / exposed	1 / 395 (0.25%)	0 / 399 (0.00%)	2 / 402 (0.50%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Erysipelas			
subjects affected / exposed	1 / 395 (0.25%)	1 / 399 (0.25%)	0 / 402 (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
Diverticulitis intestinal haemorrhagic			
subjects affected / exposed	1 / 395 (0.25%)	0 / 399 (0.00%)	0 / 402 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	2 / 395 (0.51%)	0 / 399 (0.00%)	1 / 402 (0.25%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			

subjects affected / exposed	1 / 395 (0.25%)	0 / 399 (0.00%)	0 / 402 (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
COVID-19 pneumonia			
subjects affected / exposed	1 / 395 (0.25%)	4 / 399 (1.00%)	1 / 402 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 4	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
COVID-19			
subjects affected / exposed	1 / 395 (0.25%)	5 / 399 (1.25%)	7 / 402 (1.74%)
occurrences causally related to treatment / all	0 / 1	0 / 5	0 / 7
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 3
Acarodermatitis			
subjects affected / exposed	1 / 395 (0.25%)	0 / 399 (0.00%)	0 / 402 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory tract infection			
subjects affected / exposed	1 / 395 (0.25%)	0 / 399 (0.00%)	0 / 402 (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
Clostridium difficile infection			
subjects affected / exposed	0 / 395 (0.00%)	0 / 399 (0.00%)	1 / 402 (0.25%)
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 bacterial			
subjects affected / exposed	0 / 395 (0.00%)	0 / 399 (0.00%)	0 / 402 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	1 / 395 (0.25%)	1 / 399 (0.25%)	1 / 402 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Diabetes mellitus			

subjects affected / exposed	0 / 395 (0.00%)	1 / 399 (0.25%)	0 / 402 (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
Hyperkalaemia			
subjects affected / exposed	1 / 395 (0.25%)	0 / 399 (0.00%)	0 / 402 (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
Hypoglycaemia			
subjects affected / exposed	0 / 395 (0.00%)	1 / 399 (0.25%)	0 / 402 (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
Decreased appetite			
subjects affected / exposed	0 / 395 (0.00%)	0 / 399 (0.00%)	0 / 402 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Asundexian 20 mg		
Total subjects affected by serious adverse events			
subjects affected / exposed	82 / 397 (20.65%)		
number of deaths (all causes)	7		
number of deaths resulting from adverse events	3		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma gastric			
subjects affected / exposed	1 / 397 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Bladder neoplasm			
subjects affected / exposed	1 / 397 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Bronchial carcinoma			
subjects affected / exposed	1 / 397 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Lymphoma				
subjects affected / exposed	0 / 397 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Malignant melanoma				
subjects affected / exposed	0 / 397 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Non-Hodgkin's lymphoma				
subjects affected / exposed	1 / 397 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pancreatic carcinoma				
subjects affected / exposed	0 / 397 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Tongue neoplasm malignant stage unspecified				
subjects affected / exposed	0 / 397 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Transitional cell carcinoma				
subjects affected / exposed	0 / 397 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Tumour haemorrhage				
subjects affected / exposed	1 / 397 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Prostate cancer				
subjects affected / exposed	0 / 397 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pancreatic neoplasm				

subjects affected / exposed	1 / 397 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Urethral cancer				
subjects affected / exposed	0 / 397 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vascular disorders				
Shock				
subjects affected / exposed	0 / 397 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vascular stenosis				
subjects affected / exposed	0 / 397 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypertensive urgency				
subjects affected / exposed	0 / 397 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypertension				
subjects affected / exposed	1 / 397 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Haematoma				
subjects affected / exposed	0 / 397 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Giant cell arteritis				
subjects affected / exposed	0 / 397 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Arterial rupture				

subjects affected / exposed	0 / 397 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Aortic stenosis				
subjects affected / exposed	0 / 397 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Peripheral arterial occlusive disease				
subjects affected / exposed	0 / 397 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Surgical and medical procedures				
Percutaneous coronary intervention				
subjects affected / exposed	0 / 397 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac resynchronisation therapy				
subjects affected / exposed	0 / 397 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Sigmoidectomy				
subjects affected / exposed	0 / 397 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Polypectomy				
subjects affected / exposed	1 / 397 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Transurethral bladder resection				
subjects affected / exposed	1 / 397 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Coronary arterial stent insertion				

subjects affected / exposed	0 / 397 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Revascularisation procedure				
subjects affected / exposed	0 / 397 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
General disorders and administration site conditions				
Chest discomfort				
subjects affected / exposed	0 / 397 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Asthenia				
subjects affected / exposed	0 / 397 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Inflammation				
subjects affected / exposed	1 / 397 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Death				
subjects affected / exposed	0 / 397 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Malaise				
subjects affected / exposed	1 / 397 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pyrexia				
subjects affected / exposed	1 / 397 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Chest pain				

subjects affected / exposed	5 / 397 (1.26%)			
occurrences causally related to treatment / all	0 / 5			
deaths causally related to treatment / all	0 / 0			
Vascular stent stenosis				
subjects affected / exposed	2 / 397 (0.50%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Vascular stent thrombosis				
subjects affected / exposed	1 / 397 (0.25%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Non-cardiac chest pain				
subjects affected / exposed	1 / 397 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Reproductive system and breast disorders				
Uterine polyp				
subjects affected / exposed	1 / 397 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Prostatitis				
subjects affected / exposed	1 / 397 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Acute respiratory failure				
subjects affected / exposed	0 / 397 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bronchitis chronic				
subjects affected / exposed	0 / 397 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Pleural effusion				
subjects affected / exposed	1 / 397 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hyperventilation				
subjects affected / exposed	1 / 397 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Epistaxis				
subjects affected / exposed	1 / 397 (0.25%)			
occurrences causally related to treatment / all	4 / 4			
deaths causally related to treatment / all	0 / 0			
Dyspnoea				
subjects affected / exposed	1 / 397 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Chronic obstructive pulmonary disease				
subjects affected / exposed	0 / 397 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pulmonary embolism				
subjects affected / exposed	2 / 397 (0.50%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Pulmonary oedema				
subjects affected / exposed	0 / 397 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pulmonary hypertension				
subjects affected / exposed	0 / 397 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pulmonary fibrosis				

subjects affected / exposed	0 / 397 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory failure				
subjects affected / exposed	1 / 397 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Investigations				
Haemoglobin decreased				
subjects affected / exposed	0 / 397 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Coagulation factor VIII level increased				
subjects affected / exposed	0 / 397 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatic enzyme increased				
subjects affected / exposed	1 / 397 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Von Willebrand's factor antigen increased				
subjects affected / exposed	0 / 397 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Von Willebrand's factor activity increased				
subjects affected / exposed	0 / 397 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Arterial bruit				
subjects affected / exposed	0 / 397 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Injury, poisoning and procedural complications			
Femoral neck fracture			
subjects affected / exposed	0 / 397 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Periprocedural myocardial infarction			
subjects affected / exposed	1 / 397 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Urinary retention postoperative			
subjects affected / exposed	1 / 397 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Head injury			
subjects affected / exposed	0 / 397 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vaccination complication			
subjects affected / exposed	1 / 397 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Subdural haematoma			
subjects affected / exposed	0 / 397 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Road traffic accident			
subjects affected / exposed	0 / 397 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Contusion			
subjects affected / exposed	1 / 397 (0.25%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	9 / 397 (2.27%)		
occurrences causally related to treatment / all	0 / 12		
deaths causally related to treatment / all	0 / 0		
Angina pectoris			
subjects affected / exposed	4 / 397 (1.01%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Angina unstable			
subjects affected / exposed	1 / 397 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Atrial fibrillation			
subjects affected / exposed	2 / 397 (0.50%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Atrioventricular block complete			
subjects affected / exposed	2 / 397 (0.50%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Atrioventricular block second degree			
subjects affected / exposed	0 / 397 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac failure acute			
subjects affected / exposed	1 / 397 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac failure			
subjects affected / exposed	4 / 397 (1.01%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 0		
Cardiac arrest			

subjects affected / exposed	1 / 397 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Cardiac failure chronic				
subjects affected / exposed	0 / 397 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Coronary artery disease				
subjects affected / exposed	1 / 397 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cardiogenic shock				
subjects affected / exposed	1 / 397 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Cardiac tamponade				
subjects affected / exposed	0 / 397 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac failure congestive				
subjects affected / exposed	0 / 397 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Coronary artery embolism				
subjects affected / exposed	1 / 397 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Coronary artery stenosis				
subjects affected / exposed	1 / 397 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Mitral valve incompetence				

subjects affected / exposed	0 / 397 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Interventricular septum rupture				
subjects affected / exposed	0 / 397 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Dressler's syndrome				
subjects affected / exposed	0 / 397 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Coronary artery thrombosis				
subjects affected / exposed	1 / 397 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Myocardial infarction				
subjects affected / exposed	2 / 397 (0.50%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Supraventricular tachycardia				
subjects affected / exposed	1 / 397 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pericardial effusion				
subjects affected / exposed	0 / 397 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Palpitations				
subjects affected / exposed	0 / 397 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Myocardial ischaemia				

subjects affected / exposed	2 / 397 (0.50%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Ventricular fibrillation				
subjects affected / exposed	0 / 397 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Coronary artery dissection				
subjects affected / exposed	0 / 397 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Intracardiac thrombus				
subjects affected / exposed	0 / 397 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ventricular tachycardia				
subjects affected / exposed	1 / 397 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Stress cardiomyopathy				
subjects affected / exposed	0 / 397 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Coronary artery perforation				
subjects affected / exposed	0 / 397 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac ventricular thrombosis				
subjects affected / exposed	0 / 397 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Acute coronary syndrome				

subjects affected / exposed	0 / 397 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiopulmonary failure				
subjects affected / exposed	0 / 397 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Sinus node dysfunction				
subjects affected / exposed	0 / 397 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
Altered state of consciousness				
subjects affected / exposed	0 / 397 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ataxia				
subjects affected / exposed	0 / 397 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cerebral haemorrhage				
subjects affected / exposed	0 / 397 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cerebral infarction				
subjects affected / exposed	0 / 397 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cerebrovascular accident				
subjects affected / exposed	1 / 397 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Dizziness				

subjects affected / exposed	0 / 397 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Dizziness postural				
subjects affected / exposed	1 / 397 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Myelitis transverse				
subjects affected / exposed	0 / 397 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Sciatica				
subjects affected / exposed	0 / 397 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Syncope				
subjects affected / exposed	2 / 397 (0.50%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Metabolic encephalopathy				
subjects affected / exposed	0 / 397 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ischaemic stroke				
subjects affected / exposed	1 / 397 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hypoxic-ischaemic encephalopathy				
subjects affected / exposed	0 / 397 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Transient ischaemic attack				

subjects affected / exposed	0 / 397 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Spinal epidural haematoma			
subjects affected / exposed	1 / 397 (0.25%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Ischaemic cerebral infarction			
subjects affected / exposed	0 / 397 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 397 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 397 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 397 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Colitis ulcerative			
subjects affected / exposed	0 / 397 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Colitis			
subjects affected / exposed	1 / 397 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Abdominal pain upper				
subjects affected / exposed	1 / 397 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastritis				
subjects affected / exposed	0 / 397 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Intestinal obstruction				
subjects affected / exposed	1 / 397 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Haematochezia				
subjects affected / exposed	1 / 397 (0.25%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Haematemesis				
subjects affected / exposed	0 / 397 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Melaena				
subjects affected / exposed	1 / 397 (0.25%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Pancreatitis				
subjects affected / exposed	0 / 397 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pancreatitis chronic				
subjects affected / exposed	1 / 397 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Proctalgia				

subjects affected / exposed	0 / 397 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Mechanical ileus				
subjects affected / exposed	0 / 397 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Rectal ulcer haemorrhage				
subjects affected / exposed	0 / 397 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Upper gastrointestinal haemorrhage				
subjects affected / exposed	0 / 397 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vomiting				
subjects affected / exposed	1 / 397 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Rectal haemorrhage				
subjects affected / exposed	1 / 397 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Large intestine polyp				
subjects affected / exposed	0 / 397 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastric antral vascular ectasia				
subjects affected / exposed	0 / 397 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatobiliary disorders				
Bile duct stone				

subjects affected / exposed	1 / 397 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cholecystitis				
subjects affected / exposed	1 / 397 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Ischaemic hepatitis				
subjects affected / exposed	0 / 397 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatitis toxic				
subjects affected / exposed	1 / 397 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hepatic function abnormal				
subjects affected / exposed	0 / 397 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cholecystitis acute				
subjects affected / exposed	0 / 397 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Portal hypertension				
subjects affected / exposed	0 / 397 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Skin and subcutaneous tissue disorders				
Angioedema				
subjects affected / exposed	0 / 397 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Diabetic foot				

subjects affected / exposed	1 / 397 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Henoch-Schonlein purpura				
subjects affected / exposed	0 / 397 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Renal and urinary disorders				
Renal artery stenosis				
subjects affected / exposed	0 / 397 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nephrolithiasis				
subjects affected / exposed	1 / 397 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Haematuria				
subjects affected / exposed	0 / 397 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Renal colic				
subjects affected / exposed	0 / 397 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Acute kidney injury				
subjects affected / exposed	2 / 397 (0.50%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Renal impairment				
subjects affected / exposed	0 / 397 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Urinary retention				

subjects affected / exposed	2 / 397 (0.50%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Ureterolithiasis				
subjects affected / exposed	1 / 397 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal and connective tissue disorders				
Lumbar spinal stenosis				
subjects affected / exposed	0 / 397 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Osteoarthritis				
subjects affected / exposed	1 / 397 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Rhabdomyolysis				
subjects affected / exposed	0 / 397 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Tenosynovitis				
subjects affected / exposed	0 / 397 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Intervertebral disc protrusion				
subjects affected / exposed	1 / 397 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Appendicitis				
subjects affected / exposed	0 / 397 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Cystitis			
subjects affected / exposed	0 / 397 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Diverticulitis			
subjects affected / exposed	2 / 397 (0.50%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Pneumonia aspiration			
subjects affected / exposed	0 / 397 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis			
subjects affected / exposed	0 / 397 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Erysipelas			
subjects affected / exposed	0 / 397 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Diverticulitis intestinal haemorrhagic			
subjects affected / exposed	0 / 397 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	1 / 397 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Sepsis			
subjects affected / exposed	0 / 397 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
COVID-19 pneumonia			

subjects affected / exposed	0 / 397 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
COVID-19				
subjects affected / exposed	1 / 397 (0.25%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Acarodermatitis				
subjects affected / exposed	0 / 397 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory tract infection				
subjects affected / exposed	0 / 397 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Clostridium difficile infection				
subjects affected / exposed	0 / 397 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Urinary tract infection bacterial				
subjects affected / exposed	1 / 397 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Urinary tract infection				
subjects affected / exposed	1 / 397 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Metabolism and nutrition disorders				
Diabetes mellitus				
subjects affected / exposed	0 / 397 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hyperkalaemia				

subjects affected / exposed	0 / 397 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypoglycaemia			
subjects affected / exposed	0 / 397 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Decreased appetite			
subjects affected / exposed	1 / 397 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Asundexian 10 mg	Placebo	Asundexian 50 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	89 / 395 (22.53%)	107 / 399 (26.82%)	94 / 402 (23.38%)
Vascular disorders			
Hypertension			
subjects affected / exposed	22 / 395 (5.57%)	30 / 399 (7.52%)	15 / 402 (3.73%)
occurrences (all)	23	30	15
Nervous system disorders			
Dizziness			
subjects affected / exposed	18 / 395 (4.56%)	19 / 399 (4.76%)	21 / 402 (5.22%)
occurrences (all)	19	22	22
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	13 / 395 (3.29%)	17 / 399 (4.26%)	15 / 402 (3.73%)
occurrences (all)	15	20	15
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	22 / 395 (5.57%)	18 / 399 (4.51%)	22 / 402 (5.47%)
occurrences (all)	23	19	25
Respiratory, thoracic and mediastinal disorders			

Dyspnoea			
subjects affected / exposed	21 / 395 (5.32%)	23 / 399 (5.76%)	21 / 402 (5.22%)
occurrences (all)	21	25	23
Epistaxis			
subjects affected / exposed	17 / 395 (4.30%)	20 / 399 (5.01%)	21 / 402 (5.22%)
occurrences (all)	25	26	29

Non-serious adverse events	Asundexian 20 mg		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	118 / 397 (29.72%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	27 / 397 (6.80%)		
occurrences (all)	29		
Nervous system disorders			
Dizziness			
subjects affected / exposed	19 / 397 (4.79%)		
occurrences (all)	22		
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	29 / 397 (7.30%)		
occurrences (all)	32		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	21 / 397 (5.29%)		
occurrences (all)	22		
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	27 / 397 (6.80%)		
occurrences (all)	28		
Epistaxis			
subjects affected / exposed	19 / 397 (4.79%)		
occurrences (all)	45		

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

Online references

http://www.ncbi.nlm.nih.gov/pubmed/36030390