Clinical trial results:
A Global, Phase 2, Randomized, Double-Blind, Placebo-Controlled, Dose-Ranging Study of BMS-986177, an Oral Factor XIa Inhibitor, for the Prevention of New Ischemic Stroke or New Covert Brain Infarction in Patients Receiving Aspirin and Clopidogrel Following Acute Ischemic Stroke or Transient Ischemic Attack (TIA)

Summary

EudraCT number	2017-005029-19
Trial protocol	CZ DE ES SE HU NO FI BE GB AT DK GR IT
Global end of trial date	31 March 2022

Results information

Result version number	v2 (current)
This version publication date	13 May 2023
First version publication date	17 April 2023
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	CV010-031

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03766581
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Bristol-Myers Squibb
Sponsor organisation address	Chaussee de la Hulpe 185, Brussels, Belgium, 1170
Public contact	EU Study Start-Up Unit, Bristol-Myers Squibb International Corporation, Clinical.Trials@bms.com
Scientific contact	Bristol-Myers Squibb Study Director, Bristol-Myers Squibb, Clinical.Trials@bms.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	13 May 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	31 March 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The purpose of this clinical study is to estimate the dose-response relationship of milvexian in participants with ischemic stroke or transient ischemic attack (TIA) treated with aspirin and clopidogrel.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Conference on Harmonization Good Clinical Practice Guidelines. All the local regulatory requirements pertinent to safety of trial participants were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	27 January 2019
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	Argentina: 23
Country: Number of subjects enrolled	Australia: 49
Country: Number of subjects enrolled	Austria: 12
Country: Number of subjects enrolled	Belgium: 55
Country: Number of subjects enrolled	Brazil: 41
Country: Number of subjects enrolled	Canada: 126
Country: Number of subjects enrolled	Chile: 4
Country: Number of subjects enrolled	Czechia: 13
Country: Number of subjects enrolled	Denmark: 43
Country: Number of subjects enrolled	Finland: 33
Country: Number of subjects enrolled	France: 104
Country: Number of subjects enrolled	Germany: 100
Country: Number of subjects enrolled	Greece: 211
Country: Number of subjects enrolled	Hungary: 221
Country: Number of subjects enrolled	Israel: 64
Country: Number of subjects enrolled	Italy: 56
Country: Number of subjects enrolled	Japan: 295
Country: Number of subjects enrolled	Korea, Republic of: 91
Country: Number of subjects enrolled	Mexico: 1
Country: Number of subjects enrolled	Norway: 10

Country: Number of subjects enrolled	Poland: 160
Country: Number of subjects enrolled	Russian Federation: 9
Country: Number of subjects enrolled	Spain: 342
Country: Number of subjects enrolled	Sweden: 27
Country: Number of subjects enrolled	Switzerland: 25
Country: Number of subjects enrolled	United Kingdom: 39
Country: Number of subjects enrolled	United States: 212
Worldwide total number of subjects	2366
EEA total number of subjects	1387

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)	720
From 65 to 84 years	1481
85 years and over	165

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

2366 participants were randomized and 2334 treated. 1 participant was randomized to Milvexian 200 mg BID, but received Milvexian 25 mg QD.

Period 1

Period 1 title	Randomization
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Loading dose of Clopidogrel 300 mg + Aspirin 100 mg followed by Placebo + Aspirin 100 mg QD + Clopidogrel 75 mg QD on days 1-21 and Placebo + Aspirin 100 mg QD on days 22-90. All administered orally.

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

Dosage and administration details:

Loading dose of Clopidogrel 300 mg + Aspirin 100 mg followed by Placebo + Aspirin 100 mg QD + Clopidogrel 75 mg QD on days 1-21 and Placebo + Aspirin 100 mg QD on days 22-90. All administered orally.

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

Dosage and administration details:

Loading dose of Clopidogrel 300 mg + Aspirin 100 mg followed by Placebo + Aspirin 100 mg QD + Clopidogrel 75 mg QD on days 1-21 and Placebo + Aspirin 100 mg QD on days 22-90. All administered orally.

Investigational medicinal product name	Aspirin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Loading dose of Clopidogrel 300 mg + Aspirin 100 mg followed by Placebo + Aspirin 100 mg QD + Clopidogrel 75 mg QD on days 1-21 and Placebo + Aspirin 100 mg QD on days 22-90. All administered orally.

Arm title	Milvexian 25 mg QD

Arm description:

Loading dose of Clopidogrel 300 mg + Aspirin 100 mg followed by Milvexian 25 mg QD + Aspirin 100 mg QD + Clopidogrel 75 mg QD on days 1-21 and Milvexian 25 mg QD + Aspirin 100 mg QD on days 22-90. All administered orally.

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

Dosage and administration details:

Loading dose of Clopidogrel 300 mg + Aspirin 100 mg followed by Milvexian 25 mg QD + Aspirin 100 mg QD + Clopidogrel 75 mg QD on days 1-21 and Milvexian 25 mg QD + Aspirin 100 mg QD on days 22-90. All administered orally.

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

Dosage and administration details:

Loading dose of Clopidogrel 300 mg + Aspirin 100 mg followed by Milvexian 25 mg QD + Aspirin 100 mg QD + Clopidogrel 75 mg QD on days 1-21 and Milvexian 25 mg QD + Aspirin 100 mg QD on days 22-90. All administered orally.

Investigational medicinal product name	Aspirin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Loading dose of Clopidogrel 300 mg + Aspirin 100 mg followed by Milvexian 25 mg QD + Aspirin 100 mg QD + Clopidogrel 75 mg QD on days 1-21 and Milvexian 25 mg QD + Aspirin 100 mg QD on days 22-90. All administered orally.

Arm title	Milvexian 25 mg BID

Arm description:

Loading dose of Clopidogrel 300 mg + Aspirin 100 mg followed by Milvexian 25 mg BID + Aspirin 100 mg QD + Clopidogrel 75 mg QD on days 1-21 and Milvexian 25 mg BID + Aspirin 100 mg QD on days 22-90. All administered orally.

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

Dosage and administration details:

Loading dose of Clopidogrel 300 mg + Aspirin 100 mg followed by Milvexian 25 mg BID + Aspirin 100 mg QD + Clopidogrel 75 mg QD on days 1-21 and Milvexian 25 mg BID + Aspirin 100 mg QD on days 22-90. All administered orally.

Investigational medicinal product name	Aspirin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Loading dose of Clopidogrel 300 mg + Aspirin 100 mg followed by Milvexian 25 mg BID + Aspirin 100 mg QD + Clopidogrel 75 mg QD on days 1-21 and Milvexian 25 mg BID + Aspirin 100 mg QD on days

22-90. All administered orally.

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

Dosage and administration details:

Loading dose of Clopidogrel 300 mg + Aspirin 100 mg followed by Milvexian 25 mg BID + Aspirin 100 mg QD + Clopidogrel 75 mg QD on days 1-21 and Milvexian 25 mg BID + Aspirin 100 mg QD on days 22-90. All administered orally.

Arm title	Milvexian 50 mg BID

Arm description:

Loading dose of Clopidogrel 300 mg + Aspirin 100 mg followed by Milvexian 50 mg BID + Aspirin 100 mg QD + Clopidogrel 75 mg QD on days 1-21 and Milvexian 50 mg BID + Aspirin 100 mg QD on days 22-90. All administered orally.

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

Dosage and administration details:

Loading dose of Clopidogrel 300 mg + Aspirin 100 mg followed by Milvexian 50 mg BID + Aspirin 100 mg QD + Clopidogrel 75 mg QD on days 1-21 and Milvexian 50 mg BID + Aspirin 100 mg QD on days 22-90. All administered orally.

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

Dosage and administration details:

Loading dose of Clopidogrel 300 mg + Aspirin 100 mg followed by Milvexian 50 mg BID + Aspirin 100 mg QD + Clopidogrel 75 mg QD on days 1-21 and Milvexian 50 mg BID + Aspirin 100 mg QD on days 22-90. All administered orally.

Investigational medicinal product name	Aspirin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Loading dose of Clopidogrel 300 mg + Aspirin 100 mg followed by Milvexian 50 mg BID + Aspirin 100 mg QD + Clopidogrel 75 mg QD on days 1-21 and Milvexian 50 mg BID + Aspirin 100 mg QD on days 22-90. All administered orally.

Arm title	Milvexian 100 mg BID

Arm description:

Loading dose of Clopidogrel 300 mg + Aspirin 100 mg followed by Milvexian 100 mg BID + Aspirin 100 mg QD + Clopidogrel 75 mg QD on days 1-21 and Milvexian 100 mg BID + Aspirin 100 mg QD on days 22-90. All administered orally.

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

Dosage and administration details:

Loading dose of Clopidogrel 300 mg + Aspirin 100 mg followed by Milvexian 100 mg BID + Aspirin 100 mg QD + Clopidogrel 75 mg QD on days 1-21 and Milvexian 100 mg BID + Aspirin 100 mg QD on days 22-90. All administered orally.

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

Dosage and administration details:

Loading dose of Clopidogrel 300 mg + Aspirin 100 mg followed by Milvexian 100 mg BID + Aspirin 100 mg QD + Clopidogrel 75 mg QD on days 1-21 and Milvexian 100 mg BID + Aspirin 100 mg QD on days 22-90. All administered orally.

Investigational medicinal product name	Aspirin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Loading dose of Clopidogrel 300 mg + Aspirin 100 mg followed by Milvexian 100 mg BID + Aspirin 100 mg QD + Clopidogrel 75 mg QD on days 1-21 and Milvexian 100 mg BID + Aspirin 100 mg QD on days 22-90. All administered orally.

Arm title	Milvexian 200 mg BID

Arm description:

Loading dose of Clopidogrel 300 mg + Aspirin 100 mg followed by Milvexian 200 mg BID + Aspirin 100 mg QD + Clopidogrel 75 mg QD on days 1-21 and Milvexian 200 mg BID + Aspirin 100 mg QD on days 22-90. All administered orally.

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

Dosage and administration details:

Loading dose of Clopidogrel 300 mg + Aspirin 100 mg followed by Milvexian 200 mg BID + Aspirin 100 mg QD + Clopidogrel 75 mg QD on days 1-21 and Milvexian 200 mg BID + Aspirin 100 mg QD on days 22-90. All administered orally.

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

Dosage and administration details:

Loading dose of Clopidogrel 300 mg + Aspirin 100 mg followed by Milvexian 200 mg BID + Aspirin 100 mg QD + Clopidogrel 75 mg QD on days 1-21 and Milvexian 200 mg BID + Aspirin 100 mg QD on days 22-90. All administered orally.

Investigational medicinal product name	Aspirin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Loading dose of Clopidogrel 300 mg + Aspirin 100 mg followed by Milvexian 200 mg BID + Aspirin 100 mg QD + Clopidogrel 75 mg QD on days 1-21 and Milvexian 200 mg BID + Aspirin 100 mg QD on days 22-90. All administered orally.

Arm title	Milvexian 50 mg QD

Arm description:

Loading dose of Clopidogrel 300 mg + Aspirin 100 mg followed by Milvexian 50 mg QD + Aspirin 100 mg QD + Clopidogrel 75 mg QD on days 1-21 and Milvexian 50 mg QD + Aspirin 100 mg QD on days 22-90. All administered orally.

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

Dosage and administration details:

Loading dose of Clopidogrel 300 mg + Aspirin 100 mg followed by Milvexian 50 mg QD + Aspirin 100 mg QD + Clopidogrel 75 mg QD on days 1-21 and Milvexian 50 mg QD + Aspirin 100 mg QD on days 22-90. All administered orally.

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

Dosage and administration details:

Loading dose of Clopidogrel 300 mg + Aspirin 100 mg followed by Milvexian 50 mg QD + Aspirin 100 mg QD + Clopidogrel 75 mg QD on days 1-21 and Milvexian 50 mg QD + Aspirin 100 mg QD on days 22-90. All administered orally.

Investigational medicinal product name	Aspirin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Loading dose of Clopidogrel 300 mg + Aspirin 100 mg followed by Milvexian 50 mg QD + Aspirin 100 mg QD + Clopidogrel 75 mg QD on days 1-21 and Milvexian 50 mg QD + Aspirin 100 mg QD on days 22-90. All administered orally.

Arm title	Milvexian 100 mg QD

Arm description:

Loading dose of Clopidogrel 300 mg + Aspirin 100 mg followed by Milvexian 100 mg QD + Aspirin 100 mg QD + Clopidogrel 75 mg QD on days 1-21 and Milvexian 100 mg QD + Aspirin 100 mg QD on days 22-90. All administered orally.

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

Dosage and administration details:

Loading dose of Clopidogrel 300 mg + Aspirin 100 mg followed by Milvexian 100 mg QD + Aspirin 100 mg QD + Clopidogrel 75 mg QD on days 1-21 and Milvexian 100 mg QD + Aspirin 100 mg QD on days 22-90. All administered orally.

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

Dosage and administration details:

Loading dose of Clopidogrel 300 mg + Aspirin 100 mg followed by Milvexian 100 mg QD + Aspirin 100

mg QD + Clopidogrel 75 mg QD on days 1-21 and Milvexian 100 mg QD + Aspirin 100 mg QD on days 22-90. All administered orally.

Investigational medicinal product name	Aspirin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Loading dose of Clopidogrel 300 mg + Aspirin 100 mg followed by Milvexian 100 mg QD + Aspirin 100 mg QD + Clopidogrel 75 mg QD on days 1-21 and Milvexian 100 mg QD + Aspirin 100 mg QD on days 22-90. All administered orally.

Number of subjects in period 1	Placebo	Milvexian 25 mg QD	Milvexian 25 mg BID
Started	691	328	318
Completed	682	324	313
Not completed	9	4	5
Participant withdrew consent	1	-	1
Participant no longer meets study criteria	5	3	4
Other reasons	2	1	-
Participant request to discontinue study treatment	1	-	-

Number of subjects in period 1	Milvexian 50 mg BID	Milvexian 100 mg BID	Milvexian 200 mg BID
Started	328	310	351
Completed	325	306	345
Not completed	3	4	6
Participant withdrew consent	2	1	1
Participant no longer meets study criteria	-	2	3
Other reasons	1	-	-
Participant request to discontinue study treatment	-	1	2

Number of subjects in period 1	Milvexian 50 mg QD	Milvexian 100 mg QD
Started	22	18
Completed	22	17
Not completed	0	1
Participant withdrew consent	-	-
Participant no longer meets study criteria	-	1
Other reasons	-	-
Participant request to discontinue study treatment	-	-

Period 2

Period 2 title	Treatment
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Loading dose of Clopidogrel 300 mg + Aspirin 100 mg followed by Placebo + Aspirin 100 mg QD + Clopidogrel 75 mg QD on days 1-21 and Placebo + Aspirin 100 mg QD on days 22-90. All administered orally.

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

Dosage and administration details:

Loading dose of Clopidogrel 300 mg + Aspirin 100 mg followed by Placebo + Aspirin 100 mg QD + Clopidogrel 75 mg QD on days 1-21 and Placebo + Aspirin 100 mg QD on days 22-90. All administered orally.

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

Dosage and administration details:

Loading dose of Clopidogrel 300 mg + Aspirin 100 mg followed by Placebo + Aspirin 100 mg QD + Clopidogrel 75 mg QD on days 1-21 and Placebo + Aspirin 100 mg QD on days 22-90. All administered orally.

Investigational medicinal product name	Aspirin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Loading dose of Clopidogrel 300 mg + Aspirin 100 mg followed by Placebo + Aspirin 100 mg QD + Clopidogrel 75 mg QD on days 1-21 and Placebo + Aspirin 100 mg QD on days 22-90. All administered orally.

Arm title	Milvexian 25 mg QD

Arm description:

Loading dose of Clopidogrel 300 mg + Aspirin 100 mg followed by Milvexian 25 mg QD + Aspirin 100 mg QD + Clopidogrel 75 mg QD on days 1-21 and Milvexian 25 mg QD + Aspirin 100 mg QD on days 22-90. All administered orally.

Arm type	Experimental

Investigational medicinal product name	Clopidogrel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Loading dose of Clopidogrel 300 mg + Aspirin 100 mg followed by Milvexian 25 mg QD + Aspirin 100 mg QD + Clopidogrel 75 mg QD on days 1-21 and Milvexian 25 mg QD + Aspirin 100 mg QD on days 22-90. All administered orally.

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

Dosage and administration details:

Loading dose of Clopidogrel 300 mg + Aspirin 100 mg followed by Milvexian 25 mg QD + Aspirin 100 mg QD + Clopidogrel 75 mg QD on days 1-21 and Milvexian 25 mg QD + Aspirin 100 mg QD on days 22-90. All administered orally.

Investigational medicinal product name	Aspirin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Loading dose of Clopidogrel 300 mg + Aspirin 100 mg followed by Milvexian 25 mg QD + Aspirin 100 mg QD + Clopidogrel 75 mg QD on days 1-21 and Milvexian 25 mg QD + Aspirin 100 mg QD on days 22-90. All administered orally.

Arm title	Milvexian 25 mg BID

Arm description:

Loading dose of Clopidogrel 300 mg + Aspirin 100 mg followed by Milvexian 25 mg BID + Aspirin 100 mg QD + Clopidogrel 75 mg QD on days 1-21 and Milvexian 25 mg BID + Aspirin 100 mg QD on days 22-90. All administered orally.

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

Dosage and administration details:

Loading dose of Clopidogrel 300 mg + Aspirin 100 mg followed by Milvexian 25 mg BID + Aspirin 100 mg QD + Clopidogrel 75 mg QD on days 1-21 and Milvexian 25 mg BID + Aspirin 100 mg QD on days 22-90. All administered orally.

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

Dosage and administration details:

Loading dose of Clopidogrel 300 mg + Aspirin 100 mg followed by Milvexian 25 mg BID + Aspirin 100 mg QD + Clopidogrel 75 mg QD on days 1-21 and Milvexian 25 mg BID + Aspirin 100 mg QD on days 22-90. All administered orally.

Investigational medicinal product name	Aspirin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet

Routes of administration	Oral use

Dosage and administration details:

Loading dose of Clopidogrel 300 mg + Aspirin 100 mg followed by Milvexian 25 mg BID + Aspirin 100 mg QD + Clopidogrel 75 mg QD on days 1-21 and Milvexian 25 mg BID + Aspirin 100 mg QD on days 22-90. All administered orally.

Arm title	Milvexian 50 mg BID

Arm description:

Loading dose of Clopidogrel 300 mg + Aspirin 100 mg followed by Milvexian 50 mg BID + Aspirin 100 mg QD + Clopidogrel 75 mg QD on days 1-21 and Milvexian 50 mg BID + Aspirin 100 mg QD on days 22-90. All administered orally.

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

Dosage and administration details:

Loading dose of Clopidogrel 300 mg + Aspirin 100 mg followed by Milvexian 50 mg BID + Aspirin 100 mg QD + Clopidogrel 75 mg QD on days 1-21 and Milvexian 50 mg BID + Aspirin 100 mg QD on days 22-90. All administered orally.

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

Dosage and administration details:

Loading dose of Clopidogrel 300 mg + Aspirin 100 mg followed by Milvexian 50 mg BID + Aspirin 100 mg QD + Clopidogrel 75 mg QD on days 1-21 and Milvexian 50 mg BID + Aspirin 100 mg QD on days 22-90. All administered orally.

Investigational medicinal product name	Aspirin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Loading dose of Clopidogrel 300 mg + Aspirin 100 mg followed by Milvexian 50 mg BID + Aspirin 100 mg QD + Clopidogrel 75 mg QD on days 1-21 and Milvexian 50 mg BID + Aspirin 100 mg QD on days 22-90. All administered orally.

Arm title	Milvexian 100 mg BID

Arm description:

Loading dose of Clopidogrel 300 mg + Aspirin 100 mg followed by Milvexian 100 mg BID + Aspirin 100 mg QD + Clopidogrel 75 mg QD on days 1-21 and Milvexian 100 mg BID + Aspirin 100 mg QD on days 22-90. All administered orally.

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

Dosage and administration details:

Loading dose of Clopidogrel 300 mg + Aspirin 100 mg followed by Milvexian 100 mg BID + Aspirin 100 mg QD + Clopidogrel 75 mg QD on days 1-21 and Milvexian 100 mg BID + Aspirin 100 mg QD on days 22-90. All administered orally.

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

Dosage and administration details:

Loading dose of Clopidogrel 300 mg + Aspirin 100 mg followed by Milvexian 100 mg BID + Aspirin 100 mg QD + Clopidogrel 75 mg QD on days 1-21 and Milvexian 100 mg BID + Aspirin 100 mg QD on days 22-90. All administered orally.

Investigational medicinal product name	Aspirin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Loading dose of Clopidogrel 300 mg + Aspirin 100 mg followed by Milvexian 100 mg BID + Aspirin 100 mg QD + Clopidogrel 75 mg QD on days 1-21 and Milvexian 100 mg BID + Aspirin 100 mg QD on days 22-90. All administered orally.

Arm title	Milvexian 200 mg BID

Arm description:

Loading dose of Clopidogrel 300 mg + Aspirin 100 mg followed by Milvexian 200 mg BID + Aspirin 100 mg QD + Clopidogrel 75 mg QD on days 1-21 and Milvexian 200 mg BID + Aspirin 100 mg QD on days 22-90. All administered orally.

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

Dosage and administration details:

Loading dose of Clopidogrel 300 mg + Aspirin 100 mg followed by Milvexian 200 mg BID + Aspirin 100 mg QD + Clopidogrel 75 mg QD on days 1-21 and Milvexian 200 mg BID + Aspirin 100 mg QD on days 22-90. All administered orally.

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

Dosage and administration details:

Loading dose of Clopidogrel 300 mg + Aspirin 100 mg followed by Milvexian 200 mg BID + Aspirin 100 mg QD + Clopidogrel 75 mg QD on days 1-21 and Milvexian 200 mg BID + Aspirin 100 mg QD on days 22-90. All administered orally.

Investigational medicinal product name	Aspirin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Loading dose of Clopidogrel 300 mg + Aspirin 100 mg followed by Milvexian 200 mg BID + Aspirin 100 mg QD + Clopidogrel 75 mg QD on days 1-21 and Milvexian 200 mg BID + Aspirin 100 mg QD on days 22-90. All administered orally.

Arm title	Milvexian 50 mg QD

Arm description:

Loading dose of Clopidogrel 300 mg + Aspirin 100 mg followed by Milvexian 50 mg QD + Aspirin 100 mg QD + Clopidogrel 75 mg QD on days 1-21 and Milvexian 50 mg QD + Aspirin 100 mg QD on days

22-90. All administered orally.

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

Dosage and administration details:

Loading dose of Clopidogrel 300 mg + Aspirin 100 mg followed by Milvexian 50 mg QD + Aspirin 100 mg QD + Clopidogrel 75 mg QD on days 1-21 and Milvexian 50 mg QD + Aspirin 100 mg QD on days 22-90. All administered orally.

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

Dosage and administration details:

Loading dose of Clopidogrel 300 mg + Aspirin 100 mg followed by Milvexian 50 mg QD + Aspirin 100 mg QD + Clopidogrel 75 mg QD on days 1-21 and Milvexian 50 mg QD + Aspirin 100 mg QD on days 22-90. All administered orally.

Investigational medicinal product name	Aspirin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Loading dose of Clopidogrel 300 mg + Aspirin 100 mg followed by Milvexian 50 mg QD + Aspirin 100 mg QD + Clopidogrel 75 mg QD on days 1-21 and Milvexian 50 mg QD + Aspirin 100 mg QD on days 22-90. All administered orally.

Arm title	Milvexian 100 mg QD

Arm description:

Loading dose of Clopidogrel 300 mg + Aspirin 100 mg followed by Milvexian 100 mg QD + Aspirin 100 mg QD + Clopidogrel 75 mg QD on days 1-21 and Milvexian 100 mg QD + Aspirin 100 mg QD on days 22-90. All administered orally.

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

Dosage and administration details:

Loading dose of Clopidogrel 300 mg + Aspirin 100 mg followed by Milvexian 100 mg QD + Aspirin 100 mg QD + Clopidogrel 75 mg QD on days 1-21 and Milvexian 100 mg QD + Aspirin 100 mg QD on days 22-90. All administered orally.

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

Dosage and administration details:

Loading dose of Clopidogrel 300 mg + Aspirin 100 mg followed by Milvexian 100 mg QD + Aspirin 100 mg QD + Clopidogrel 75 mg QD on days 1-21 and Milvexian 100 mg QD + Aspirin 100 mg QD on days 22-90. All administered orally.

Investigational medicinal product name	Aspirin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Loading dose of Clopidogrel 300 mg + Aspirin 100 mg followed by Milvexian 100 mg QD + Aspirin 100 mg QD + Clopidogrel 75 mg QD on days 1-21 and Milvexian 100 mg QD + Aspirin 100 mg QD on days 22-90. All administered orally.

Number of subjects in period 2	Placebo	Milvexian 25 mg QD	Milvexian 25 mg BID
Started	682	325	313
Completed	529	260	242
Not completed	153	65	71
Participant request to discontinue treatment	34	6	10
Adverse event, serious fatal	1	-	-
Participant withdrew consent	11	4	5
Poor/Non compliance	2	2	1
Adverse event, non-fatal	82	44	47
Participant no longer meets study criteria	9	1	5
Other reasons	13	8	3
Lost to follow-up	1	-	-

Number of subjects in period 2	Milvexian 50 mg BID	Milvexian 100 mg BID	Milvexian 200 mg BID
Started	325	306	344
Completed	251	230	240
Not completed	74	76	104
Participant request to discontinue treatment	10	14	15
Adverse event, serious fatal	-	-	-
Participant withdrew consent	5	4	4
Poor/Non compliance	1	1	1
Adverse event, non-fatal	46	50	77
Participant no longer meets study criteria	4	4	4
Other reasons	7	3	3
Lost to follow-up	1	-	-

Number of subjects in period 2	Milvexian 50 mg QD	Milvexian 100 mg QD
Started	22	17
Completed	15	14
Not completed	7	3

Participant request to discontinue treatment	-	1
Adverse event, serious fatal	-	-
Participant withdrew consent	-	-
Poor/Non compliance	-	-
Adverse event, non-fatal	5	2
Participant no longer meets study criteria	2	-
Other reasons	-	-
Lost to follow-up	-	-

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Loading dose of Clopidogrel 300 mg + Aspirin 100 mg followed by Placebo + Aspirin 100 mg QD + Clopidogrel 75 mg QD on days 1-21 and Placebo + Aspirin 100 mg QD on days 22-90. All administered orally.	
Reporting group title	Milvexian 25 mg QD
Reporting group description:	
Loading dose of Clopidogrel 300 mg + Aspirin 100 mg followed by Milvexian 25 mg QD + Aspirin 100 mg QD + Clopidogrel 75 mg QD on days 1-21 and Milvexian 25 mg QD + Aspirin 100 mg QD on days 22-90. All administered orally.	
Reporting group title	Milvexian 25 mg BID
Reporting group description:	
Loading dose of Clopidogrel 300 mg + Aspirin 100 mg followed by Milvexian 25 mg BID + Aspirin 100 mg QD + Clopidogrel 75 mg QD on days 1-21 and Milvexian 25 mg BID + Aspirin 100 mg QD on days 22-90. All administered orally.	
Reporting group title	Milvexian 50 mg BID
Reporting group description:	
Loading dose of Clopidogrel 300 mg + Aspirin 100 mg followed by Milvexian 50 mg BID + Aspirin 100 mg QD + Clopidogrel 75 mg QD on days 1-21 and Milvexian 50 mg BID + Aspirin 100 mg QD on days 22-90. All administered orally.	
Reporting group title	Milvexian 100 mg BID
Reporting group description:	
Loading dose of Clopidogrel 300 mg + Aspirin 100 mg followed by Milvexian 100 mg BID + Aspirin 100 mg QD + Clopidogrel 75 mg QD on days 1-21 and Milvexian 100 mg BID + Aspirin 100 mg QD on days 22-90. All administered orally.	
Reporting group title	Milvexian 200 mg BID
Reporting group description:	
Loading dose of Clopidogrel 300 mg + Aspirin 100 mg followed by Milvexian 200 mg BID + Aspirin 100 mg QD + Clopidogrel 75 mg QD on days 1-21 and Milvexian 200 mg BID + Aspirin 100 mg QD on days 22-90. All administered orally.	
Reporting group title	Milvexian 50 mg QD
Reporting group description:	
Loading dose of Clopidogrel 300 mg + Aspirin 100 mg followed by Milvexian 50 mg QD + Aspirin 100 mg QD + Clopidogrel 75 mg QD on days 1-21 and Milvexian 50 mg QD + Aspirin 100 mg QD on days 22-90. All administered orally.	
Reporting group title	Milvexian 100 mg QD
Reporting group description:	
Loading dose of Clopidogrel 300 mg + Aspirin 100 mg followed by Milvexian 100 mg QD + Aspirin 100 mg QD + Clopidogrel 75 mg QD on days 1-21 and Milvexian 100 mg QD + Aspirin 100 mg QD on days 22-90. All administered orally.	

Reporting group values	Placebo	Milvexian 25 mg QD	Milvexian 25 mg BID
Number of subjects	691	328	318
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)	208	90	97
From 65-84 years	441	208	193
85 years and over	42	30	28
Age Continuous			
Units: Years			
arithmetic mean	69.1	70.9	70.1
standard deviation	± 10.58	± 10.66	± 11.34
Sex: Female, Male			
Units:			
Female	254	109	118
Male	437	219	200
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	10	4	2
Not Hispanic or Latino	62	20	22
Unknown or Not Reported	619	304	294
Race/Ethnicity, Customized			
Race			
Units: Subjects			
White	549	257	246
Black or African American	15	5	6
Asian	35	12	21
Native Hawaiian or Other Pacific Islander	0	1	1
Asian Indian	2	1	2
Chinese	0	0	0
Japanese	84	46	40
Malay	1	0	0
Asian Other	0	0	0
Other	5	6	2

Reporting group values	Milvexian 50 mg BID	Milvexian 100 mg BID	Milvexian 200 mg BID
Number of subjects	328	310	351
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)	108	92	106
From 65-84 years	201	198	221
85 years and over	19	20	24
Age Continuous			
Units: Years			
arithmetic mean	69.3	69.7	69.5
standard deviation	± 10.69	± 10.59	± 11.11

Sex: Female, Male Units:			
Female	121	112	128
Male	207	198	223
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	1	2	1
Not Hispanic or Latino	23	29	27
Unknown or Not Reported	304	279	323
Race/Ethnicity, Customized			
Race			
Units: Subjects			
White	260	251	288
Black or African American	8	3	5
Asian	13	11	17
Native Hawaiian or Other Pacific Islander	0	0	0
Asian Indian	1	0	0
Chinese	0	1	0
Japanese	41	39	40
Malay	0	0	0
Asian Other	1	0	0
Other	4	5	1

Reporting group values	Milvexian 50 mg QD	Milvexian 100 mg QD	Total
Number of subjects	22	18	2366
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)	10	9	720
From 65-84 years	11	8	1481
85 years and over	1	1	165
Age Continuous Units: Years			
arithmetic mean	65.7	65.4	
standard deviation	± 10.64	± 11.65	-
Sex: Female, Male Units:			
Female	7	10	859
Male	15	8	1507
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	1	1	22
Not Hispanic or Latino	7	7	197
Unknown or Not Reported	14	10	2147

Race/Ethnicity, Customized			
Race			
Units: Subjects			
White	18	15	1884
Black or African American	3	3	48
Asian	0	0	109
Native Hawaiian or Other Pacific Islander	0	0	2
Asian Indian	0	0	6
Chinese	0	0	1
Japanese	0	0	290
Malay	0	0	1
Asian Other	0	0	1
Other	1	0	24

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Loading dose of Clopidogrel 300 mg + Aspirin 100 mg followed by Placebo + Aspirin 100 mg QD + Clopidogrel 75 mg QD on days 1-21 and Placebo + Aspirin 100 mg QD on days 22-90. All administered orally.	
Reporting group title	Milvexian 25 mg QD
Reporting group description:	
Loading dose of Clopidogrel 300 mg + Aspirin 100 mg followed by Milvexian 25 mg QD + Aspirin 100 mg QD + Clopidogrel 75 mg QD on days 1-21 and Milvexian 25 mg QD + Aspirin 100 mg QD on days 22-90. All administered orally.	
Reporting group title	Milvexian 25 mg BID
Reporting group description:	
Loading dose of Clopidogrel 300 mg + Aspirin 100 mg followed by Milvexian 25 mg BID + Aspirin 100 mg QD + Clopidogrel 75 mg QD on days 1-21 and Milvexian 25 mg BID + Aspirin 100 mg QD on days 22-90. All administered orally.	
Reporting group title	Milvexian 50 mg BID
Reporting group description:	
Loading dose of Clopidogrel 300 mg + Aspirin 100 mg followed by Milvexian 50 mg BID + Aspirin 100 mg QD + Clopidogrel 75 mg QD on days 1-21 and Milvexian 50 mg BID + Aspirin 100 mg QD on days 22-90. All administered orally.	
Reporting group title	Milvexian 100 mg BID
Reporting group description:	
Loading dose of Clopidogrel 300 mg + Aspirin 100 mg followed by Milvexian 100 mg BID + Aspirin 100 mg QD + Clopidogrel 75 mg QD on days 1-21 and Milvexian 100 mg BID + Aspirin 100 mg QD on days 22-90. All administered orally.	
Reporting group title	Milvexian 200 mg BID
Reporting group description:	
Loading dose of Clopidogrel 300 mg + Aspirin 100 mg followed by Milvexian 200 mg BID + Aspirin 100 mg QD + Clopidogrel 75 mg QD on days 1-21 and Milvexian 200 mg BID + Aspirin 100 mg QD on days 22-90. All administered orally.	
Reporting group title	Milvexian 50 mg QD
Reporting group description:	
Loading dose of Clopidogrel 300 mg + Aspirin 100 mg followed by Milvexian 50 mg QD + Aspirin 100 mg QD + Clopidogrel 75 mg QD on days 1-21 and Milvexian 50 mg QD + Aspirin 100 mg QD on days 22-90. All administered orally.	
Reporting group title	Milvexian 100 mg QD
Reporting group description:	
Loading dose of Clopidogrel 300 mg + Aspirin 100 mg followed by Milvexian 100 mg QD + Aspirin 100 mg QD + Clopidogrel 75 mg QD on days 1-21 and Milvexian 100 mg QD + Aspirin 100 mg QD on days 22-90. All administered orally.	
Reporting group title	Placebo
Reporting group description:	
Loading dose of Clopidogrel 300 mg + Aspirin 100 mg followed by Placebo + Aspirin 100 mg QD + Clopidogrel 75 mg QD on days 1-21 and Placebo + Aspirin 100 mg QD on days 22-90. All administered orally.	
Reporting group title	Milvexian 25 mg QD
Reporting group description:	
Loading dose of Clopidogrel 300 mg + Aspirin 100 mg followed by Milvexian 25 mg QD + Aspirin 100 mg QD + Clopidogrel 75 mg QD on days 1-21 and Milvexian 25 mg QD + Aspirin 100 mg QD on days 22-90. All administered orally.	
Reporting group title	Milvexian 25 mg BID
Reporting group description:	
Loading dose of Clopidogrel 300 mg + Aspirin 100 mg followed by Milvexian 25 mg BID + Aspirin 100 mg QD + Clopidogrel 75 mg QD on days 1-21 and Milvexian 25 mg BID + Aspirin 100 mg QD on days	

22-90. All administered orally.

Reporting group title	Milvexian 50 mg BID

Reporting group description:

Loading dose of Clopidogrel 300 mg + Aspirin 100 mg followed by Milvexian 50 mg BID + Aspirin 100 mg QD + Clopidogrel 75 mg QD on days 1-21 and Milvexian 50 mg BID + Aspirin 100 mg QD on days 22-90. All administered orally.

Reporting group title	Milvexian 100 mg BID

Reporting group description:

Loading dose of Clopidogrel 300 mg + Aspirin 100 mg followed by Milvexian 100 mg BID + Aspirin 100 mg QD + Clopidogrel 75 mg QD on days 1-21 and Milvexian 100 mg BID + Aspirin 100 mg QD on days 22-90. All administered orally.

Reporting group title	Milvexian 200 mg BID

Reporting group description:

Loading dose of Clopidogrel 300 mg + Aspirin 100 mg followed by Milvexian 200 mg BID + Aspirin 100 mg QD + Clopidogrel 75 mg QD on days 1-21 and Milvexian 200 mg BID + Aspirin 100 mg QD on days 22-90. All administered orally.

Reporting group title	Milvexian 50 mg QD

Reporting group description:

Loading dose of Clopidogrel 300 mg + Aspirin 100 mg followed by Milvexian 50 mg QD + Aspirin 100 mg QD + Clopidogrel 75 mg QD on days 1-21 and Milvexian 50 mg QD + Aspirin 100 mg QD on days 22-90. All administered orally.

Reporting group title	Milvexian 100 mg QD

Reporting group description:

Loading dose of Clopidogrel 300 mg + Aspirin 100 mg followed by Milvexian 100 mg QD + Aspirin 100 mg QD + Clopidogrel 75 mg QD on days 1-21 and Milvexian 100 mg QD + Aspirin 100 mg QD on days 22-90. All administered orally.

Primary: Percent of Participants with Model Based Assessment of Composite of New Ischemic Stroke During Treatment and New Covert Brain Infarction (FLAIR + DWI) Detected by MRI by Day 90

End point title	Percent of Participants with Model Based Assessment of Composite of New Ischemic Stroke During Treatment and New Covert Brain Infarction (FLAIR + DWI) Detected by MRI by Day 90[1]

End point description:

Model based assessment estimate for composite event is a customized statistical analysis called MCP-MOD (Multiple Comparison Procedures, MODel) estimation, which is used to check for dose-response relationship. 95% confidence interval (CI) for composite event based on bootstrap (10000 samples).

End point type	Primary

End point timeframe:

From randomization to up to 90 days after randomization

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Endpoints are cohort specific and do not report for all arms.

End point values	Placebo	Milvexian 25 mg QD	Milvexian 25 mg BID	Milvexian 50 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	625	308	287	306
Units: Percentage of participants				
number (confidence interval 95%)	16.8 (14.2 to 19.4)	16.7 (14.4 to 19.0)	16.6 (14.5 to 18.7)	15.6 (13.6 to 17.9)

End point values	Milvexian 100 mg BID	Milvexian 200 mg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	277	317		
Units: Percentage of participants				
number (confidence interval 95%)	15.4 (13.0 to 18.0)	15.3 (12.3 to 20.4)		

Statistical analyses

Statistical analysis title	Milvexian 25 mg QD over Placebo
Statistical analysis description:	
Multiple Comparison Procedures, MODel (MCP-MOD). 95% confidence interval (CI) for composite event based on bootstrap (10000 samples).	
Comparison groups	Placebo v Milvexian 25 mg QD
Number of subjects included in analysis	933
Analysis specification	Pre-specified
Analysis type	superiority
Method	MCP-MOD
Parameter estimate	Relative Risk (RR)
Point estimate	0.99
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.87
upper limit	1.1

Statistical analysis title	Milvexian 200 mg BID over Placebo
Statistical analysis description:	
Multiple Comparison Procedures, MODel (MCP-MOD). 95% confidence interval (CI) for composite event based on bootstrap (10000 samples).	
Comparison groups	Placebo v Milvexian 200 mg BID
Number of subjects included in analysis	942
Analysis specification	Pre-specified
Analysis type	superiority
Method	MCP-MOD
Parameter estimate	Relative Risk (RR)
Point estimate	0.91
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.69
upper limit	1.31

Statistical analysis title	Milvexian 100 mg BID over Placebo
Statistical analysis description:	
Multiple Comparison Procedures, MODel (MCP-MOD). 95% confidence interval (CI) for composite event based on bootstrap (10000 samples).	
Comparison groups	Placebo v Milvexian 100 mg BID
Number of subjects included in analysis	902
Analysis specification	Pre-specified
Analysis type	superiority
Method	MCP-MOD
Parameter estimate	Relative Risk (RR)
Point estimate	0.92
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.73
upper limit	1.18

Statistical analysis title	Milvexian 25 mg BID over Placebo
Statistical analysis description:	
Multiple Comparison Procedures, MODel (MCP-MOD). 95% confidence interval (CI) for composite event based on bootstrap (10000 samples).	
Comparison groups	Placebo v Milvexian 25 mg BID
Number of subjects included in analysis	912
Analysis specification	Pre-specified
Analysis type	superiority
Method	MCP-MOD
Parameter estimate	Relative Risk (RR)
Point estimate	0.99
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.83
upper limit	1.15

Statistical analysis title	Milvexian 50 mg BID over Placebo
Statistical analysis description:	
Multiple Comparison Procedures, MODel (MCP-MOD). 95% confidence interval (CI) for composite event based on bootstrap (10000 samples).	
Comparison groups	Placebo v Milvexian 50 mg BID

Number of subjects included in analysis	931
Analysis specification	Pre-specified
Analysis type	superiority
Method	MCP-MOD
Parameter estimate	Relative Risk (RR)
Point estimate	0.93
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.76
upper limit	1.16

Secondary: Percent of Participants with Major Bleeding According to BARC Type 3 and 5

End point title	Percent of Participants with Major Bleeding According to BARC Type 3 and 5

End point description:

Percent of participants with major bleeding based on the Bleeding Academic Research Consortium (BARC) Types 3 and 5 definitions. BARC bleeding types:
3a = Overt bleeding plus hemoglobin drop of 3 to < 5 g/dL transfusion with overt bleeding
3b = Overt bleeding plus hemoglobin drop ≥5 g/dL; cardiac tamponade; bleeding requiring surgical intervention for control; bleeding requiring IV vasoactive agents
3c = Intracranial hemorrhage,
5a = Probable fatal bleeding
5b = Definite fatal bleeding

End point type	Secondary

End point timeframe:

From first dose to up to 107 days after first dose

End point values	Placebo	Milvexian 25 mg QD	Milvexian 25 mg BID	Milvexian 50 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	682	325	313	325
Units: Percentage of participants				
number (confidence interval 95%)	0.6 (0.2 to 1.5)	0.6 (0.1 to 2.2)	0.6 (0.1 to 2.3)	1.5 (0.5 to 3.6)

End point values	Milvexian 100 mg BID	Milvexian 200 mg BID	Milvexian 50 mg QD	Milvexian 100 mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	306	344	22	17
Units: Percentage of participants				
number (confidence interval 95%)	1.6 (0.5 to 3.8)	1.5 (0.5 to 3.4)	0 (0 to 15.4)	0 (0 to 19.5)

Statistical analyses

No statistical analyses for this end point

Secondary: Percent of Participants with Bleeding Based on BARC Types 1-5

End point title	Percent of Participants with Bleeding Based on BARC Types 1-5

End point description:

Percent of participants with bleeding based on Bleeding Academic Research Consortium (BARC) Type 1 to 5. BARC bleeding types: 0=No bleeding. 1=Not actionable bleeding. 2=Overt, actionable sign of hemorrhage requiring nonsurgical, medical intervention by a health-care professional, leading to hospitalization or increased level of care, or prompting evaluation. 3a=Overt bleeding plus hemoglobin drop of 3 to < 5 g/dL. 3b=Overt bleeding plus hemoglobin drop ≥5 g/dL; cardiac tamponade; bleeding requiring surgical intervention; bleeding requiring IV vasoactive agents. 3c=Intracranial hemorrhage; intraocular bleed compromising vision. 4=CABG-related bleeding, perioperative intracranial bleeding within 48 hours, reoperation after closure of sternotomy to control bleeding, transfusion of ≥5 U whole blood or packed red blood cells within a 48-hour period, chest tube output more than or equal to 2L within a 24-hour period. 5a=Probable fatal bleeding. 5b=Definite fatal bleeding.

End point type	Secondary

End point timeframe:

From first dose to up to 107 days after first dose

End point values	Placebo	Milvexian 25 mg QD	Milvexian 25 mg BID	Milvexian 50 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	682	325	313	325
Units: Participants				
TYPE 1	41	26	16	28
TYPE 2	9	7	9	7
TYPE 3A	2	1	1	1
TYPE 3B	0	1	1	1
TYPE 3C	2	0	0	3
TYPE 4	0	0	0	0
TYPE 5A	0	0	0	0
TYPE 5B	0	0	0	0

End point values	Milvexian 100 mg BID	Milvexian 200 mg BID	Milvexian 50 mg QD	Milvexian 100 mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	306	344	22	17
Units: Participants				
TYPE 1	25	22	5	2
TYPE 2	10	8	1	1
TYPE 3A	2	3	0	0
TYPE 3B	3	1	0	0
TYPE 3C	0	1	0	0
TYPE 4	0	0	0	0
TYPE 5A	0	0	0	0
TYPE 5B	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Bleeding Based on ISTH-Defined Criteria

End point title	Number of Participants with Bleeding Based on ISTH-Defined Criteria

End point description:

Number of participants with bleeding based on International Society on Thrombosis and Hemostasis (ISTH). ISTH Bleeding Types: 1) Fatal bleeding and/or 2) Symptomatic bleeding in a critical area or organ, such as intracranial, intraspinal, intraocular, retroperitoneal, intraarticular or pericardial, or intramuscular with compartment syndrome and/or 3) Bleeding causing a fall in hemoglobin level of ≥2 g/dL, or leading to transfusion of ≥2 units of whole blood or red cells.

End point type	Secondary

End point timeframe:

From first dose to up to 107 days after first dose

End point values	Placebo	Milvexian 25 mg QD	Milvexian 25 mg BID	Milvexian 50 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	682	325	313	325
Units: Participants				
Major	4	2	2	5
Clinically Relevant Non-Major (CRNM)	7	8	9	7
Major or CRNM	11	10	11	12
Minor Bleed	43	25	16	28

End point values	Milvexian 100 mg BID	Milvexian 200 mg BID	Milvexian 50 mg QD	Milvexian 100 mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	306	344	22	17
Units: Participants				
Major	6	5	0	0
Clinically Relevant Non-Major (CRNM)	8	8	1	1
Major or CRNM	14	13	1	1
Minor Bleed	26	22	5	2

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Bleeding Based on PLATO-Defined Criteria

End point title	Number of Participants with Bleeding Based on PLATO-Defined Criteria

End point description:

Number of participants with bleeding based on Platelet Inhibition and Patient Outcomes (PLATO) defined criteria. PLATO bleeding definitions:
1. Major Life-threatening: Fatal, Intracranial, Intrapericardial with cardiac tamponade, Resulting in hypovolemic shock or severe hypotension that requires pressors or surgery, Clinically overt or apparent bleeding associated with decrease in hemoglobin >5 g/dL, Requiring transfusion of ≥4 U whole blood or packed red blood cells (PRBCs)
2. Other Major: Significantly disabling (eg, intraocular with permanent vision loss), Associated drop in hemoglobin of 3 to 5 g/dL, Requiring transfusion of 2 to 3 U whole blood or PRBCs
3. Any Major: Any one of the above criteria
4. Minor: Bleeding that does not meet criteria for PLATO Major bleeding, and requiring medical intervention

End point type	Secondary

End point timeframe:

From first dose to up to 107 days after first dose

End point values	Placebo	Milvexian 25 mg QD	Milvexian 25 mg BID	Milvexian 50 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	682	325	313	325
Units: Participants				
MAJOR LIFE-THREATENING	2	1	1	4
OTHER MAJOR BLEEDING	2	1	1	1
ANY MAJOR	4	2	2	5
MINOR	7	6	7	7
MINIMAL	43	27	18	28

End point values	Milvexian 100 mg BID	Milvexian 200 mg BID	Milvexian 50 mg QD	Milvexian 100 mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	306	344	22	17
Units: Participants				
MAJOR LIFE-THREATENING	3	2	0	0
OTHER MAJOR BLEEDING	2	3	0	0
ANY MAJOR	5	5	0	0
MINOR	9	9	0	1
MINIMAL	26	21	6	2

Statistical analyses

No statistical analyses for this end point

Secondary: Percent of Participants with Descriptive Assessment of Composite of New Ischemic Stroke During Treatment and New Covert Brain Infarction (FLAIR + DWI) Detected by MRI by Day 90

End point title	Percent of Participants with Descriptive Assessment of Composite of New Ischemic Stroke During Treatment and New Covert Brain Infarction (FLAIR + DWI) Detected by MRI by Day 90

End point description:

Descriptive Assessment of Composite of New Ischemic Stroke During Treatment and New Covert Brain Infarction (FLAIR + DWI) Detected by MRI by Day 90.

End point type	Secondary

End point timeframe:

From randomization to up to 90 days after randomization

End point values	Placebo	Milvexian 25 mg QD	Milvexian 25 mg BID	Milvexian 50 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	625	308	287	306
Units: Percentage of participants				
number (not applicable)	16.6	16.2	18.5	14.1

End point values	Milvexian 100 mg BID	Milvexian 200 mg BID	Milvexian 50 mg QD	Milvexian 100 mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	277	317	21	16
Units: Percentage of participants				
number (not applicable)	14.8	16.4	19.0	18.8

Statistical analyses

No statistical analyses for this end point

Secondary: National Institutes of Health Stroke Scale (NIHSS)

End point title	National Institutes of Health Stroke Scale (NIHSS)

End point description:

The NIHSS is an 11-item neurologic examination stroke scale used to evaluate the effect of acute cerebral infarction on the levels of consciousness, language, neglect, visual-field loss, extraocular movement, motor strength, ataxia, dysarthria, and sensory loss. A trained observer rates the patent's ability to answer questions and perform activities. The score for each ability is a number between 0 and 4, 0 being normal functioning and 4 being completely impaired. The patient's NIHSS score is calculated by adding the number for each element of the scale; 42 is the highest score possible. In the NIHSS, the higher the score, the more impaired a stroke participant is. 99999 = Not Available

End point type	Secondary

End point timeframe:

At baseline, on Days 21 and 90, and at the time of a new stroke event

End point values	Placebo	Milvexian 25 mg QD	Milvexian 25 mg BID	Milvexian 50 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	684	324	311	326
Units: Score on a scale				
arithmetic mean (standard deviation)				
Baseline	1.6 (± 1.87)	1.7 (± 1.68)	1.6 (± 1.73)	1.6 (± 1.79)
Day 21	0.9 (± 2.11)	0.8 (± 1.35)	0.8 (± 1.43)	0.8 (± 1.58)
Day 90	0.5 (± 1.40)	0.6 (± 1.06)	0.6 (± 1.51)	0.6 (± 1.14)
First recurrent stroke	6.2 (± 5.01)	4.6 (± 6.79)	5.4 (± 3.17)	4.6 (± 4.30)

End point values	Milvexian 100 mg BID	Milvexian 200 mg BID	Milvexian 50 mg QD	Milvexian 100 mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	305	348	22	17
Units: Score on a scale				
arithmetic mean (standard deviation)				
Baseline	1.8 (± 1.81)	1.6 (± 1.79)	1.1 (± 1.44)	2.0 (± 1.70)
Day 21	0.8 (± 1.48)	0.9 (± 1.88)	0.8 (± 1.90)	0.9 (± 1.39)
Day 90	0.6 (± 1.32)	0.6 (± 1.29)	0.3 (± 0.72)	0.6 (± 1.45)
First recurrent stroke	7.1 (± 4.68)	4.4 (± 4.60)	5.3 (± 3.06)	1.0 (± 99999)

Statistical analyses

No statistical analyses for this end point

Secondary: Composite of Percent of Participants with New Ischemic Stroke, MI and All Cause Death

End point title	Composite of Percent of Participants with New Ischemic Stroke, MI and All Cause Death

End point description:

Composite of percent of participants of new ischemic stroke, (Myocardial Infarction) MI and all cause death.

End point type	Secondary

End point timeframe:

From randomization to up to 90 days after randomization

End point values	Placebo	Milvexian 25 mg QD	Milvexian 25 mg BID	Milvexian 50 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	691	328	318	328
Units: Percentage of participants				
number (confidence interval 95%)	6.1 (4.3 to 7.9)	5.2 (2.8 to 7.6)	4.7 (2.4 to 7.0)	4.9 (2.5 to 7.2)

End point values	Milvexian 100 mg BID	Milvexian 200 mg BID	Milvexian 50 mg QD	Milvexian 100 mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	310	351	22	18
Units: Percentage of participants				
number (confidence interval 95%)	5.2 (2.7 to 7.6)	9.4 (6.3 to 12.5)	18.2 (2.1 to 34.3)	5.6 (0 to 16.1)

Statistical analyses

No statistical analyses for this end point

Secondary: Modified Rankin Scale (mRS)

End point title	Modified Rankin Scale (mRS)

End point description:

The Modified Rankin Score (mRS) is a 6-point disability scale with possible scores ranging from 0 to 6.
0 = No symptoms at all
1 = No significant disability despite symptoms; able to carry out all usual duties and activities
2 = Slight disability; unable to carry out all previous activities, but able to look after own affairs without assistance
3 = Moderate disability; requiring some help, but able to walk without assistance
4 = Moderately severe disability; unable to walk and attend to bodily needs without assistance
5 = Severe disability; bedridden, incontinent and requiring constant nursing care and attention
6 = Dead
99999 = Not Available

End point type	Secondary

End point timeframe:

At baseline, on Days 21 and 90, and at the time of a new stroke event

End point values	Placebo	Milvexian 25 mg QD	Milvexian 25 mg BID	Milvexian 50 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	688	326	314	328
Units: Score on a scale				
arithmetic mean (standard deviation)				
Baseline	0.5 (± 0.87)	0.6 (± 0.95)	0.6 (± 0.96)	0.5 (± 0.86)
Day 21	1.0 (± 1.18)	1.0 (± 1.13)	0.9 (± 1.15)	0.9 (± 1.15)
Day 90	0.7 (± 1.04)	0.8 (± 1.04)	0.8 (± 1.07)	0.7 (± 1.01)
First recurrent stroke	3.0 (± 1.60)	2.7 (± 1.03)	2.6 (± 1.35)	2.3 (± 1.62)

End point values	Milvexian 100 mg BID	Milvexian 200 mg BID	Milvexian 50 mg QD	Milvexian 100 mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	309	349	22	17
Units: Score on a scale				
arithmetic mean (standard deviation)				
Baseline	0.5 (± 0.89)	0.6 (± 0.95)	0.2 (± 0.53)	0.7 (± 0.99)
Day 21	1.0 (± 1.17)	0.9 (± 1.19)	0.9 (± 1.27)	1.3 (± 1.14)
Day 90	0.7 (± 1.01)	0.8 (± 1.05)	0.6 (± 1.05)	1.0 (± 1.11)
First recurrent stroke	2.9 (± 1.64)	1.8 (± 1.72)	2.0 (± 0.00)	1.0 (± 99999)

Statistical analyses

No statistical analyses for this end point

Secondary: Montreal Cognitive Assessment (MoCA)

End point title	Montreal Cognitive Assessment (MoCA)

End point description:

The Montreal Cognitive Assessment (MoCA) is a survey with a summed score. MoCA score ranges between a lowest score of 0 to a highest score of 30. A score of:
- ≥26 points: indicates normal cognitive function
- 18–25 points: Mild cognitive impairment
- 10–17 points: Moderate cognitive impairment
- fewer than 10 points: Severe cognitive impairment

99999 = Not Available

End point type	Secondary

End point timeframe:

At baseline, on Days 21 and 90, and at the time of a new stroke event

End point values	Placebo	Milvexian 25 mg QD	Milvexian 25 mg BID	Milvexian 50 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	541	257	235	257
Units: Score on a scale				
arithmetic mean (standard deviation)				
Baseline	22.3 (± 5.06)	21.6 (± 5.59)	22.0 (± 5.18)	22.5 (± 4.82)
Day 21	24.0 (± 4.77)	23.9 (± 5.01)	24.0 (± 4.70)	24.3 (± 4.57)
Day 90	24.6 (± 4.54)	24.0 (± 4.69)	24.2 (± 4.80)	24.4 (± 4.48)
First recurrent stroke	23.2 (± 6.63)	17.3 (± 6.11)	25.3 (± 2.31)	19.0 (± 8.49)

End point values	Milvexian 100 mg BID	Milvexian 200 mg BID	Milvexian 50 mg QD	Milvexian 100 mg QD

Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	235	276	17	14
Units: Score on a scale				
arithmetic mean (standard deviation)				
Baseline	22.4 (± 5.04)	22.1 (± 5.31)	24.4 (± 3.84)	22.0 (± 4.59)
Day 21	23.6 (± 4.48)	24.0 (± 4.96)	26.4 (± 2.61)	24.1 (± 4.70)
Day 90	24.5 (± 4.36)	24.2 (± 5.05)	25.0 (± 4.72)	26.4 (± 1.69)
First recurrent stroke	3.0 (± 99999)	23.1 (± 7.08)	11.0 (± 99999)	22.0 (± 99999)

Statistical analyses

No statistical analyses for this end point

Secondary: Digit Symbol Substitution Test (DSST)

End point title	Digit Symbol Substitution Test (DSST)

End point description:

The Descriptive Summary of the Digit Symbol Substitution Test (DSST) is a scale item, with a lowest score of 0 and highest total score of 135. Higher score indicates better cognitive functioning.

99999 = Not Available

End point type	Secondary

End point timeframe:

At baseline, on Days 21 and 90, and at the time of a new stroke event

End point values	Placebo	Milvexian 25 mg QD	Milvexian 25 mg BID	Milvexian 50 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	493	238	209	234
Units: Score on a scale				
arithmetic mean (standard deviation)				
Baseline	34.9 (± 22.36)	31.2 (± 18.87)	32.9 (± 22.89)	37.2 (± 25.67)
Day 21	41.2 (± 22.14)	38.9 (± 19.27)	40.2 (± 21.60)	45.1 (± 25.77)
Day 90	42.8 (± 21.18)	41.7 (± 21.66)	41.3 (± 20.29)	45.2 (± 21.86)
First recurrent stroke	36.3 (± 13.56)	28.0 (± 20.95)	42.0 (± 4.36)	40.5 (± 2.12)

End point values	Milvexian 100 mg BID	Milvexian 200 mg BID	Milvexian 50 mg QD	Milvexian 100 mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	220	257	17	14
Units: Score on a scale				
arithmetic mean (standard deviation)				
Baseline	33.7 (± 21.89)	31.7 (± 19.15)	47.1 (± 29.34)	29.2 (± 18.16)
Day 21	41.2 (± 22.87)	39.1 (± 21.35)	54.6 (± 32.73)	37.1 (± 20.13)
Day 90	45.5 (± 23.44)	41.4 (± 21.97)	47.5 (± 27.48)	40.7 (± 17.46)
First recurrent stroke	23.0 (± 99999)	27.5 (± 16.96)	9.0 (± 99999)	47.0 (± 99999)

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Clinically Significant Vital Sign Abnormalities

End point title	Number of Participants with Clinically Significant Vital Sign Abnormalities

End point description:

Number of participants with clinically significant vital sign abnormalities. Vital signs included heart rate and diastolic and systolic blood pressure.

End point type	Secondary

End point timeframe:

From first dose to up to 90 days after first dose

End point values	Placebo	Milvexian 25 mg QD	Milvexian 25 mg BID	Milvexian 50 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	682	325	313	325
Units: Participants	0	0	0	0

End point values	Milvexian 100 mg BID	Milvexian 200 mg BID	Milvexian 50 mg QD	Milvexian 100 mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	306	344	22	17
Units: Participants	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Adverse Events (AEs)

End point title	Number of Participants with Adverse Events (AEs)

End point description:

AE: include all non-serious adverse events with onset on or after first dose date and within 2 days after the last dose of study treatment.

End point type	Secondary

End point timeframe:

From first dose to 2 days after last dose of study therapy (up to approximately 107 days)

End point values	Placebo	Milvexian 25 mg QD	Milvexian 25 mg BID	Milvexian 50 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	682	325	313	325
Units: Participants	399	190	186	192

End point values	Milvexian 100 mg BID	Milvexian 200 mg BID	Milvexian 50 mg QD	Milvexian 100 mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	306	344	22	17
Units: Participants	193	211	11	13

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Clinically Significant Physical Examination Abnormalities

End point title	Number of Participants with Clinically Significant Physical Examination Abnormalities

End point description:

Number of participants with clinically significant physical examination abnormalities.

End point type	Secondary

End point timeframe:

From first dose to up to 90 days after first dose

End point values	Placebo	Milvexian 25 mg QD	Milvexian 25 mg BID	Milvexian 50 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	682	325	313	325
Units: Participants	0	0	0	0

End point values	Milvexian 100 mg BID	Milvexian 200 mg BID	Milvexian 50 mg QD	Milvexian 100 mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	306	344	22	17
Units: Participants	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Clinically Significant Electrocardiogram (ECG) Abnormalities

End point title	Number of Participants with Clinically Significant Electrocardiogram (ECG) Abnormalities

End point description:

Number of participants with clinically significant ECG abnormalities.

End point type	Secondary

End point timeframe:

From first dose to up to 90 days after first dose

End point values	Placebo	Milvexian 25 mg QD	Milvexian 25 mg BID	Milvexian 50 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	682	325	313	325
Units: Participants	0	0	0	0

End point values	Milvexian 100 mg BID	Milvexian 200 mg BID	Milvexian 50 mg QD	Milvexian 100 mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	306	344	22	17
Units: Participants	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Clinically Significant Laboratory Abnormalities - Liver

End point title	Number of Participants with Clinically Significant Laboratory Abnormalities - Liver

End point description:

The number of treated participants who experienced a laboratory abnormality of the liver during the course of the study.

Aspartate aminotransferase (AST)
Alanine aminotransferase (ALT)

Upper Limit of Normal (ULN)
Results reported in International System of Units (SI)

End point type	Secondary

End point timeframe:

From first dose to up to approximately 38 months

End point values	Placebo	Milvexian 25 mg QD	Milvexian 25 mg BID	Milvexian 50 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	642	303	280	306
Units: Participants				
ALT > 3x ULN	4	2	0	2
ALT > 5x ULN	1	0	0	0
ALT > 10x ULN	1	0	0	0
ALT > 20x ULN	0	0	0	0
AST > 3x ULN	6	5	1	4
AST > 5x ULN	3	2	1	0
AST > 10x ULN	1	0	0	0
AST > 20x ULN	0	0	0	0
ALP > 2x ULN	4	5	1	6
Total Bilirubin > 1.5x ULN	10	6	2	7
Total Bilirubin > 2x ULN	3	1	1	2
ALT/AST elevation >3xULN w/ total bili >2xULN	0	0	0	0

End point values	Milvexian 100 mg BID	Milvexian 200 mg BID	Milvexian 50 mg QD	Milvexian 100 mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	281	324	21	16
Units: Participants				
ALT > 3x ULN	3	3	0	0
ALT > 5x ULN	2	2	0	0
ALT > 10x ULN	1	1	0	0
ALT > 20x ULN	1	0	0	0
AST > 3x ULN	3	3	1	0
AST > 5x ULN	2	1	1	0
AST > 10x ULN	1	0	0	0
AST > 20x ULN	1	0	0	0
ALP > 2x ULN	4	2	0	0
Total Bilirubin > 1.5x ULN	5	2	0	0
Total Bilirubin > 2x ULN	2	1	0	0
ALT/AST elevation >3xULN w/ total bili >2xULN	1	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change from Baseline in Factor XI Clotting Activity

End point title	Percent Change from Baseline in Factor XI Clotting Activity

End point description:

Percent change from baseline in factor XI clotting activity via exposure response.

End point type	Secondary

End point timeframe:

Baseline and day 90

End point values	Placebo	Milvexian 25 mg QD	Milvexian 25 mg BID	Milvexian 50 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	503	251	223	228
Units: Seconds				
arithmetic mean (standard error)	4.48 (± 3.455)	-8.88 (± 1.280)	-1767 (± 1.900)	-37.20 (± 1.655)

End point values	Milvexian 100 mg BID	Milvexian 200 mg BID	Milvexian 50 mg QD	Milvexian 100 mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	216	236	15	13
Units: Seconds				
arithmetic mean (standard error)	-61.52 (± 1.869)	-70.25 (± 3.043)	3.86 (± 13.754)	-44.27 (± 6.501)

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change from Baseline in aPTT Activity

End point title	Percent Change from Baseline in aPTT Activity

End point description:

Percent change from baseline in activated partial thromboplastin time (aPTT) activity via exposure response.

End point type	Secondary

End point timeframe:

Baseline and day 90

End point values	Placebo	Milvexian 25 mg QD	Milvexian 25 mg BID	Milvexian 50 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	503	251	226	241
Units: Seconds				
arithmetic mean (standard error)	2.47 (± 0.768)	38.72 (± 2.264)	58.30 (± 3.195)	97.32 (± 3.601)

End point values	Milvexian 100 mg BID	Milvexian 200 mg BID	Milvexian 50 mg QD	Milvexian 100 mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	214	232	14	14
Units: Seconds				
arithmetic mean (standard error)	140.76 (± 5.154)	193.64 (± 7.041)	48.48 (± 11.243)	118.06 (± 13.840)

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetic Parameter - Estimated Clearance (CL)

End point title	Pharmacokinetic Parameter - Estimated Clearance (CL)[2]

End point description:

Pharmacokinetic Parameter - Estimated Clearance (CL). CL is derived from plasma concentration versus time data. PK parameters were generated using a Population Pharmacokinetics (PPK) model. Summary statistics for these individual predicted PK parameters and exposures were stratified by dose. The PPK model analysis was based on combined PK data collected on days 1, 21, and 90.

End point type	Secondary

End point timeframe:

From first dose to up to 90 days after first dose

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Endpoints are cohort specific and do not report for all arms.

End point values	Milvexian 25 mg QD	Milvexian 25 mg BID	Milvexian 50 mg BID	Milvexian 100 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	323	307	323	303
Units: L/h				
geometric mean (geometric coefficient of variation)	8.15 (± 34)	8.01 (± 34.3)	7.54 (± 32.8)	7.08 (± 31.3)

End point values	Milvexian 200 mg BID			
Subject group type	Reporting group			
Number of subjects analysed	341			

Units: L/h				
geometric mean (geometric coefficient of variation)	7.43 (± 32.9)			

Statistical analyses

No statistical analyses for this end point

Secondary: Volume of DWI-Positive Infarct (s) on the DWI Sequence

End point title	Volume of DWI-Positive Infarct (s) on the DWI Sequence

End point description:

Total Volume of diffusion-weighted imaging MRI (DWI)-Positive Infarct (s) on the DWI Sequence.

End point type	Secondary

End point timeframe:

From randomization to up to 90 days after randomization

End point values	Placebo	Milvexian 25 mg QD	Milvexian 25 mg BID	Milvexian 50 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	516	242	241	256
Units: mL				
arithmetic mean (standard deviation)	4.6 (± 7.7)	6.0 (± 13.2)	4.2 (± 9.4)	6.3 (± 14.0)

End point values	Milvexian 100 mg BID	Milvexian 200 mg BID	Milvexian 50 mg QD	Milvexian 100 mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	237	278	16	12
Units: mL				
arithmetic mean (standard deviation)	4.3 (± 7.4)	6.1 (± 10.1)	3.8 (± 5.5)	10.6 (± 8.5)

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetic Parameter - Volume of the Central Compartment (VC)

End point title	Pharmacokinetic Parameter - Volume of the Central Compartment (VC)[3]

End point description:

Pharmacokinetic Parameter - Volume of the Central Compartment (VC). VC is derived from plasma concentration versus time data. PK parameters were generated using a Population Pharmacokinetics (PPK) model. Summary statistics for these individual predicted PK parameters and exposures were stratified by dose. The PPK model analysis was based on combined PK data collected on days 1, 21, and 90.

End point type	Secondary

End point timeframe:

From first dose to up to 90 days after first dose

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Endpoints are cohort specific and do not report for all arms.

End point values	Milvexian 25 mg QD	Milvexian 25 mg BID	Milvexian 50 mg BID	Milvexian 100 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	323	307	323	303
Units: Liter				
geometric mean (geometric coefficient of variation)	34.9 (± 152)	31.4 (± 138)	30.9 (± 145)	28.9 (± 149)

End point values	Milvexian 200 mg BID			
Subject group type	Reporting group			
Number of subjects analysed	341			
Units: Liter				
geometric mean (geometric coefficient of variation)	31.6 (± 181)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of DWI-Positive Infarct (s) on the DWI Sequence

End point title	Number of DWI-Positive Infarct (s) on the DWI Sequence

End point description:

Number of diffusion-weighted imaging MRI (DWI)-Positive Infarct (s) on the DWI Sequence.

End point type	Secondary

End point timeframe:

From randomization to up to 90 days after randomization

End point values	Placebo	Milvexian 25 mg QD	Milvexian 25 mg BID	Milvexian 50 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	516	242	241	256
Units: DWI-Positive Infarct(s)				
arithmetic mean (standard deviation)	4.5 (± 5.7)	4.6 (± 7.0)	4.6 (± 5.8)	3.7 (± 4.1)

End point values	Milvexian 100 mg BID	Milvexian 200 mg BID	Milvexian 50 mg QD	Milvexian 100 mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	237	278	16	12
Units: DWI-Positive Infarct(s)				
arithmetic mean (standard deviation)	4.3 (± 5.2)	4.2 (± 5.1)	1.6 (± 1.1)	4.2 (± 4.3)

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Percent of Participants with Ischemic Stroke Events

End point title	Percent of Participants with Ischemic Stroke Events

End point description:

Secondary analysis of symptomatic ischemic stroke events. Clinical events are included up to day 90. Wald 95% CI within group. Undetermined stroke is included.

End point type	Other pre-specified

End point timeframe:

From randomization to up to 90 days after randomization

End point values	Placebo	Milvexian 25 mg QD	Milvexian 25 mg BID	Milvexian 50 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	691	328	318	328
Units: Percentage of participants				
number (confidence interval 95%)				
Ischemic stroke	5.5 (3.8 to 7.2)	4.6 (2.3 to 6.8)	3.8 (1.7 to 5.9)	4.0 (1.9 to 6.1)
Undetermined stroke	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)

End point values	Milvexian 100 mg BID	Milvexian 200 mg BID	Milvexian 50 mg QD	Milvexian 100 mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	310	351	22	18
Units: Percentage of participants				
number (confidence interval 95%)				
Ischemic stroke	3.5 (1.5 to 5.6)	7.7 (4.9 to 10.5)	13.6 (0.0 to 28.0)	5.6 (0.0 to 16.1)
Undetermined stroke	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)

Statistical analyses

Statistical analysis title	Milvexian 25 mg QD over Placebo

Statistical analysis description:	
Wald Confidence Limits. 95% CIs for RR are constructed using Wald Confidence Limits.	
Comparison groups	Placebo v Milvexian 25 mg QD
Number of subjects included in analysis	1019
Analysis specification	Pre-specified
Analysis type	superiority
Method	Wald Confidence Limits
Parameter estimate	Relative Risk (RR)
Point estimate	0.83
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.46
upper limit	1.49

Statistical analysis title	Milvexian 25 mg BID over Placebo
Statistical analysis description:	
Wald Confidence Limits. 95% CIs for RR are constructed using Wald Confidence Limits.	
Comparison groups	Placebo v Milvexian 25 mg BID
Number of subjects included in analysis	1009
Analysis specification	Pre-specified
Analysis type	superiority
Method	Wald Confidence Limits
Parameter estimate	Relative Risk (RR)
Point estimate	0.69
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.36
upper limit	1.3

Statistical analysis title	Milvexian 50 mg BID over Placebo
Statistical analysis description:	
Wald Confidence Limits. 95% CIs for RR are constructed using Wald Confidence Limits.	
Comparison groups	Placebo v Milvexian 50 mg BID
Number of subjects included in analysis	1019
Analysis specification	Pre-specified
Analysis type	superiority
Method	Wald Confidence Limits
Parameter estimate	Relative Risk (RR)
Point estimate	0.72
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.39
upper limit	1.33

Statistical analysis title	Milvexian 100 mg BID over Placebo
Statistical analysis description: Wald Confidence Limits. 95% CIs for RR are constructed using Wald Confidence Limits.	
Comparison groups	Placebo v Milvexian 100 mg BID
Number of subjects included in analysis	1001
Analysis specification	Pre-specified
Analysis type	superiority
Method	Wald Confidence Limits
Parameter estimate	Relative Risk (RR)
Point estimate	0.65
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.33
upper limit	1.25

Statistical analysis title	Milvexian 200 mg BID
Statistical analysis description: Wald Confidence Limits. 95% CIs for RR are constructed using Wald Confidence Limits.	
Comparison groups	Placebo v Milvexian 200 mg BID
Number of subjects included in analysis	1042
Analysis specification	Pre-specified
Analysis type	superiority
Method	Wald Confidence Limits
Parameter estimate	Relative Risk (RR)
Point estimate	1.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.87
upper limit	2.25

Statistical analysis title	Milvexian 50 mg QD over Placebo
Statistical analysis description: Wald Confidence Limits. 95% CIs for RR are constructed using Wald Confidence Limits.	
Comparison groups	Placebo v Milvexian 50 mg QD
Number of subjects included in analysis	713
Analysis specification	Pre-specified
Analysis type	superiority
Method	Wald Confidence Limits
Parameter estimate	Relative Risk (RR)
Point estimate	2.48

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.83
upper limit	7.42

Statistical analysis title	Milvexian 100 mg QD over Placebo
Statistical analysis description:	
Wald Confidence Limits. 95% CIs for RR are constructed using Wald Confidence Limits.	
Comparison groups	Placebo v Milvexian 100 mg QD
Number of subjects included in analysis	709
Analysis specification	Pre-specified
Analysis type	superiority
Method	Wald Confidence Limits
Parameter estimate	Relative Risk (RR)
Point estimate	1.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.15
upper limit	6.96

Adverse events

Adverse events information

Timeframe for reporting adverse events:

SAEs and NSAEs were assessed from first dose to 7 days after last dose of study therapy (up to approximately 112 days).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.0

Reporting groups

Reporting group title	Placebo

Reporting group description:

Loading dose of Clopidogrel 300 mg + Aspirin 100 mg followed by Placebo + Aspirin 100 mg QD + Clopidogrel 75 mg QD on days 1-21 and Placebo + Aspirin 100 mg QD on days 22-90. All administered orally.

Reporting group title	Milvexian 25 mg QD

Reporting group description:

Loading dose of Clopidogrel 300 mg + Aspirin 100 mg followed by Milvexian 25 mg QD + Aspirin 100 mg QD + Clopidogrel 75 mg QD on days 1-21 and Milvexian 25 mg QD + Aspirin 100 mg QD on days 22-90. All administered orally.

Reporting group title	Milvexian 50 mg QD

Reporting group description:

Loading dose of Clopidogrel 300 mg + Aspirin 100 mg followed by Milvexian 50 mg QD + Aspirin 100 mg QD + Clopidogrel 75 mg QD on days 1-21 and Milvexian 50 mg QD + Aspirin 100 mg QD on days 22-90. All administered orally.

Reporting group title	Milvexian 100 mg QD

Reporting group description:

Loading dose of Clopidogrel 300 mg + Aspirin 100 mg followed by Milvexian 100 mg QD + Aspirin 100 mg QD + Clopidogrel 75 mg QD on days 1-21 and Milvexian 100 mg QD + Aspirin 100 mg QD on days 22-90. All administered orally.

Reporting group title	Milvexian 50 mg BID

Reporting group description:

Loading dose of Clopidogrel 300 mg + Aspirin 100 mg followed by Milvexian 50 mg BID + Aspirin 100 mg QD + Clopidogrel 75 mg QD on days 1-21 and Milvexian 50 mg BID + Aspirin 100 mg QD on days 22-90. All administered orally.

Reporting group title	Milvexian 25 mg BID

Reporting group description:

Loading dose of Clopidogrel 300 mg + Aspirin 100 mg followed by Milvexian 25 mg BID + Aspirin 100 mg QD + Clopidogrel 75 mg QD on days 1-21 and Milvexian 25 mg BID + Aspirin 100 mg QD on days 22-90. All administered orally.

Reporting group title	Milvexian 100 mg BID

Reporting group description:

Loading dose of Clopidogrel 300 mg + Aspirin 100 mg followed by Milvexian 100 mg BID + Aspirin 100 mg QD + Clopidogrel 75 mg QD on days 1-21 and Milvexian 100 mg BID + Aspirin 100 mg QD on days 22-90. All administered orally.

Reporting group title	Milvexian 200 mg BID

Reporting group description:

Loading dose of Clopidogrel 300 mg + Aspirin 100 mg followed by Milvexian 200 mg BID + Aspirin 100 mg QD + Clopidogrel 75 mg QD on days 1-21 and Milvexian 200 mg BID + Aspirin 100 mg QD on days 22-90. All administered orally.

Serious adverse events	Placebo	Milvexian 25 mg QD	Milvexian 50 mg QD
Total subjects affected by serious adverse events			
subjects affected / exposed	94 / 682 (13.78%)	37 / 325 (11.38%)	5 / 22 (22.73%)
number of deaths (all causes)	5	4	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
B-cell lymphoma			
subjects affected / exposed	0 / 682 (0.00%)	0 / 325 (0.00%)	0 / 22 (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
Breast cancer			
subjects affected / exposed	0 / 682 (0.00%)	0 / 325 (0.00%)	0 / 22 (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
Invasive ductal breast carcinoma			
subjects affected / exposed	0 / 682 (0.00%)	0 / 325 (0.00%)	0 / 22 (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
Intestinal adenocarcinoma			
subjects affected / exposed	0 / 682 (0.00%)	0 / 325 (0.00%)	0 / 22 (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
Colon cancer			
subjects affected / exposed	0 / 682 (0.00%)	1 / 325 (0.31%)	0 / 22 (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
Lung neoplasm malignant			
subjects affected / exposed	0 / 682 (0.00%)	0 / 325 (0.00%)	0 / 22 (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
Metastases to lung			
subjects affected / exposed	0 / 682 (0.00%)	1 / 325 (0.31%)	0 / 22 (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

Metastatic neoplasm			
subjects affected / exposed	0 / 682 (0.00%)	0 / 325 (0.00%)	0 / 22 (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
Sinonasal papilloma			
subjects affected / exposed	0 / 682 (0.00%)	1 / 325 (0.31%)	0 / 22 (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
Squamous cell carcinoma of lung			
subjects affected / exposed	0 / 682 (0.00%)	0 / 325 (0.00%)	0 / 22 (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
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 682 (0.00%)	0 / 325 (0.00%)	0 / 22 (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
Hypertension			
subjects affected / exposed	0 / 682 (0.00%)	0 / 325 (0.00%)	0 / 22 (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
Malignant hypertension			
subjects affected / exposed	0 / 682 (0.00%)	0 / 325 (0.00%)	0 / 22 (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
Orthostatic hypotension			
subjects affected / exposed	0 / 682 (0.00%)	0 / 325 (0.00%)	0 / 22 (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
Peripheral artery thrombosis			
subjects affected / exposed	1 / 682 (0.15%)	0 / 325 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral arterial occlusive disease			

subjects affected / exposed	0 / 682 (0.00%)	1 / 325 (0.31%)	0 / 22 (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
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 682 (0.15%)	0 / 325 (0.00%)	0 / 22 (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
Asthenia			
subjects affected / exposed	1 / 682 (0.15%)	0 / 325 (0.00%)	0 / 22 (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
Sudden cardiac death			
subjects affected / exposed	0 / 682 (0.00%)	0 / 325 (0.00%)	0 / 22 (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			
Benign prostatic hyperplasia			
subjects affected / exposed	0 / 682 (0.00%)	0 / 325 (0.00%)	0 / 22 (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			
Dyspnoea			
subjects affected / exposed	0 / 682 (0.00%)	1 / 325 (0.31%)	0 / 22 (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
Acute respiratory failure			
subjects affected / exposed	1 / 682 (0.15%)	0 / 325 (0.00%)	0 / 22 (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 oedema			

subjects affected / exposed	0 / 682 (0.00%)	0 / 325 (0.00%)	0 / 22 (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 failure			
subjects affected / exposed	0 / 682 (0.00%)	1 / 325 (0.31%)	0 / 22 (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
Pulmonary embolism			
subjects affected / exposed	0 / 682 (0.00%)	1 / 325 (0.31%)	0 / 22 (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
Pleural effusion			
subjects affected / exposed	1 / 682 (0.15%)	0 / 325 (0.00%)	0 / 22 (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
Psychiatric disorders			
Anxiety disorder			
subjects affected / exposed	1 / 682 (0.15%)	0 / 325 (0.00%)	0 / 22 (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
Mania			
subjects affected / exposed	0 / 682 (0.00%)	0 / 325 (0.00%)	0 / 22 (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
Investigations			
Ejection fraction decreased			
subjects affected / exposed	0 / 682 (0.00%)	0 / 325 (0.00%)	0 / 22 (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
Activated partial thromboplastin time prolonged			
subjects affected / exposed	0 / 682 (0.00%)	0 / 325 (0.00%)	0 / 22 (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

Liver function test increased			
subjects affected / exposed	1 / 682 (0.15%)	0 / 325 (0.00%)	0 / 22 (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
Injury, poisoning and procedural complications			
Accidental overdose			
subjects affected / exposed	1 / 682 (0.15%)	0 / 325 (0.00%)	0 / 22 (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
Cystitis radiation			
subjects affected / exposed	0 / 682 (0.00%)	0 / 325 (0.00%)	0 / 22 (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
Femur fracture			
subjects affected / exposed	1 / 682 (0.15%)	0 / 325 (0.00%)	0 / 22 (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
Fibula fracture			
subjects affected / exposed	0 / 682 (0.00%)	0 / 325 (0.00%)	0 / 22 (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
Post procedural stroke			
subjects affected / exposed	1 / 682 (0.15%)	0 / 325 (0.00%)	0 / 22 (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
Post procedural haemorrhage			
subjects affected / exposed	0 / 682 (0.00%)	1 / 325 (0.31%)	0 / 22 (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
Forearm fracture			
subjects affected / exposed	0 / 682 (0.00%)	0 / 325 (0.00%)	0 / 22 (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

Procedural haemorrhage			
subjects affected / exposed	0 / 682 (0.00%)	0 / 325 (0.00%)	0 / 22 (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
Radius fracture			
subjects affected / exposed	0 / 682 (0.00%)	0 / 325 (0.00%)	0 / 22 (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
Reactive gastropathy			
subjects affected / exposed	1 / 682 (0.15%)	0 / 325 (0.00%)	0 / 22 (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
Skin laceration			
subjects affected / exposed	0 / 682 (0.00%)	1 / 325 (0.31%)	0 / 22 (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
Subdural haematoma			
subjects affected / exposed	1 / 682 (0.15%)	0 / 325 (0.00%)	0 / 22 (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
Congenital, familial and genetic disorders			
Atrial septal defect			
subjects affected / exposed	0 / 682 (0.00%)	1 / 325 (0.31%)	0 / 22 (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 disorders			
Acute myocardial infarction			
subjects affected / exposed	2 / 682 (0.29%)	0 / 325 (0.00%)	1 / 22 (4.55%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			
subjects affected / exposed	4 / 682 (0.59%)	3 / 325 (0.92%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Atrial flutter			
subjects affected / exposed	0 / 682 (0.00%)	1 / 325 (0.31%)	0 / 22 (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
Atrial tachycardia			
subjects affected / exposed	0 / 682 (0.00%)	0 / 325 (0.00%)	0 / 22 (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
Atrioventricular block complete			
subjects affected / exposed	1 / 682 (0.15%)	0 / 325 (0.00%)	0 / 22 (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
Angina pectoris			
subjects affected / exposed	1 / 682 (0.15%)	1 / 325 (0.31%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina unstable			
subjects affected / exposed	1 / 682 (0.15%)	0 / 325 (0.00%)	0 / 22 (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
Bradycardia			
subjects affected / exposed	0 / 682 (0.00%)	0 / 325 (0.00%)	0 / 22 (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 arrest			
subjects affected / exposed	2 / 682 (0.29%)	0 / 325 (0.00%)	0 / 22 (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
Atrioventricular block second degree			
subjects affected / exposed	0 / 682 (0.00%)	0 / 325 (0.00%)	0 / 22 (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 failure			

subjects affected / exposed	1 / 682 (0.15%)	0 / 325 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure acute			
subjects affected / exposed	1 / 682 (0.15%)	0 / 325 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure congestive			
subjects affected / exposed	1 / 682 (0.15%)	0 / 325 (0.00%)	0 / 22 (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 ventricular thrombosis			
subjects affected / exposed	0 / 682 (0.00%)	1 / 325 (0.31%)	0 / 22 (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
Coronary artery disease			
subjects affected / exposed	1 / 682 (0.15%)	0 / 325 (0.00%)	0 / 22 (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
Intracardiac thrombus			
subjects affected / exposed	0 / 682 (0.00%)	0 / 325 (0.00%)	0 / 22 (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 cardiomyopathy			
subjects affected / exposed	0 / 682 (0.00%)	0 / 325 (0.00%)	0 / 22 (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	0 / 682 (0.00%)	1 / 325 (0.31%)	0 / 22 (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
Nodal rhythm			

subjects affected / exposed	0 / 682 (0.00%)	0 / 325 (0.00%)	0 / 22 (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 ischaemia			
subjects affected / exposed	1 / 682 (0.15%)	0 / 325 (0.00%)	0 / 22 (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
Pericarditis			
subjects affected / exposed	0 / 682 (0.00%)	0 / 325 (0.00%)	0 / 22 (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
Sinus tachycardia			
subjects affected / exposed	0 / 682 (0.00%)	1 / 325 (0.31%)	0 / 22 (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
Prinzmetal angina			
subjects affected / exposed	1 / 682 (0.15%)	0 / 325 (0.00%)	0 / 22 (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			
Aphasia			
subjects affected / exposed	1 / 682 (0.15%)	0 / 325 (0.00%)	0 / 22 (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
Basilar artery occlusion			
subjects affected / exposed	0 / 682 (0.00%)	0 / 325 (0.00%)	0 / 22 (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
Carotid artery thrombosis			
subjects affected / exposed	0 / 682 (0.00%)	0 / 325 (0.00%)	0 / 22 (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
Carotid artery stenosis			

subjects affected / exposed	4 / 682 (0.59%)	0 / 325 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Brain stem stroke			
subjects affected / exposed	1 / 682 (0.15%)	0 / 325 (0.00%)	0 / 22 (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
Basilar migraine			
subjects affected / exposed	0 / 682 (0.00%)	0 / 325 (0.00%)	0 / 22 (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
Basilar artery stenosis			
subjects affected / exposed	0 / 682 (0.00%)	0 / 325 (0.00%)	0 / 22 (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
Cerebral infarction			
subjects affected / exposed	4 / 682 (0.59%)	1 / 325 (0.31%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Cerebral ischaemia			
subjects affected / exposed	1 / 682 (0.15%)	0 / 325 (0.00%)	0 / 22 (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 venous thrombosis			
subjects affected / exposed	1 / 682 (0.15%)	0 / 325 (0.00%)	0 / 22 (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
Dementia			
subjects affected / exposed	0 / 682 (0.00%)	0 / 325 (0.00%)	0 / 22 (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
Dysarthria			

subjects affected / exposed	0 / 682 (0.00%)	1 / 325 (0.31%)	0 / 22 (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
Embolic cerebral infarction			
subjects affected / exposed	0 / 682 (0.00%)	0 / 325 (0.00%)	0 / 22 (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
Encephalopathy			
subjects affected / exposed	0 / 682 (0.00%)	0 / 325 (0.00%)	0 / 22 (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
Epilepsy			
subjects affected / exposed	0 / 682 (0.00%)	1 / 325 (0.31%)	0 / 22 (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
Focal dyscognitive seizures			
subjects affected / exposed	0 / 682 (0.00%)	0 / 325 (0.00%)	0 / 22 (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
Generalised tonic-clonic seizure			
subjects affected / exposed	1 / 682 (0.15%)	0 / 325 (0.00%)	0 / 22 (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
Haemorrhagic transformation stroke			
subjects affected / exposed	1 / 682 (0.15%)	0 / 325 (0.00%)	0 / 22 (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
Intracranial aneurysm			
subjects affected / exposed	0 / 682 (0.00%)	1 / 325 (0.31%)	0 / 22 (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
Myasthenia gravis crisis			

subjects affected / exposed	1 / 682 (0.15%)	0 / 325 (0.00%)	0 / 22 (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
Mental impairment			
subjects affected / exposed	0 / 682 (0.00%)	0 / 325 (0.00%)	0 / 22 (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
Lacunar stroke			
subjects affected / exposed	1 / 682 (0.15%)	0 / 325 (0.00%)	0 / 22 (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	21 / 682 (3.08%)	9 / 325 (2.77%)	3 / 22 (13.64%)
occurrences causally related to treatment / all	0 / 21	0 / 9	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic cerebral infarction			
subjects affected / exposed	3 / 682 (0.44%)	1 / 325 (0.31%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myelopathy			
subjects affected / exposed	0 / 682 (0.00%)	0 / 325 (0.00%)	0 / 22 (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
Partial seizures			
subjects affected / exposed	1 / 682 (0.15%)	0 / 325 (0.00%)	0 / 22 (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
Neurological symptom			
subjects affected / exposed	0 / 682 (0.00%)	0 / 325 (0.00%)	0 / 22 (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
Peroneal nerve palsy			

subjects affected / exposed	1 / 682 (0.15%)	0 / 325 (0.00%)	0 / 22 (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
Pseudostroke			
subjects affected / exposed	1 / 682 (0.15%)	0 / 325 (0.00%)	0 / 22 (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
Sedation complication			
subjects affected / exposed	0 / 682 (0.00%)	0 / 325 (0.00%)	0 / 22 (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
Seizure			
subjects affected / exposed	1 / 682 (0.15%)	0 / 325 (0.00%)	0 / 22 (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
Stroke in evolution			
subjects affected / exposed	5 / 682 (0.73%)	2 / 325 (0.62%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 6	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	2 / 682 (0.29%)	1 / 325 (0.31%)	0 / 22 (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
Toxic encephalopathy			
subjects affected / exposed	0 / 682 (0.00%)	1 / 325 (0.31%)	0 / 22 (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
Transient ischaemic attack			
subjects affected / exposed	8 / 682 (1.17%)	1 / 325 (0.31%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 8	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vertebral artery dissection			

subjects affected / exposed	0 / 682 (0.00%)	0 / 325 (0.00%)	0 / 22 (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
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 682 (0.00%)	1 / 325 (0.31%)	0 / 22 (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
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	1 / 682 (0.15%)	0 / 325 (0.00%)	0 / 22 (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
Vertigo positional			
subjects affected / exposed	0 / 682 (0.00%)	0 / 325 (0.00%)	0 / 22 (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
Eye disorders			
Retinal detachment			
subjects affected / exposed	0 / 682 (0.00%)	0 / 325 (0.00%)	0 / 22 (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
Gastrointestinal disorders			
Diverticulum intestinal haemorrhagic			
subjects affected / exposed	0 / 682 (0.00%)	0 / 325 (0.00%)	0 / 22 (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
Duodenal ulcer			
subjects affected / exposed	0 / 682 (0.00%)	1 / 325 (0.31%)	0 / 22 (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
Duodenal ulcer haemorrhage			

subjects affected / exposed	0 / 682 (0.00%)	0 / 325 (0.00%)	0 / 22 (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
Duodenal ulcer perforation			
subjects affected / exposed	0 / 682 (0.00%)	0 / 325 (0.00%)	0 / 22 (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
Gastric ulcer haemorrhage			
subjects affected / exposed	1 / 682 (0.15%)	1 / 325 (0.31%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Faecaloma			
subjects affected / exposed	0 / 682 (0.00%)	0 / 325 (0.00%)	0 / 22 (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
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 682 (0.00%)	0 / 325 (0.00%)	0 / 22 (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
Nausea			
subjects affected / exposed	0 / 682 (0.00%)	0 / 325 (0.00%)	0 / 22 (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
Mallory-Weiss syndrome			
subjects affected / exposed	0 / 682 (0.00%)	0 / 325 (0.00%)	0 / 22 (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
Haemorrhoidal haemorrhage			
subjects affected / exposed	0 / 682 (0.00%)	0 / 325 (0.00%)	0 / 22 (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
Oesophagitis haemorrhagic			

subjects affected / exposed	0 / 682 (0.00%)	0 / 325 (0.00%)	0 / 22 (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
Peptic ulcer haemorrhage			
subjects affected / exposed	0 / 682 (0.00%)	0 / 325 (0.00%)	0 / 22 (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
Pancreatitis acute			
subjects affected / exposed	2 / 682 (0.29%)	0 / 325 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper gastrointestinal haemorrhage			
subjects affected / exposed	0 / 682 (0.00%)	0 / 325 (0.00%)	0 / 22 (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	0 / 682 (0.00%)	0 / 325 (0.00%)	0 / 22 (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
Small intestinal haemorrhage			
subjects affected / exposed	0 / 682 (0.00%)	0 / 325 (0.00%)	0 / 22 (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
Hepatobiliary disorders			
Hepatitis fulminant			
subjects affected / exposed	0 / 682 (0.00%)	0 / 325 (0.00%)	0 / 22 (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
Cholelithiasis			
subjects affected / exposed	0 / 682 (0.00%)	0 / 325 (0.00%)	0 / 22 (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
Cholecystitis acute			

subjects affected / exposed	0 / 682 (0.00%)	0 / 325 (0.00%)	0 / 22 (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
Cholecystitis			
subjects affected / exposed	2 / 682 (0.29%)	0 / 325 (0.00%)	0 / 22 (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
Skin and subcutaneous tissue disorders			
Diabetic foot			
subjects affected / exposed	0 / 682 (0.00%)	0 / 325 (0.00%)	0 / 22 (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
Drug eruption			
subjects affected / exposed	0 / 682 (0.00%)	1 / 325 (0.31%)	0 / 22 (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
Rash macular			
subjects affected / exposed	0 / 682 (0.00%)	0 / 325 (0.00%)	0 / 22 (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
Toxic epidermal necrolysis			
subjects affected / exposed	0 / 682 (0.00%)	0 / 325 (0.00%)	1 / 22 (4.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urticaria			
subjects affected / exposed	0 / 682 (0.00%)	0 / 325 (0.00%)	0 / 22 (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
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	3 / 682 (0.44%)	0 / 325 (0.00%)	0 / 22 (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 haemorrhagic			

subjects affected / exposed	0 / 682 (0.00%)	0 / 325 (0.00%)	0 / 22 (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
Prerenal failure			
subjects affected / exposed	0 / 682 (0.00%)	0 / 325 (0.00%)	0 / 22 (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
Nephropathy toxic			
subjects affected / exposed	0 / 682 (0.00%)	0 / 325 (0.00%)	0 / 22 (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 / 682 (0.00%)	0 / 325 (0.00%)	0 / 22 (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
Renal tubular necrosis			
subjects affected / exposed	0 / 682 (0.00%)	0 / 325 (0.00%)	0 / 22 (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
Renal failure			
subjects affected / exposed	0 / 682 (0.00%)	0 / 325 (0.00%)	0 / 22 (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
Musculoskeletal and connective tissue disorders			
Osteoarthritis			
subjects affected / exposed	0 / 682 (0.00%)	0 / 325 (0.00%)	0 / 22 (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
Musculoskeletal chest pain			
subjects affected / exposed	0 / 682 (0.00%)	0 / 325 (0.00%)	0 / 22 (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			

Arthritis bacterial			
subjects affected / exposed	1 / 682 (0.15%)	0 / 325 (0.00%)	0 / 22 (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			
subjects affected / exposed	5 / 682 (0.73%)	2 / 325 (0.62%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 5	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	0 / 682 (0.00%)	1 / 325 (0.31%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	1 / 682 (0.15%)	0 / 325 (0.00%)	0 / 22 (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 / 682 (0.00%)	0 / 325 (0.00%)	0 / 22 (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
Cystitis			
subjects affected / exposed	0 / 682 (0.00%)	0 / 325 (0.00%)	0 / 22 (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
Clostridium difficile infection			
subjects affected / exposed	0 / 682 (0.00%)	1 / 325 (0.31%)	0 / 22 (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
Diverticulitis intestinal perforated			
subjects affected / exposed	0 / 682 (0.00%)	0 / 325 (0.00%)	0 / 22 (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
Febrile infection			

subjects affected / exposed	0 / 682 (0.00%)	0 / 325 (0.00%)	0 / 22 (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
Gastroenteritis			
subjects affected / exposed	1 / 682 (0.15%)	0 / 325 (0.00%)	0 / 22 (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
Infected dermal cyst			
subjects affected / exposed	1 / 682 (0.15%)	0 / 325 (0.00%)	0 / 22 (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
Large intestine infection			
subjects affected / exposed	0 / 682 (0.00%)	1 / 325 (0.31%)	0 / 22 (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
Osteomyelitis			
subjects affected / exposed	1 / 682 (0.15%)	0 / 325 (0.00%)	0 / 22 (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
Pneumonia			
subjects affected / exposed	3 / 682 (0.44%)	0 / 325 (0.00%)	1 / 22 (4.55%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	1 / 682 (0.15%)	0 / 325 (0.00%)	0 / 22 (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
Septic shock			
subjects affected / exposed	0 / 682 (0.00%)	0 / 325 (0.00%)	0 / 22 (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
Pneumonia aspiration			

subjects affected / exposed	1 / 682 (0.15%)	0 / 325 (0.00%)	0 / 22 (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
Staphylococcal bacteraemia			
subjects affected / exposed	0 / 682 (0.00%)	0 / 325 (0.00%)	0 / 22 (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
Wound infection pseudomonas			
subjects affected / exposed	0 / 682 (0.00%)	0 / 325 (0.00%)	0 / 22 (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
Tuberculosis			
subjects affected / exposed	1 / 682 (0.15%)	0 / 325 (0.00%)	0 / 22 (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
Urinary tract infection			
subjects affected / exposed	1 / 682 (0.15%)	2 / 325 (0.62%)	0 / 22 (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
Urosepsis			
subjects affected / exposed	1 / 682 (0.15%)	0 / 325 (0.00%)	0 / 22 (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
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 682 (0.00%)	0 / 325 (0.00%)	0 / 22 (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
Hyperglycaemia			
subjects affected / exposed	0 / 682 (0.00%)	0 / 325 (0.00%)	0 / 22 (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
Hyperkalaemia			

subjects affected / exposed	0 / 682 (0.00%)	1 / 325 (0.31%)	0 / 22 (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
Hyponatraemia			
subjects affected / exposed	1 / 682 (0.15%)	0 / 325 (0.00%)	0 / 22 (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 / 682 (0.00%)	0 / 325 (0.00%)	0 / 22 (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
Type 2 diabetes mellitus			
subjects affected / exposed	0 / 682 (0.00%)	0 / 325 (0.00%)	0 / 22 (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	Milvexian 100 mg QD	Milvexian 50 mg BID	Milvexian 25 mg BID
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 17 (17.65%)	41 / 325 (12.62%)	39 / 313 (12.46%)
number of deaths (all causes)	0	3	3
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
B-cell lymphoma			
subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	1 / 313 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Breast cancer			
subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	0 / 313 (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
Invasive ductal breast carcinoma			
subjects affected / exposed	0 / 17 (0.00%)	1 / 325 (0.31%)	0 / 313 (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

Intestinal adenocarcinoma			
subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	1 / 313 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colon cancer			
subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	0 / 313 (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
Lung neoplasm malignant			
subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	0 / 313 (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
Metastases to lung			
subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	0 / 313 (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
Metastatic neoplasm			
subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	1 / 313 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Sinonasal papilloma			
subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	0 / 313 (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
Squamous cell carcinoma of lung			
subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	0 / 313 (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
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	1 / 313 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertension			

subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	1 / 313 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malignant hypertension			
subjects affected / exposed	0 / 17 (0.00%)	1 / 325 (0.31%)	0 / 313 (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
Orthostatic hypotension			
subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	0 / 313 (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
Peripheral artery thrombosis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	0 / 313 (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
Peripheral arterial occlusive disease			
subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	0 / 313 (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
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	0 / 313 (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
Asthenia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	0 / 313 (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
Sudden cardiac death			
subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	0 / 313 (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			

Benign prostatic hyperplasia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	0 / 313 (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			
Dyspnoea			
subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	0 / 313 (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
Acute respiratory failure			
subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	0 / 313 (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
Pulmonary oedema			
subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	1 / 313 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			
subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	0 / 313 (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
Pulmonary embolism			
subjects affected / exposed	0 / 17 (0.00%)	1 / 325 (0.31%)	0 / 313 (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
Pleural effusion			
subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	0 / 313 (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
Psychiatric disorders			
Anxiety disorder			
subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	0 / 313 (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

Mania			
subjects affected / exposed	0 / 17 (0.00%)	1 / 325 (0.31%)	0 / 313 (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
Investigations			
Ejection fraction decreased			
subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	0 / 313 (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
Activated partial thromboplastin time prolonged			
subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	0 / 313 (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
Liver function test increased			
subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	0 / 313 (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
Injury, poisoning and procedural complications			
Accidental overdose			
subjects affected / exposed	0 / 17 (0.00%)	1 / 325 (0.31%)	1 / 313 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cystitis radiation			
subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	1 / 313 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femur fracture			
subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	0 / 313 (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
Fibula fracture			

subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	0 / 313 (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
Post procedural stroke			
subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	0 / 313 (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
Post procedural haemorrhage			
subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	0 / 313 (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
Forearm fracture			
subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	1 / 313 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Procedural haemorrhage			
subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	1 / 313 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Radius fracture			
subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	1 / 313 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reactive gastropathy			
subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	0 / 313 (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
Skin laceration			
subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	0 / 313 (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 / 17 (0.00%)	1 / 325 (0.31%)	0 / 313 (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
Congenital, familial and genetic disorders			
Atrial septal defect			
subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	0 / 313 (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	0 / 17 (0.00%)	0 / 325 (0.00%)	0 / 313 (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
Atrial fibrillation			
subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	1 / 313 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial flutter			
subjects affected / exposed	0 / 17 (0.00%)	1 / 325 (0.31%)	0 / 313 (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
Atrial tachycardia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	0 / 313 (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
Atrioventricular block complete			
subjects affected / exposed	0 / 17 (0.00%)	1 / 325 (0.31%)	0 / 313 (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
Angina pectoris			
subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	0 / 313 (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

Angina unstable			
subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	0 / 313 (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
Bradycardia			
subjects affected / exposed	0 / 17 (0.00%)	1 / 325 (0.31%)	0 / 313 (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 arrest			
subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	0 / 313 (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
Atrioventricular block second degree			
subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	0 / 313 (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 failure			
subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	2 / 313 (0.64%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Cardiac failure acute			
subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	0 / 313 (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 failure congestive			
subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	0 / 313 (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 ventricular thrombosis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	0 / 313 (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 disease			

subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	0 / 313 (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
Intracardiac thrombus			
subjects affected / exposed	0 / 17 (0.00%)	1 / 325 (0.31%)	0 / 313 (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 cardiomyopathy			
subjects affected / exposed	0 / 17 (0.00%)	1 / 325 (0.31%)	0 / 313 (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 infarction			
subjects affected / exposed	0 / 17 (0.00%)	1 / 325 (0.31%)	0 / 313 (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
Nodal rhythm			
subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	0 / 313 (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 ischaemia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	0 / 313 (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
Pericarditis			
subjects affected / exposed	0 / 17 (0.00%)	1 / 325 (0.31%)	0 / 313 (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 tachycardia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	0 / 313 (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
Prinzmetal angina			

subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	0 / 313 (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
Nervous system disorders			
Aphasia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	0 / 313 (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
Basilar artery occlusion			
subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	0 / 313 (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
Carotid artery thrombosis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	0 / 313 (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
Carotid artery stenosis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	0 / 313 (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
Brain stem stroke			
subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	0 / 313 (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
Basilar migraine			
subjects affected / exposed	1 / 17 (5.88%)	0 / 325 (0.00%)	0 / 313 (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
Basilar artery stenosis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	0 / 313 (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
Cerebral infarction			

subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	1 / 313 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral ischaemia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	0 / 313 (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
Cerebral venous thrombosis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	0 / 313 (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
Dementia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	0 / 313 (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
Dysarthria			
subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	0 / 313 (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
Embolic cerebral infarction			
subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	0 / 313 (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
Encephalopathy			
subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	0 / 313 (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
Epilepsy			
subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	0 / 313 (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
Focal dyscognitive seizures			

subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	1 / 313 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Generalised tonic-clonic seizure			
subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	0 / 313 (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
Haemorrhagic transformation stroke			
subjects affected / exposed	0 / 17 (0.00%)	2 / 325 (0.62%)	0 / 313 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intracranial aneurysm			
subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	0 / 313 (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
Myasthenia gravis crisis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	0 / 313 (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
Mental impairment			
subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	0 / 313 (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
Lacunar stroke			
subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	0 / 313 (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 stroke			
subjects affected / exposed	1 / 17 (5.88%)	10 / 325 (3.08%)	6 / 313 (1.92%)
occurrences causally related to treatment / all	0 / 1	0 / 10	0 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic cerebral infarction			

subjects affected / exposed	0 / 17 (0.00%)	2 / 325 (0.62%)	3 / 313 (0.96%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myelopathy			
subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	1 / 313 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Partial seizures			
subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	0 / 313 (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
Neurological symptom			
subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	0 / 313 (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
Peroneal nerve palsy			
subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	0 / 313 (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
Pseudostroke			
subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	0 / 313 (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
Sedation complication			
subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	1 / 313 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seizure			
subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	1 / 313 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stroke in evolution			

subjects affected / exposed	1 / 17 (5.88%)	1 / 325 (0.31%)	4 / 313 (1.28%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 17 (0.00%)	1 / 325 (0.31%)	0 / 313 (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
Toxic encephalopathy			
subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	0 / 313 (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
Transient ischaemic attack			
subjects affected / exposed	0 / 17 (0.00%)	1 / 325 (0.31%)	4 / 313 (1.28%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vertebral artery dissection			
subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	0 / 313 (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
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	0 / 313 (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
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	2 / 313 (0.64%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vertigo positional			
subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	0 / 313 (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
Eye disorders			

Retinal detachment			
subjects affected / exposed	0 / 17 (0.00%)	1 / 325 (0.31%)	0 / 313 (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
Gastrointestinal disorders			
Diverticulum intestinal haemorrhagic			
subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	0 / 313 (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
Duodenal ulcer			
subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	0 / 313 (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
Duodenal ulcer haemorrhage			
subjects affected / exposed	0 / 17 (0.00%)	1 / 325 (0.31%)	0 / 313 (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
Duodenal ulcer perforation			
subjects affected / exposed	0 / 17 (0.00%)	1 / 325 (0.31%)	0 / 313 (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 ulcer haemorrhage			
subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	0 / 313 (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
Faecaloma			
subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	1 / 313 (0.32%)
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 haemorrhage			
subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	1 / 313 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			

subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	0 / 313 (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
Mallory-Weiss syndrome			
subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	0 / 313 (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
Haemorrhoidal haemorrhage			
subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	1 / 313 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophagitis haemorrhagic			
subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	0 / 313 (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
Peptic ulcer haemorrhage			
subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	0 / 313 (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
Pancreatitis acute			
subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	0 / 313 (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
Upper gastrointestinal haemorrhage			
subjects affected / exposed	0 / 17 (0.00%)	1 / 325 (0.31%)	0 / 313 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal haemorrhage			
subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	0 / 313 (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
Small intestinal haemorrhage			

subjects affected / exposed	0 / 17 (0.00%)	1 / 325 (0.31%)	0 / 313 (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			
Hepatitis fulminant			
subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	0 / 313 (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
Cholelithiasis			
subjects affected / exposed	0 / 17 (0.00%)	1 / 325 (0.31%)	0 / 313 (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 / 17 (0.00%)	0 / 325 (0.00%)	0 / 313 (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
Cholecystitis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	0 / 313 (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
Skin and subcutaneous tissue disorders			
Diabetic foot			
subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	2 / 313 (0.64%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Drug eruption			
subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	0 / 313 (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
Rash macular			
subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	0 / 313 (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
Toxic epidermal necrolysis			

subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	0 / 313 (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
Urticaria			
subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	0 / 313 (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
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 17 (0.00%)	1 / 325 (0.31%)	0 / 313 (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
Cystitis haemorrhagic			
subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	1 / 313 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prerenal failure			
subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	0 / 313 (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
Nephropathy toxic			
subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	0 / 313 (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 / 17 (0.00%)	0 / 325 (0.00%)	0 / 313 (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
Renal tubular necrosis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	0 / 313 (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
Renal failure			

subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	0 / 313 (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
Musculoskeletal and connective tissue disorders			
Osteoarthritis			
subjects affected / exposed	0 / 17 (0.00%)	1 / 325 (0.31%)	0 / 313 (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 chest pain			
subjects affected / exposed	0 / 17 (0.00%)	1 / 325 (0.31%)	0 / 313 (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
Infections and infestations			
Arthritis bacterial			
subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	0 / 313 (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
COVID-19			
subjects affected / exposed	0 / 17 (0.00%)	1 / 325 (0.31%)	2 / 313 (0.64%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	0 / 17 (0.00%)	1 / 325 (0.31%)	0 / 313 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	0 / 313 (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
Diverticulitis			
subjects affected / exposed	0 / 17 (0.00%)	1 / 325 (0.31%)	0 / 313 (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

Cystitis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	0 / 313 (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
Clostridium difficile infection			
subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	0 / 313 (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
Diverticulitis intestinal perforated			
subjects affected / exposed	0 / 17 (0.00%)	1 / 325 (0.31%)	0 / 313 (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
Febrile infection			
subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	1 / 313 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 17 (0.00%)	1 / 325 (0.31%)	0 / 313 (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
Infected dermal cyst			
subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	0 / 313 (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
Large intestine infection			
subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	0 / 313 (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
Osteomyelitis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	0 / 313 (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
Pneumonia			

subjects affected / exposed	0 / 17 (0.00%)	1 / 325 (0.31%)	0 / 313 (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
Sepsis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	0 / 313 (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
Septic shock			
subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	1 / 313 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia aspiration			
subjects affected / exposed	0 / 17 (0.00%)	1 / 325 (0.31%)	0 / 313 (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
Staphylococcal bacteraemia			
subjects affected / exposed	0 / 17 (0.00%)	1 / 325 (0.31%)	0 / 313 (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
Wound infection pseudomonas			
subjects affected / exposed	0 / 17 (0.00%)	1 / 325 (0.31%)	0 / 313 (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
Tuberculosis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	0 / 313 (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	0 / 17 (0.00%)	1 / 325 (0.31%)	0 / 313 (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
Urosepsis			

subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	0 / 313 (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
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	0 / 313 (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
Hyperglycaemia			
subjects affected / exposed	0 / 17 (0.00%)	1 / 325 (0.31%)	0 / 313 (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	0 / 17 (0.00%)	0 / 325 (0.00%)	0 / 313 (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
Hyponatraemia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	0 / 313 (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
Hypoglycaemia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	1 / 313 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Type 2 diabetes mellitus			
subjects affected / exposed	0 / 17 (0.00%)	0 / 325 (0.00%)	1 / 313 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Milvexian 100 mg BID	Milvexian 200 mg BID	
Total subjects affected by serious adverse events			
subjects affected / exposed	42 / 306 (13.73%)	54 / 344 (15.70%)	
number of deaths (all causes)	5	5	
number of deaths resulting from adverse events			

Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
B-cell lymphoma			
subjects affected / exposed	0 / 306 (0.00%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast cancer			
subjects affected / exposed	0 / 306 (0.00%)	1 / 344 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Invasive ductal breast carcinoma			
subjects affected / exposed	0 / 306 (0.00%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal adenocarcinoma			
subjects affected / exposed	0 / 306 (0.00%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colon cancer			
subjects affected / exposed	0 / 306 (0.00%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung neoplasm malignant			
subjects affected / exposed	1 / 306 (0.33%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases to lung			
subjects affected / exposed	0 / 306 (0.00%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastatic neoplasm			
subjects affected / exposed	0 / 306 (0.00%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Sinonasal papilloma			
subjects affected / exposed	0 / 306 (0.00%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma of lung			
subjects affected / exposed	1 / 306 (0.33%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 306 (0.00%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertension			
subjects affected / exposed	0 / 306 (0.00%)	1 / 344 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant hypertension			
subjects affected / exposed	0 / 306 (0.00%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Orthostatic hypotension			
subjects affected / exposed	0 / 306 (0.00%)	1 / 344 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral artery thrombosis			
subjects affected / exposed	0 / 306 (0.00%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral arterial occlusive disease			
subjects affected / exposed	0 / 306 (0.00%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration			

site conditions			
Pyrexia			
subjects affected / exposed	0 / 306 (0.00%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Asthenia			
subjects affected / exposed	1 / 306 (0.33%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sudden cardiac death			
subjects affected / exposed	1 / 306 (0.33%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Reproductive system and breast disorders			
Benign prostatic hyperplasia			
subjects affected / exposed	1 / 306 (0.33%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 306 (0.00%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute respiratory failure			
subjects affected / exposed	0 / 306 (0.00%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary oedema			
subjects affected / exposed	0 / 306 (0.00%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			

subjects affected / exposed	0 / 306 (0.00%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	0 / 306 (0.00%)	1 / 344 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
subjects affected / exposed	1 / 306 (0.33%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Anxiety disorder			
subjects affected / exposed	0 / 306 (0.00%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mania			
subjects affected / exposed	0 / 306 (0.00%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Ejection fraction decreased			
subjects affected / exposed	1 / 306 (0.33%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Activated partial thromboplastin time prolonged			
subjects affected / exposed	0 / 306 (0.00%)	1 / 344 (0.29%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liver function test increased			
subjects affected / exposed	0 / 306 (0.00%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Injury, poisoning and procedural complications			
Accidental overdose			
subjects affected / exposed	0 / 306 (0.00%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cystitis radiation			
subjects affected / exposed	0 / 306 (0.00%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femur fracture			
subjects affected / exposed	0 / 306 (0.00%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fibula fracture			
subjects affected / exposed	0 / 306 (0.00%)	1 / 344 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural stroke			
subjects affected / exposed	0 / 306 (0.00%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural haemorrhage			
subjects affected / exposed	0 / 306 (0.00%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Forearm fracture			
subjects affected / exposed	0 / 306 (0.00%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Procedural haemorrhage			
subjects affected / exposed	0 / 306 (0.00%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Radius fracture			
subjects affected / exposed	0 / 306 (0.00%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reactive gastropathy			
subjects affected / exposed	0 / 306 (0.00%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin laceration			
subjects affected / exposed	1 / 306 (0.33%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subdural haematoma			
subjects affected / exposed	0 / 306 (0.00%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congenital, familial and genetic disorders			
Atrial septal defect			
subjects affected / exposed	0 / 306 (0.00%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 306 (0.00%)	1 / 344 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	3 / 306 (0.98%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial flutter			
subjects affected / exposed	0 / 306 (0.00%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Atrial tachycardia			
subjects affected / exposed	1 / 306 (0.33%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrioventricular block complete			
subjects affected / exposed	1 / 306 (0.33%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina pectoris			
subjects affected / exposed	0 / 306 (0.00%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina unstable			
subjects affected / exposed	0 / 306 (0.00%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bradycardia			
subjects affected / exposed	1 / 306 (0.33%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac arrest			
subjects affected / exposed	0 / 306 (0.00%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrioventricular block second degree			
subjects affected / exposed	0 / 306 (0.00%)	1 / 344 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure			
subjects affected / exposed	0 / 306 (0.00%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure acute			

subjects affected / exposed	0 / 306 (0.00%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure congestive			
subjects affected / exposed	1 / 306 (0.33%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac ventricular thrombosis			
subjects affected / exposed	0 / 306 (0.00%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery disease			
subjects affected / exposed	1 / 306 (0.33%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intracardiac thrombus			
subjects affected / exposed	0 / 306 (0.00%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic cardiomyopathy			
subjects affected / exposed	0 / 306 (0.00%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			
subjects affected / exposed	2 / 306 (0.65%)	1 / 344 (0.29%)	
occurrences causally related to treatment / all	1 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nodal rhythm			
subjects affected / exposed	0 / 306 (0.00%)	1 / 344 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial ischaemia			

subjects affected / exposed	0 / 306 (0.00%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericarditis			
subjects affected / exposed	0 / 306 (0.00%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinus tachycardia			
subjects affected / exposed	0 / 306 (0.00%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prinzmetal angina			
subjects affected / exposed	0 / 306 (0.00%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Aphasia			
subjects affected / exposed	0 / 306 (0.00%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Basilar artery occlusion			
subjects affected / exposed	1 / 306 (0.33%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carotid artery thrombosis			
subjects affected / exposed	0 / 306 (0.00%)	1 / 344 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carotid artery stenosis			
subjects affected / exposed	0 / 306 (0.00%)	1 / 344 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brain stem stroke			

subjects affected / exposed	0 / 306 (0.00%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Basilar migraine			
subjects affected / exposed	0 / 306 (0.00%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Basilar artery stenosis			
subjects affected / exposed	1 / 306 (0.33%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral infarction			
subjects affected / exposed	1 / 306 (0.33%)	2 / 344 (0.58%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral ischaemia			
subjects affected / exposed	0 / 306 (0.00%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral venous thrombosis			
subjects affected / exposed	0 / 306 (0.00%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dementia			
subjects affected / exposed	1 / 306 (0.33%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysarthria			
subjects affected / exposed	0 / 306 (0.00%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Embolic cerebral infarction			

subjects affected / exposed	0 / 306 (0.00%)	1 / 344 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Encephalopathy			
subjects affected / exposed	0 / 306 (0.00%)	1 / 344 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epilepsy			
subjects affected / exposed	0 / 306 (0.00%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Focal dyscognitive seizures			
subjects affected / exposed	0 / 306 (0.00%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Generalised tonic-clonic seizure			
subjects affected / exposed	0 / 306 (0.00%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhagic transformation stroke			
subjects affected / exposed	0 / 306 (0.00%)	1 / 344 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intracranial aneurysm			
subjects affected / exposed	0 / 306 (0.00%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myasthenia gravis crisis			
subjects affected / exposed	0 / 306 (0.00%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mental impairment			

subjects affected / exposed	1 / 306 (0.33%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lacunar stroke			
subjects affected / exposed	0 / 306 (0.00%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic stroke			
subjects affected / exposed	7 / 306 (2.29%)	11 / 344 (3.20%)	
occurrences causally related to treatment / all	0 / 7	0 / 11	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic cerebral infarction			
subjects affected / exposed	1 / 306 (0.33%)	3 / 344 (0.87%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myelopathy			
subjects affected / exposed	0 / 306 (0.00%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Partial seizures			
subjects affected / exposed	0 / 306 (0.00%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neurological symptom			
subjects affected / exposed	1 / 306 (0.33%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peroneal nerve palsy			
subjects affected / exposed	0 / 306 (0.00%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pseudostroke			

subjects affected / exposed	0 / 306 (0.00%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sedation complication			
subjects affected / exposed	0 / 306 (0.00%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seizure			
subjects affected / exposed	1 / 306 (0.33%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stroke in evolution			
subjects affected / exposed	1 / 306 (0.33%)	8 / 344 (2.33%)	
occurrences causally related to treatment / all	0 / 1	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	1 / 306 (0.33%)	1 / 344 (0.29%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Toxic encephalopathy			
subjects affected / exposed	0 / 306 (0.00%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient ischaemic attack			
subjects affected / exposed	4 / 306 (1.31%)	4 / 344 (1.16%)	
occurrences causally related to treatment / all	0 / 4	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vertebral artery dissection			
subjects affected / exposed	1 / 306 (0.33%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			

subjects affected / exposed	0 / 306 (0.00%)	1 / 344 (0.29%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 306 (0.00%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vertigo positional			
subjects affected / exposed	1 / 306 (0.33%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Retinal detachment			
subjects affected / exposed	0 / 306 (0.00%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Diverticulum intestinal haemorrhagic			
subjects affected / exposed	1 / 306 (0.33%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenal ulcer			
subjects affected / exposed	0 / 306 (0.00%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenal ulcer haemorrhage			
subjects affected / exposed	0 / 306 (0.00%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenal ulcer perforation			
subjects affected / exposed	0 / 306 (0.00%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Gastric ulcer haemorrhage			
subjects affected / exposed	1 / 306 (0.33%)	2 / 344 (0.58%)	
occurrences causally related to treatment / all	1 / 1	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Faecaloma			
subjects affected / exposed	0 / 306 (0.00%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 306 (0.00%)	1 / 344 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	0 / 306 (0.00%)	1 / 344 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mallory-Weiss syndrome			
subjects affected / exposed	0 / 306 (0.00%)	1 / 344 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhoidal haemorrhage			
subjects affected / exposed	0 / 306 (0.00%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophagitis haemorrhagic			
subjects affected / exposed	1 / 306 (0.33%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peptic ulcer haemorrhage			
subjects affected / exposed	1 / 306 (0.33%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis acute			

subjects affected / exposed	0 / 306 (0.00%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper gastrointestinal haemorrhage			
subjects affected / exposed	0 / 306 (0.00%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal haemorrhage			
subjects affected / exposed	0 / 306 (0.00%)	1 / 344 (0.29%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal haemorrhage			
subjects affected / exposed	0 / 306 (0.00%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Hepatitis fulminant			
subjects affected / exposed	1 / 306 (0.33%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cholelithiasis			
subjects affected / exposed	0 / 306 (0.00%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis acute			
subjects affected / exposed	1 / 306 (0.33%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis			
subjects affected / exposed	0 / 306 (0.00%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			

Diabetic foot			
subjects affected / exposed	0 / 306 (0.00%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Drug eruption			
subjects affected / exposed	0 / 306 (0.00%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rash macular			
subjects affected / exposed	0 / 306 (0.00%)	1 / 344 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Toxic epidermal necrolysis			
subjects affected / exposed	0 / 306 (0.00%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urticaria			
subjects affected / exposed	1 / 306 (0.33%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 306 (0.00%)	4 / 344 (1.16%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cystitis haemorrhagic			
subjects affected / exposed	0 / 306 (0.00%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prerenal failure			
subjects affected / exposed	0 / 306 (0.00%)	1 / 344 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephropathy toxic			

subjects affected / exposed	0 / 306 (0.00%)	2 / 344 (0.58%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematuria			
subjects affected / exposed	1 / 306 (0.33%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal tubular necrosis			
subjects affected / exposed	0 / 306 (0.00%)	1 / 344 (0.29%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal failure			
subjects affected / exposed	0 / 306 (0.00%)	2 / 344 (0.58%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Osteoarthritis			
subjects affected / exposed	0 / 306 (0.00%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal chest pain			
subjects affected / exposed	0 / 306 (0.00%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Arthritis bacterial			
subjects affected / exposed	0 / 306 (0.00%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19			
subjects affected / exposed	0 / 306 (0.00%)	2 / 344 (0.58%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	

Bronchitis			
subjects affected / exposed	0 / 306 (0.00%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	0 / 306 (0.00%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulitis			
subjects affected / exposed	0 / 306 (0.00%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cystitis			
subjects affected / exposed	0 / 306 (0.00%)	1 / 344 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium difficile infection			
subjects affected / exposed	0 / 306 (0.00%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulitis intestinal perforated			
subjects affected / exposed	0 / 306 (0.00%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile infection			
subjects affected / exposed	0 / 306 (0.00%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	0 / 306 (0.00%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infected dermal cyst			

subjects affected / exposed	0 / 306 (0.00%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestine infection			
subjects affected / exposed	0 / 306 (0.00%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteomyelitis			
subjects affected / exposed	0 / 306 (0.00%)	1 / 344 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pneumonia			
subjects affected / exposed	2 / 306 (0.65%)	1 / 344 (0.29%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Sepsis			
subjects affected / exposed	0 / 306 (0.00%)	1 / 344 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic shock			
subjects affected / exposed	0 / 306 (0.00%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia aspiration			
subjects affected / exposed	0 / 306 (0.00%)	1 / 344 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal bacteraemia			
subjects affected / exposed	0 / 306 (0.00%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound infection pseudomonas			

subjects affected / exposed	0 / 306 (0.00%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tuberculosis			
subjects affected / exposed	0 / 306 (0.00%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	0 / 306 (0.00%)	5 / 344 (1.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urosepsis			
subjects affected / exposed	0 / 306 (0.00%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 306 (0.33%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperglycaemia			
subjects affected / exposed	0 / 306 (0.00%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperkalaemia			
subjects affected / exposed	1 / 306 (0.33%)	1 / 344 (0.29%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyponatraemia			
subjects affected / exposed	0 / 306 (0.00%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoglycaemia			

subjects affected / exposed	0 / 306 (0.00%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Type 2 diabetes mellitus			
subjects affected / exposed	0 / 306 (0.00%)	0 / 344 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Placebo	Milvexian 25 mg QD	Milvexian 50 mg QD
Total subjects affected by non-serious adverse events			
subjects affected / exposed	178 / 682 (26.10%)	81 / 325 (24.92%)	6 / 22 (27.27%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Melanocytic naevus			
subjects affected / exposed	0 / 682 (0.00%)	0 / 325 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Hypertension			
subjects affected / exposed	56 / 682 (8.21%)	21 / 325 (6.46%)	0 / 22 (0.00%)
occurrences (all)	60	21	0
Hypotension			
subjects affected / exposed	5 / 682 (0.73%)	2 / 325 (0.62%)	0 / 22 (0.00%)
occurrences (all)	5	2	0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	6 / 682 (0.88%)	2 / 325 (0.62%)	0 / 22 (0.00%)
occurrences (all)	6	2	0
Feeling cold			
subjects affected / exposed	0 / 682 (0.00%)	0 / 325 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Non-cardiac chest pain			
subjects affected / exposed	1 / 682 (0.15%)	1 / 325 (0.31%)	0 / 22 (0.00%)
occurrences (all)	1	2	0
Thirst			

subjects affected / exposed	1 / 682 (0.15%)	0 / 325 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	0 / 682 (0.00%)	1 / 325 (0.31%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Epistaxis			
subjects affected / exposed	10 / 682 (1.47%)	2 / 325 (0.62%)	2 / 22 (9.09%)
occurrences (all)	12	4	5
Psychiatric disorders			
Mental status changes			
subjects affected / exposed	0 / 682 (0.00%)	0 / 325 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Disorientation			
subjects affected / exposed	0 / 682 (0.00%)	0 / 325 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Depressed mood			
subjects affected / exposed	0 / 682 (0.00%)	0 / 325 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Anxiety			
subjects affected / exposed	5 / 682 (0.73%)	3 / 325 (0.92%)	1 / 22 (4.55%)
occurrences (all)	5	3	1
Investigations			
Activated partial thromboplastin time prolonged			
subjects affected / exposed	0 / 682 (0.00%)	0 / 325 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Skin abrasion			
subjects affected / exposed	1 / 682 (0.15%)	2 / 325 (0.62%)	0 / 22 (0.00%)
occurrences (all)	1	2	0
Road traffic accident			
subjects affected / exposed	0 / 682 (0.00%)	0 / 325 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			

Dizziness			
subjects affected / exposed	7 / 682 (1.03%)	4 / 325 (1.23%)	0 / 22 (0.00%)
occurrences (all)	7	4	0
Headache			
subjects affected / exposed	23 / 682 (3.37%)	16 / 325 (4.92%)	3 / 22 (13.64%)
occurrences (all)	24	16	3
Tremor			
subjects affected / exposed	3 / 682 (0.44%)	0 / 325 (0.00%)	0 / 22 (0.00%)
occurrences (all)	3	0	0
Paraesthesia			
subjects affected / exposed	3 / 682 (0.44%)	0 / 325 (0.00%)	1 / 22 (4.55%)
occurrences (all)	3	0	1
Syncope			
subjects affected / exposed	1 / 682 (0.15%)	1 / 325 (0.31%)	0 / 22 (0.00%)
occurrences (all)	1	1	0
Blood and lymphatic system disorders			
Leukocytosis			
subjects affected / exposed	1 / 682 (0.15%)	1 / 325 (0.31%)	0 / 22 (0.00%)
occurrences (all)	1	1	0
Iron deficiency anaemia			
subjects affected / exposed	1 / 682 (0.15%)	0 / 325 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Increased tendency to bruise			
subjects affected / exposed	2 / 682 (0.29%)	0 / 325 (0.00%)	0 / 22 (0.00%)
occurrences (all)	2	0	0
Anaemia			
subjects affected / exposed	4 / 682 (0.59%)	1 / 325 (0.31%)	0 / 22 (0.00%)
occurrences (all)	4	1	0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	5 / 682 (0.73%)	3 / 325 (0.92%)	0 / 22 (0.00%)
occurrences (all)	5	3	0
Constipation			
subjects affected / exposed	44 / 682 (6.45%)	22 / 325 (6.77%)	0 / 22 (0.00%)
occurrences (all)	46	22	0
Flatulence			

subjects affected / exposed	1 / 682 (0.15%)	0 / 325 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Gingival bleeding			
subjects affected / exposed	3 / 682 (0.44%)	0 / 325 (0.00%)	0 / 22 (0.00%)
occurrences (all)	8	0	0
Nausea			
subjects affected / exposed	14 / 682 (2.05%)	11 / 325 (3.38%)	1 / 22 (4.55%)
occurrences (all)	15	12	1
Rectal haemorrhage			
subjects affected / exposed	1 / 682 (0.15%)	0 / 325 (0.00%)	2 / 22 (9.09%)
occurrences (all)	1	0	2
Vomiting			
subjects affected / exposed	7 / 682 (1.03%)	7 / 325 (2.15%)	0 / 22 (0.00%)
occurrences (all)	7	7	0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	2 / 682 (0.29%)	0 / 325 (0.00%)	0 / 22 (0.00%)
occurrences (all)	2	0	0
Pollakiuria			
subjects affected / exposed	2 / 682 (0.29%)	1 / 325 (0.31%)	0 / 22 (0.00%)
occurrences (all)	2	1	0
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	17 / 682 (2.49%)	8 / 325 (2.46%)	0 / 22 (0.00%)
occurrences (all)	19	9	0
Metabolism and nutrition disorders			
Hypomagnesaemia			
subjects affected / exposed	1 / 682 (0.15%)	0 / 325 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Hypocalcaemia			
subjects affected / exposed	1 / 682 (0.15%)	0 / 325 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Hyperkalaemia			
subjects affected / exposed	2 / 682 (0.29%)	2 / 325 (0.62%)	0 / 22 (0.00%)
occurrences (all)	2	2	0

Non-serious adverse events	Milvexian 100 mg	Milvexian 50 mg BID	Milvexian 25 mg BID

	QD		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	11 / 17 (64.71%)	92 / 325 (28.31%)	83 / 313 (26.52%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Melanocytic naevus			
subjects affected / exposed	1 / 17 (5.88%)	0 / 325 (0.00%)	0 / 313 (0.00%)
occurrences (all)	1	0	0
Vascular disorders			
Hypertension			
subjects affected / exposed	2 / 17 (11.76%)	24 / 325 (7.38%)	23 / 313 (7.35%)
occurrences (all)	3	24	23
Hypotension			
subjects affected / exposed	1 / 17 (5.88%)	4 / 325 (1.23%)	2 / 313 (0.64%)
occurrences (all)	1	4	2
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	2 / 17 (11.76%)	1 / 325 (0.31%)	3 / 313 (0.96%)
occurrences (all)	2	1	4
Feeling cold			
subjects affected / exposed	1 / 17 (5.88%)	0 / 325 (0.00%)	0 / 313 (0.00%)
occurrences (all)	1	0	0
Non-cardiac chest pain			
subjects affected / exposed	1 / 17 (5.88%)	2 / 325 (0.62%)	1 / 313 (0.32%)
occurrences (all)	2	2	1
Thirst			
subjects affected / exposed	1 / 17 (5.88%)	0 / 325 (0.00%)	0 / 313 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	1 / 17 (5.88%)	0 / 325 (0.00%)	2 / 313 (0.64%)
occurrences (all)	1	0	2
Epistaxis			
subjects affected / exposed	0 / 17 (0.00%)	5 / 325 (1.54%)	4 / 313 (1.28%)
occurrences (all)	0	5	4
Psychiatric disorders			

Mental status changes			
subjects affected / exposed	1 / 17 (5.88%)	0 / 325 (0.00%)	0 / 313 (0.00%)
occurrences (all)	1	0	0
Disorientation			
subjects affected / exposed	1 / 17 (5.88%)	0 / 325 (0.00%)	1 / 313 (0.32%)
occurrences (all)	1	0	1
Depressed mood			
subjects affected / exposed	1 / 17 (5.88%)	1 / 325 (0.31%)	2 / 313 (0.64%)
occurrences (all)	1	1	2
Anxiety			
subjects affected / exposed	1 / 17 (5.88%)	3 / 325 (0.92%)	6 / 313 (1.92%)
occurrences (all)	1	3	6
Investigations			
Activated partial thromboplastin time prolonged			
subjects affected / exposed	1 / 17 (5.88%)	0 / 325 (0.00%)	0 / 313 (0.00%)
occurrences (all)	1	0	0
Injury, poisoning and procedural complications			
Skin abrasion			
subjects affected / exposed	1 / 17 (5.88%)	1 / 325 (0.31%)	3 / 313 (0.96%)
occurrences (all)	1	1	3
Road traffic accident			
subjects affected / exposed	1 / 17 (5.88%)	0 / 325 (0.00%)	0 / 313 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 17 (5.88%)	7 / 325 (2.15%)	4 / 313 (1.28%)
occurrences (all)	1	7	4
Headache			
subjects affected / exposed	1 / 17 (5.88%)	14 / 325 (4.31%)	12 / 313 (3.83%)
occurrences (all)	1	14	13
Tremor			
subjects affected / exposed	1 / 17 (5.88%)	0 / 325 (0.00%)	1 / 313 (0.32%)
occurrences (all)	1	0	1
Paraesthesia			
subjects affected / exposed	2 / 17 (11.76%)	0 / 325 (0.00%)	0 / 313 (0.00%)
occurrences (all)	2	0	0

Syncope			
subjects affected / exposed	1 / 17 (5.88%)	3 / 325 (0.92%)	0 / 313 (0.00%)
occurrences (all)	1	3	0
Blood and lymphatic system disorders			
Leukocytosis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 325 (0.00%)	2 / 313 (0.64%)
occurrences (all)	1	0	2
Iron deficiency anaemia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 325 (0.00%)	0 / 313 (0.00%)
occurrences (all)	1	0	0
Increased tendency to bruise			
subjects affected / exposed	1 / 17 (5.88%)	1 / 325 (0.31%)	0 / 313 (0.00%)
occurrences (all)	1	1	0
Anaemia			
subjects affected / exposed	2 / 17 (11.76%)	2 / 325 (0.62%)	2 / 313 (0.64%)
occurrences (all)	2	2	2
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 17 (5.88%)	1 / 325 (0.31%)	0 / 313 (0.00%)
occurrences (all)	1	1	0
Constipation			
subjects affected / exposed	3 / 17 (17.65%)	20 / 325 (6.15%)	17 / 313 (5.43%)
occurrences (all)	3	23	17
Flatulence			
subjects affected / exposed	1 / 17 (5.88%)	2 / 325 (0.62%)	0 / 313 (0.00%)
occurrences (all)	1	2	0
Gingival bleeding			
subjects affected / exposed	1 / 17 (5.88%)	1 / 325 (0.31%)	0 / 313 (0.00%)
occurrences (all)	1	1	0
Nausea			
subjects affected / exposed	2 / 17 (11.76%)	6 / 325 (1.85%)	6 / 313 (1.92%)
occurrences (all)	2	7	6
Rectal haemorrhage			
subjects affected / exposed	1 / 17 (5.88%)	1 / 325 (0.31%)	0 / 313 (0.00%)
occurrences (all)	1	1	0
Vomiting			

subjects affected / exposed	1 / 17 (5.88%)	3 / 325 (0.92%)	2 / 313 (0.64%)
occurrences (all)	1	3	2
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	2 / 17 (11.76%)	1 / 325 (0.31%)	1 / 313 (0.32%)
occurrences (all)	2	1	1
Pollakiuria			
subjects affected / exposed	1 / 17 (5.88%)	1 / 325 (0.31%)	0 / 313 (0.00%)
occurrences (all)	1	1	0
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	1 / 17 (5.88%)	6 / 325 (1.85%)	9 / 313 (2.88%)
occurrences (all)	1	6	10
Metabolism and nutrition disorders			
Hypomagnesaemia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 325 (0.00%)	0 / 313 (0.00%)
occurrences (all)	1	0	0
Hypocalcaemia			
subjects affected / exposed	1 / 17 (5.88%)	1 / 325 (0.31%)	0 / 313 (0.00%)
occurrences (all)	1	1	0
Hyperkalaemia			
subjects affected / exposed	1 / 17 (5.88%)	2 / 325 (0.62%)	0 / 313 (0.00%)
occurrences (all)	1	2	0

Non-serious adverse events	Milvexian 100 mg BID	Milvexian 200 mg BID	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	82 / 306 (26.80%)	90 / 344 (26.16%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Melanocytic naevus			
subjects affected / exposed	0 / 306 (0.00%)	0 / 344 (0.00%)	
occurrences (all)	0	0	
Vascular disorders			
Hypertension			
subjects affected / exposed	20 / 306 (6.54%)	19 / 344 (5.52%)	
occurrences (all)	20	19	
Hypotension			

subjects affected / exposed	1 / 306 (0.33%)	3 / 344 (0.87%)	
occurrences (all)	1	3	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	2 / 306 (0.65%)	4 / 344 (1.16%)	
occurrences (all)	2	4	
Feeling cold			
subjects affected / exposed	1 / 306 (0.33%)	0 / 344 (0.00%)	
occurrences (all)	1	0	
Non-cardiac chest pain			
subjects affected / exposed	1 / 306 (0.33%)	0 / 344 (0.00%)	
occurrences (all)	1	0	
Thirst			
subjects affected / exposed	0 / 306 (0.00%)	1 / 344 (0.29%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	0 / 306 (0.00%)	0 / 344 (0.00%)	
occurrences (all)	0	0	
Epistaxis			
subjects affected / exposed	4 / 306 (1.31%)	6 / 344 (1.74%)	
occurrences (all)	5	6	
Psychiatric disorders			
Mental status changes			
subjects affected / exposed	0 / 306 (0.00%)	0 / 344 (0.00%)	
occurrences (all)	0	0	
Disorientation			
subjects affected / exposed	1 / 306 (0.33%)	0 / 344 (0.00%)	
occurrences (all)	1	0	
Depressed mood			
subjects affected / exposed	0 / 306 (0.00%)	1 / 344 (0.29%)	
occurrences (all)	0	1	
Anxiety			
subjects affected / exposed	5 / 306 (1.63%)	3 / 344 (0.87%)	
occurrences (all)	5	3	
Investigations			

Activated partial thromboplastin time prolonged			
subjects affected / exposed	1 / 306 (0.33%)	0 / 344 (0.00%)	
occurrences (all)	1	0	
Injury, poisoning and procedural complications			
Skin abrasion			
subjects affected / exposed	1 / 306 (0.33%)	1 / 344 (0.29%)	
occurrences (all)	1	1	
Road traffic accident			
subjects affected / exposed	0 / 306 (0.00%)	0 / 344 (0.00%)	
occurrences (all)	0	0	
Nervous system disorders			
Dizziness			
subjects affected / exposed	5 / 306 (1.63%)	2 / 344 (0.58%)	
occurrences (all)	5	2	
Headache			
subjects affected / exposed	12 / 306 (3.92%)	9 / 344 (2.62%)	
occurrences (all)	13	10	
Tremor			
subjects affected / exposed	1 / 306 (0.33%)	0 / 344 (0.00%)	
occurrences (all)	1	0	
Paraesthesia			
subjects affected / exposed	1 / 306 (0.33%)	1 / 344 (0.29%)	
occurrences (all)	1	2	
Syncope			
subjects affected / exposed	0 / 306 (0.00%)	0 / 344 (0.00%)	
occurrences (all)	0	0	
Blood and lymphatic system disorders			
Leukocytosis			
subjects affected / exposed	1 / 306 (0.33%)	0 / 344 (0.00%)	
occurrences (all)	1	0	
Iron deficiency anaemia			
subjects affected / exposed	0 / 306 (0.00%)	0 / 344 (0.00%)	
occurrences (all)	0	0	
Increased tendency to bruise			
subjects affected / exposed	0 / 306 (0.00%)	0 / 344 (0.00%)	
occurrences (all)	0	0	

Anaemia			
subjects affected / exposed	5 / 306 (1.63%)	8 / 344 (2.33%)	
occurrences (all)	5	8	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	2 / 306 (0.65%)	1 / 344 (0.29%)	
occurrences (all)	2	1	
Constipation			
subjects affected / exposed	20 / 306 (6.54%)	24 / 344 (6.98%)	
occurrences (all)	20	24	
Flatulence			
subjects affected / exposed	0 / 306 (0.00%)	0 / 344 (0.00%)	
occurrences (all)	0	0	
Gingival bleeding			
subjects affected / exposed	1 / 306 (0.33%)	1 / 344 (0.29%)	
occurrences (all)	1	1	
Nausea			
subjects affected / exposed	11 / 306 (3.59%)	5 / 344 (1.45%)	
occurrences (all)	13	5	
Rectal haemorrhage			
subjects affected / exposed	1 / 306 (0.33%)	2 / 344 (0.58%)	
occurrences (all)	1	2	
Vomiting			
subjects affected / exposed	3 / 306 (0.98%)	3 / 344 (0.87%)	
occurrences (all)	3	3	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 306 (0.33%)	9 / 344 (2.62%)	
occurrences (all)	1	9	
Pollakiuria			
subjects affected / exposed	2 / 306 (0.65%)	1 / 344 (0.29%)	
occurrences (all)	2	1	
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	11 / 306 (3.59%)	12 / 344 (3.49%)	
occurrences (all)	11	13	
Metabolism and nutrition disorders			

Hypomagnesaemia			
subjects affected / exposed	0 / 306 (0.00%)	2 / 344 (0.58%)	
occurrences (all)	0	2	
Hypocalcaemia			
subjects affected / exposed	0 / 306 (0.00%)	0 / 344 (0.00%)	
occurrences (all)	0	0	
Hyperkalaemia			
subjects affected / exposed	3 / 306 (0.98%)	3 / 344 (0.87%)	
occurrences (all)	3	3	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
24 August 2019	Removed 3 QD doses groups (lowest 25 mg QD dose is maintained); keeping all BID doses. Title of the protocol was changed to reflect the new design.
09 October 2020	Updated the milestone requirement for DMC review to decide on inclusion of the 200-mg BID dose arm.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported