Clinical trial results:
A Phase 1b/2, multi-center, double-blind (principal investigators and study subjects blinded, sponsor unblinded), placebo-controlled, randomized, single-ascending dose study to assess the safety, pharmacokinetics, and pharmacodynamics of DS-1040B in subjects with acute ischemic stroke.

Summary

EudraCT number	2015-001824-43
Trial protocol	DE FR GB CZ ES SK IT
Global end of trial date	13 August 2019

Results information

Result version number	v1 (current)
This version publication date	17 August 2020
First version publication date	17 August 2020

Trial information

Trial identification

Sponsor protocol code	DS1040-A-U103

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02586233
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Daiichi Sankyo
Sponsor organisation address	211 Mt. Airy Road, Basking Ridge, United States, 07920
Public contact	Contact for Clinical Trial Information, Daiichi Sankyo Development Ltd, +1 908-992-6400, CTRinfo@dsi.com
Scientific contact	Contact for Clinical Trial Information, Daiichi Sankyo Development Ltd, +1 908-992-6400, CTRinfo@dsi.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 August 2019
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	13 August 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the safety and tolerability of DS-1040b (IV infusion over 6 hours) in subjects with AIS within 3 to 8 hours after stroke symptom onset

Protection of trial subjects:

This study was conducted in compliance with the protocol, the ethical principles that have their origin in the Declaration of Helsinki, the International Council for Harmonisation consolidated Guideline E6 for Good Clinical Practice (GCP) (CPMP/International Council for Harmonisation/135/95), the United States Food and Drug Administration GCP Regulations: Code of Federal Regulations Title 21, Parts 11, 50, 54, 56, and 312 as appropriate and other applicable local regulations.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 September 2015
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Spain: 24
Country: Number of subjects enrolled	United Kingdom: 3
Country: Number of subjects enrolled	Czech Republic: 4
Country: Number of subjects enrolled	France: 1
Country: Number of subjects enrolled	Germany: 5
Country: Number of subjects enrolled	United States: 46
Country: Number of subjects enrolled	Taiwan: 13
Country: Number of subjects enrolled	Australia: 4
Country: Number of subjects enrolled	Korea, Republic of: 6
Worldwide total number of subjects	106
EEA total number of subjects	37

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)	55
From 65 to 84 years	49
85 years and over	2

Subject disposition

Recruitment

Recruitment details:

A total of 106 participants who met all inclusion criteria and no exclusion criteria were randomized to treatment at a total of 78 clinic sites (46 in Europe, 19 in the United States, 7 in Asia, 5 in Australia, and 1 in Canada). Of the 106 participants randomized, 101 participants received treatment.

Pre-assignment

Screening details:

The study consisted of 6, sequential, ascending-dose cohorts. Participants were randomized to either DS-1040b or placebo in a 3:1 ratio.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Cohort 1: DS-1040b 0.6 mg

Arm description:

Subjects who received a single intravenous infusion of DS-1040b 0.6 mg.

Arm type	Experimental
Investigational medicinal product name	DS-1040b
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Intravenous infusion of 0.6 mg to 9.6 mg over a 6-hour period

Arm title	Cohort 2: DS-1040b 1.2 mg

Arm description:

Subjects who received a single intravenous infusion of DS-1040b 1.2 mg.

Arm type	Experimental
Investigational medicinal product name	DS-1040b
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Intravenous infusion of 0.6 mg to 9.6 mg over a 6-hour period

Arm title	Cohort 3: DS-1040b 2.4 mg

Arm description:

Subjects who received a single intravenous infusion of DS-1040b 2.4 mg.

Arm type	Experimental

Investigational medicinal product name	DS-1040b
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Intravenous infusion of 0.6 mg to 9.6 mg over a 6-hour period

Arm title	Cohort 4: DS-1040 4.8 mg

Arm description:

Subjects who received a single intravenous infusion of DS-1040b 4.8 mg.

Arm type	Experimental
Investigational medicinal product name	DS-1040b
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Intravenous infusion of 0.6 mg to 9.6 mg over a 6-hour period

Arm title	Cohort 5: DS-1040b 7.2 mg

Arm description:

Subjects who received a single intravenous infusion of DS-1040b 7.2 mg.

Arm type	Experimental
Investigational medicinal product name	DS-1040b
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Intravenous infusion of 0.6 mg to 9.6 mg over a 6-hour period

Arm title	Cohort 6: DS-1040b 9.6 mg

Arm description:

Subjects who received a single intravenous infusion of DS-1040b 9.6 mg.

Arm type	Experimental
Investigational medicinal product name	DS-1040b
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Intravenous infusion of 0.6 mg to 9.6 mg over a 6-hour period

Arm title	Placebo

Arm description:

Subjects who received a single intravenous infusion of placebo.

Arm type	Placebo
Investigational medicinal product name	0.9% sodium chloride
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:
Intravenous infusion over 6-hour period

Number of subjects in period 1	Cohort 1: DS-1040b 0.6 mg	Cohort 2: DS-1040b 1.2 mg	Cohort 3: DS-1040b 2.4 mg
Started	7	7	13
Completed	7	5	13
Not completed	0	2	0
Randomized, but did not receive treatment	-	1	-
Death	-	1	-

Number of subjects in period 1	Cohort 4: DS-1040 4.8 mg	Cohort 5: DS-1040b 7.2 mg	Cohort 6: DS-1040b 9.6 mg
Started	17	18	18
Completed	17	16	16
Not completed	0	2	2
Randomized, but did not receive treatment	-	-	2
Death	-	2	-

Number of subjects in period 1	Placebo
Started	26
Completed	24
Not completed	2
Randomized, but did not receive treatment	2
Death	-

Baseline characteristics

Reporting groups	
Reporting group title	Cohort 1: DS-1040b 0.6 mg
Reporting group description:	
Subjects who received a single intravenous infusion of DS-1040b 0.6 mg.	
Reporting group title	Cohort 2: DS-1040b 1.2 mg
Reporting group description:	
Subjects who received a single intravenous infusion of DS-1040b 1.2 mg.	
Reporting group title	Cohort 3: DS-1040b 2.4 mg
Reporting group description:	
Subjects who received a single intravenous infusion of DS-1040b 2.4 mg.	
Reporting group title	Cohort 4: DS-1040 4.8 mg
Reporting group description:	
Subjects who received a single intravenous infusion of DS-1040b 4.8 mg.	
Reporting group title	Cohort 5: DS-1040b 7.2 mg
Reporting group description:	
Subjects who received a single intravenous infusion of DS-1040b 7.2 mg.	
Reporting group title	Cohort 6: DS-1040b 9.6 mg
Reporting group description:	
Subjects who received a single intravenous infusion of DS-1040b 9.6 mg.	
Reporting group title	Placebo
Reporting group description:	
Subjects who received a single intravenous infusion of placebo.	

Reporting group values	Cohort 1: DS-1040b 0.6 mg	Cohort 2: DS-1040b 1.2 mg	Cohort 3: DS-1040b 2.4 mg
Number of subjects	7	7	13
Age categorical			
Based on Randomized Analysis Set			
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)	2	4	8
From 65-84 years	5	2	5
85 years and over	0	1	0
Age continuous			
Based on Safety Analysis Set (N=101); age data were missing for participants in some cohorts.			
Units: years			
arithmetic mean	68.2	68.2	62.7
standard deviation	± 7.8	± 10.2	± 9.7
Gender categorical			
Based on the Randomized Analysis Set			
Units: Subjects			

Female	3	2	5
Male	4	5	8

Reporting group values	Cohort 4: DS-1040 4.8 mg	Cohort 5: DS-1040b 7.2 mg	Cohort 6: DS-1040b 9.6 mg
Number of subjects	17	18	18
Age categorical			
Based on Randomized Analysis Set			
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)	8	9	10
From 65-84 years	9	9	7
85 years and over	0	0	1
Age continuous			
Based on Safety Analysis Set (N=101); age data were missing for participants in some cohorts.			
Units: years			
arithmetic mean	69.1	65.8	64.8
standard deviation	± 11.1	± 11.7	± 12.8
Gender categorical			
Based on the Randomized Analysis Set			
Units: Subjects			
Female	6	8	7
Male	11	10	11

Reporting group values	Placebo	Total	
Number of subjects	26	106	
Age categorical			
Based on Randomized Analysis Set			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	14	55	
From 65-84 years	12	49	
85 years and over	0	2	
Age continuous			
Based on Safety Analysis Set (N=101); age data were missing for participants in some cohorts.			
Units: years			
arithmetic mean	62.2		
standard deviation	± 12.3	-	

Gender categorical			
Based on the Randomized Analysis Set			
Units: Subjects			
Female	11	42	
Male	15	64	

End points

End points reporting groups

Reporting group title	Cohort 1: DS-1040b 0.6 mg
Reporting group description:	
Subjects who received a single intravenous infusion of DS-1040b 0.6 mg.	
Reporting group title	Cohort 2: DS-1040b 1.2 mg
Reporting group description:	
Subjects who received a single intravenous infusion of DS-1040b 1.2 mg.	
Reporting group title	Cohort 3: DS-1040b 2.4 mg
Reporting group description:	
Subjects who received a single intravenous infusion of DS-1040b 2.4 mg.	
Reporting group title	Cohort 4: DS-1040 4.8 mg
Reporting group description:	
Subjects who received a single intravenous infusion of DS-1040b 4.8 mg.	
Reporting group title	Cohort 5: DS-1040b 7.2 mg
Reporting group description:	
Subjects who received a single intravenous infusion of DS-1040b 7.2 mg.	
Reporting group title	Cohort 6: DS-1040b 9.6 mg
Reporting group description:	
Subjects who received a single intravenous infusion of DS-1040b 9.6 mg.	
Reporting group title	Placebo
Reporting group description:	
Subjects who received a single intravenous infusion of placebo.	
Subject analysis set title	All DS-1040b
Subject analysis set type	Safety analysis
Subject analysis set description:	
All subjects who received a single intravenous infusion of DS-1040b.	

Primary: Treatment-emergent Adverse Event Reported by >10% of Participants Following Ascending Doses of DS-1040b and a Placebo in Subjects With Acute Ischemic Stroke

End point title	Treatment-emergent Adverse Event Reported by >10% of Participants Following Ascending Doses of DS-1040b and a Placebo in Subjects With Acute Ischemic Stroke[1]
End point description:	
Treatment-emergent adverse event (TEAE) is defined as an adverse event that emerges during the treatment period (from first dose date until 30 days after the last dosing date), having been absent at predose; or reemerges during treatment, having been present at baseline but stopped prior to treatment; or worsens in severity after starting treatment relative to the pre-dose state, when the adverse event is continuous.	
End point type	Primary
End point timeframe:	
Baseline up to 90 days post last dose, up to 3 years 11 months	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive analyses were performed based on the study groups and study drugs administered for this outcome.

End point values	Cohort 1: DS-1040b 0.6 mg	Cohort 2: DS-1040b 1.2 mg	Cohort 3: DS-1040b 2.4 mg	Cohort 4: DS-1040 4.8 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	6	13	17
Units: Subjects				
number (not applicable)				
Any TEAE	5	5	10	15
Hypokalaemia	1	2	2	0
Constipation	1	2	3	1
Insomnia	0	0	1	0
Hypertension	0	0	1	3
Anxiety	0	1	0	0
Hyperglycaemia	0	0	0	1
Dyslipidaemia	0	0	0	0
Thrombocytopenia	0	1	0	0
Vomiting	0	1	0	0
Pyrexia	0	0	0	1
Vitamin B12 deficiency	0	0	0	0
Headache	3	1	2	2

End point values	Cohort 5: DS-1040b 7.2 mg	Cohort 6: DS-1040b 9.6 mg	Placebo	All DS-1040b
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	18	16	24	77
Units: Subjects				
number (not applicable)				
Any TEAE	14	14	18	63
Hypokalaemia	2	2	6	9
Constipation	5	2	5	14
Insomnia	1	3	5	5
Hypertension	1	0	3	5
Anxiety	0	2	3	3
Hyperglycaemia	1	0	3	2
Dyslipidaemia	1	1	3	2
Thrombocytopenia	0	0	3	1
Vomiting	0	0	3	1
Pyrexia	0	0	3	1
Vitamin B12 deficiency	0	0	3	0
Headache	1	4	2	13

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetic Parameter Maximum (Peak) Observed Plasma Concentration (Cmax) of DS-1040b Following Ascending Doses in Subjects With Acute Ischemic Stroke

End point title	Pharmacokinetic Parameter Maximum (Peak) Observed Plasma

	Concentration (Cmax) of DS-1040b Following Ascending Doses in Subjects With Acute Ischemic Stroke[2]

End point description:

The PK parameter of Maximum (Peak) Observed Plasma Concentration (Cmax) of DS-1040b was calculated from the plasma concentrations of DS-1040b using non-compartmental analysis.

End point type	Secondary

End point timeframe:

Predose, 0.5, 3, 6, 9, 12, 24, 48, 72, and 96 hours postdose

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: Descriptive analyses were performed based on the study groups and study drugs administered for this outcome.

End point values	Cohort 1: DS-1040b 0.6 mg	Cohort 2: DS-1040b 1.2 mg	Cohort 3: DS-1040b 2.4 mg	Cohort 4: DS-1040 4.8 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	6	13	16
Units: ng/mL				
arithmetic mean (standard deviation)				
Cmax	10.09 (± 3.26)	26.95 (± 9.39)	61.28 (± 35.67)	729.76 (± 1661.06)

End point values	Cohort 5: DS-1040b 7.2 mg	Cohort 6: DS-1040b 9.6 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17	10		
Units: ng/mL				
arithmetic mean (standard deviation)				
Cmax	191.06 (± 59.60)	203.70 (± 41.49)		

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetic Parameter Area Under the Concentration Versus Time Curve From Zero to Last Quantifiable Concentration Sampling Point (AUClast) of DS-1040b Following Ascending Doses in Subjects With Acute Ischemic Stroke

End point title	Pharmacokinetic Parameter Area Under the Concentration Versus Time Curve From Zero to Last Quantifiable Concentration Sampling Point (AUClast) of DS-1040b Following Ascending Doses in Subjects With Acute Ischemic Stroke[3]

End point description:

The PK parameter of Area Under the Concentration Versus Time Curve from Zero to Last Quantifiable Concentration Sampling Point of DS-1040b was calculated from the plasma concentrations of DS-1040b using non-compartmental analysis.

End point type	Secondary

End point timeframe:

Pre-dose, 0.5, 3, 6, 9, 12, 24, 48, 72, and 96 hours post-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: Descriptive analyses were performed based on the study groups and study drugs administered for this outcome.

End point values	Cohort 1: DS-1040b 0.6 mg	Cohort 2: DS-1040b 1.2 mg	Cohort 3: DS-1040b 2.4 mg	Cohort 4: DS-1040 4.8 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	6	13	16
Units: ng*h/mL				
arithmetic mean (standard deviation)				
AUClast	69.74 (± 16.19)	219.83 (± 95.16)	447.75 (± 199.97)	2611.87 (± 4471.65)

End point values	Cohort 5: DS-1040b 7.2 mg	Cohort 6: DS-1040b 9.6 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17	10		
Units: ng*h/mL				
arithmetic mean (standard deviation)				
AUClast	1489.21 (± 460.78)	1700.24 (± 346.43)		

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetic Parameter Terminal Half-life (t1/2) of DS-1040b Following Ascending Doses in Subjects With Acute Ischemic Stroke

End point title	Pharmacokinetic Parameter Terminal Half-life (t1/2) of DS-1040b Following Ascending Doses in Subjects With Acute Ischemic Stroke[4]

End point description:

The PK parameter of Terminal Half-life of DS-1040b was calculated from the plasma concentrations of DS-1040b using non-compartmental analysis in patients with available sample for the analysis.

End point type	Secondary

End point timeframe:

Pre-dose, 0.5, 3, 6, 9, 12, 24, 48, 72, and 96 hours post-dose

Notes:

[4] - 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: Descriptive analyses were performed based on the study groups and study drugs administered for this outcome.

End point values	Cohort 1: DS-1040b 0.6 mg	Cohort 2: DS-1040b 1.2 mg	Cohort 3: DS-1040b 2.4 mg	Cohort 4: DS-1040 4.8 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	2	7	8
Units: hours				
arithmetic mean (standard deviation)				
Terminal half-life	2.59 (± 0.46)	4.14 (± 0.17)	10.50 (± 15.02)	36.68 (± 25.94)

End point values	Cohort 5: DS-1040b 7.2 mg	Cohort 6: DS-1040b 9.6 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	8		
Units: hours				
arithmetic mean (standard deviation)				
Terminal half-life	33.37 (± 14.71)	35.86 (± 10.98)		

Statistical analyses

No statistical analyses for this end point

Secondary: Activated Form of Thrombin-activatable Fibrinolysis Inhibitor (TAFIa) Following Ascending Doses of DS-1040b and a Placebo in Subjects With Acute Ischemic Stroke

End point title	Activated Form of Thrombin-activatable Fibrinolysis Inhibitor (TAFIa) Following Ascending Doses of DS-1040b and a Placebo in Subjects With Acute Ischemic Stroke

End point description:

The enzymatic activity of thrombin-activatable fibrinolysis inhibitor was assessed using the Stago Coagulation Analyzer.

End point type	Secondary

End point timeframe:

Baseline and 6 hours postdose

End point values	Cohort 1: DS-1040b 0.6 mg	Cohort 2: DS-1040b 1.2 mg	Cohort 3: DS-1040b 2.4 mg	Cohort 4: DS-1040 4.8 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	6	13	17
Units: Mean percentage of TAFIa activity				
arithmetic mean (standard deviation)				
Baseline	96.7 (± 23.7)	97.8 (± 17.5)	100.4 (± 21.6)	105.1 (± 23.4)
6 hours postdose	93.5 (± 26.6)	98.8 (± 27.2)	86.7 (± 16.7)	75.9 (± 20.9)

End point values	Cohort 5: DS-1040b 7.2 mg	Cohort 6: DS-1040b 9.6 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	18	10	24	
Units: Mean percentage of TAFIa activity				
arithmetic mean (standard deviation)				
Baseline	108.1 (± 30.5)	112.6 (± 27.2)	100.9 (± 20.8)	
6 hours postdose	72.9 (± 22.6)	73.9 (± 14.4)	104.1 (± 24.7)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline at Day 30 in National Institute of Health Stroke Scale (NIHSS) Score Following Ascending Doses of DS-1040b and a Placebo in Subjects With Acute Ischemic Stroke

End point title	Change From Baseline at Day 30 in National Institute of Health Stroke Scale (NIHSS) Score Following Ascending Doses of DS-1040b and a Placebo in Subjects With Acute Ischemic Stroke

End point description:

The National Institute of Health Stroke Scale (NIHSS) quantifies stroke severity based on weighted evaluation findings. The score for each ability is a number between 0 and 4, with 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 indicates more impairment (worse outcome) in a stroke patient.

End point type	Secondary

End point timeframe:

30 days postdose

End point values	Cohort 1: DS-1040b 0.6 mg	Cohort 2: DS-1040b 1.2 mg	Cohort 3: DS-1040b 2.4 mg	Cohort 4: DS-1040 4.8 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	6	13	17
Units: Units on a scale				
arithmetic mean (standard deviation)				
Change from baseline in NIHSS score	-3.7 (± 2.21)	-3.0 (± 2.00)	-3.5 (± 1.71)	-2.06 (± 1.06)

End point values	Cohort 5: DS-1040b 7.2 mg	Cohort 6: DS-1040b 9.6 mg	Placebo	All DS-1040b
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	18	16	24	77
Units: Units on a scale				
arithmetic mean (standard deviation)				
Change from baseline in NIHSS score	-3.4 (± 2.70)	-6.2 (± 3.08)	-3.6 (± 4.27)	-3.9 (± 2.56)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With a Modified Rankin Scale (mRS) Score of 0 to 2 Following Ascending Doses of DS-1040b and a Placebo in Subjects With Acute Ischemic Stroke

End point title	Percentage of Participants With a Modified Rankin Scale (mRS) Score of 0 to 2 Following Ascending Doses of DS-1040b and a Placebo in Subjects With Acute Ischemic Stroke

End point description:

The modified Rankin scale (mRS) is a commonly used disability scale derived from the Rankin scale that is used to measure the degree of disability or dependence in the daily activities of people who have suffered a stroke or other causes of neurological disability. The level of disability following a stroke is assessed via a scale from 0 to 6, where 0 is no symptoms at all and 6 indicates death. Higher scores indicate worse outcome. The proportion (%) of participants with an mRS score of 0 to 2 at Day 5 (baseline) and Day 90 is being reported.

End point type	Secondary

End point timeframe:

Day 5 (baseline) and Day 90 post dose

End point values	Cohort 1: DS-1040b 0.6 mg	Cohort 2: DS-1040b 1.2 mg	Cohort 3: DS-1040b 2.4 mg	Cohort 4: DS-1040 4.8 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	6	13	17
Units: Percentage of subjects				
number (not applicable)				
Day 5 (baseline)	66.7	40.0	76.9	82.4
Day 90 postdose	85.7	60.0	76.9	82.4

End point values	Cohort 5: DS-1040b 7.2 mg	Cohort 6: DS-1040b 9.6 mg	Placebo	All DS-1040b
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	18	16	24	77
Units: Percentage of subjects				
number (not applicable)				
Day 5 (baseline)	72.2	53.3	54.2	68.9
Day 90 postdose	93.8	68.8	75.0	79.7

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Treatment-emergent adverse events (TEAEs) were collected from baseline up to 30 days post last dose, up to 3 years 11 months.

Adverse event reporting additional description:

A TEAE is defined as an adverse event (AE) that emerges from first dose date until 30 days after the last dose, having been absent at predose; or reemerges during treatment, having been present at baseline but stopped prior to treatment; or worsens in severity after starting treatment relative to the pre-dose state, when the AE is continuous.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups

Reporting group title	Cohort 1: DS-1040b 0.6 mg

Reporting group description:

Subjects who received a single intravenous infusion of DS-1040b 0.6 mg.

Reporting group title	Cohort 2: DS-1040b 1.2 mg

Reporting group description:

Subjects who received a single intravenous infusion of DS-1040b 1.2 mg.

Reporting group title	Cohort 3: DS-1040b 2.4 mg

Reporting group description:

Subjects who received a single intravenous infusion of DS-1040b 2.4 mg.

Reporting group title	Cohort 4: DS-1040 4.8 mg

Reporting group description:

Subjects who received a single intravenous infusion of DS-1040b 4.8 mg.

Reporting group title	Cohort 5: DS-1040b 7.2 mg

Reporting group description:

Subjects who received a single intravenous infusion of DS-1040b 7.2 mg.

Reporting group title	Cohort 6: DS-1040b 9.6 mg

Reporting group description:

Subjects who received a single intravenous infusion of DS-1040b 9.6 mg.

Reporting group title	Placebo

Reporting group description:

Subjects who received a single intravenous infusion of placebo.

Reporting group title	All DS-1040b

Reporting group description:

All subjects who received a single intravenous infusion of DS-1040b.

Serious adverse events	Cohort 1: DS-1040b 0.6 mg	Cohort 2: DS-1040b 1.2 mg	Cohort 3: DS-1040b 2.4 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 7 (14.29%)	4 / 6 (66.67%)	0 / 13 (0.00%)
number of deaths (all causes)	0	1	0
number of deaths resulting from adverse events	0	0	0

Vascular disorders			
Haematoma			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 13 (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			
Cardiac arrest			
subjects affected / exposed	0 / 7 (0.00%)	1 / 6 (16.67%)	0 / 13 (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
Nervous system disorders			
Carotid arteriosclerosis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 13 (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 / 7 (0.00%)	0 / 6 (0.00%)	0 / 13 (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
Cerebrovascular accident			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 13 (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
Haemorrhage intracranial			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 13 (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
Simple partial seizures			
subjects affected / exposed	1 / 7 (14.29%)	0 / 6 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal cord infarction			

subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 13 (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			
Cholestasis			
subjects affected / exposed	0 / 7 (0.00%)	1 / 6 (16.67%)	0 / 13 (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
Hepatocellular injury			
subjects affected / exposed	0 / 7 (0.00%)	1 / 6 (16.67%)	0 / 13 (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
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 13 (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			
Agitation			
subjects affected / exposed	0 / 7 (0.00%)	1 / 6 (16.67%)	0 / 13 (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
Renal and urinary disorders			
Renal failure acute			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 13 (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			
Escherichia urinary tract infection			
subjects affected / exposed	0 / 7 (0.00%)	1 / 6 (16.67%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			

subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 13 (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
Urosepsis			
subjects affected / exposed	0 / 7 (0.00%)	1 / 6 (16.67%)	0 / 13 (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

Serious adverse events	Cohort 4: DS-1040 4.8 mg	Cohort 5: DS-1040b 7.2 mg	Cohort 6: DS-1040b 9.6 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 17 (5.88%)	2 / 18 (11.11%)	2 / 16 (12.50%)
number of deaths (all causes)	0	2	0
number of deaths resulting from adverse events	0	0	0
Vascular disorders			
Haematoma			
subjects affected / exposed	1 / 17 (5.88%)	0 / 18 (0.00%)	0 / 16 (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 disorders			
Cardiac arrest			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	0 / 16 (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			
Carotid arteriosclerosis			
subjects affected / exposed	0 / 17 (0.00%)	1 / 18 (5.56%)	0 / 16 (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
Carotid artery stenosis			
subjects affected / exposed	0 / 17 (0.00%)	1 / 18 (5.56%)	0 / 16 (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
Cerebrovascular accident			

subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	0 / 16 (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
Haemorrhage intracranial			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Simple partial seizures			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	0 / 16 (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
Spinal cord infarction			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	0 / 16 (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			
Cholestasis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	0 / 16 (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
Hepatocellular injury			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	0 / 16 (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			
Pulmonary embolism			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	0 / 16 (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			
Agitation			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	0 / 16 (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			
Renal failure acute			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Escherichia urinary tract infection			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	0 / 16 (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%)	0 / 18 (0.00%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urosepsis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	0 / 16 (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	Placebo	All DS-1040b	
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 24 (16.67%)	10 / 77 (12.99%)	
number of deaths (all causes)	0	3	
number of deaths resulting from adverse events	0	0	
Vascular disorders			
Haematoma			
subjects affected / exposed	0 / 24 (0.00%)	1 / 77 (1.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Cardiac arrest			
subjects affected / exposed	1 / 24 (4.17%)	1 / 77 (1.30%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Nervous system disorders			
Carotid arteriosclerosis			

subjects affected / exposed	0 / 24 (0.00%)	1 / 77 (1.30%)	
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 / 24 (0.00%)	1 / 77 (1.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular accident			
subjects affected / exposed	1 / 24 (4.17%)	0 / 77 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhage intracranial			
subjects affected / exposed	0 / 24 (0.00%)	1 / 77 (1.30%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Simple partial seizures			
subjects affected / exposed	0 / 24 (0.00%)	1 / 77 (1.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal cord infarction			
subjects affected / exposed	1 / 24 (4.17%)	0 / 77 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholestasis			
subjects affected / exposed	0 / 24 (0.00%)	1 / 77 (1.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatocellular injury			
subjects affected / exposed	0 / 24 (0.00%)	1 / 77 (1.30%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			

Pulmonary embolism			
subjects affected / exposed	1 / 24 (4.17%)	0 / 77 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Agitation			
subjects affected / exposed	0 / 24 (0.00%)	1 / 77 (1.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Renal failure acute			
subjects affected / exposed	0 / 24 (0.00%)	1 / 77 (1.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Escherichia urinary tract infection			
subjects affected / exposed	0 / 24 (0.00%)	1 / 77 (1.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	0 / 24 (0.00%)	1 / 77 (1.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urosepsis			
subjects affected / exposed	0 / 24 (0.00%)	1 / 77 (1.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Cohort 1: DS-1040b 0.6 mg	Cohort 2: DS-1040b 1.2 mg	Cohort 3: DS-1040b 2.4 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 7 (71.43%)	5 / 6 (83.33%)	10 / 13 (76.92%)
Vascular disorders			

Arteriosclerosis			
subjects affected / exposed	1 / 7 (14.29%)	0 / 6 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Haematoma			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Hypertension			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Hypotension			
subjects affected / exposed	0 / 7 (0.00%)	1 / 6 (16.67%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 6 (16.67%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Chest discomfort			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Chest pain			
subjects affected / exposed	0 / 7 (0.00%)	1 / 6 (16.67%)	1 / 13 (7.69%)
occurrences (all)	0	1	1
Fatigue			
subjects affected / exposed	1 / 7 (14.29%)	0 / 6 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Inflammation			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Influenza like illness			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Infusion site phlebitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Pain			

subjects affected / exposed	0 / 7 (0.00%)	1 / 6 (16.67%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Peripheral swelling			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Vessel puncture site pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Bronchiectasis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Cough			
subjects affected / exposed	1 / 7 (14.29%)	0 / 6 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Dyspnoea			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Hypoxia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 6 (16.67%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Nasal obstruction			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Productive cough			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Pulmonary mass			

subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Pulmonary oedema			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Respiratory failure			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Rhinorrhoea			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Affective disorder			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Agitation			
subjects affected / exposed	0 / 7 (0.00%)	1 / 6 (16.67%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Anxiety			
subjects affected / exposed	0 / 7 (0.00%)	1 / 6 (16.67%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Confusional state			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Delirium			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Depressed mood			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Depression			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Hallucination			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0

Insomnia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Mood altered			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Sleep disorder			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Investigations			
Activated partial thromboplastin time prolonged			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Biopsy bone			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Blood albumin decreased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Blood bicarbonate decreased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Blood creatinine increased			
subjects affected / exposed	1 / 7 (14.29%)	0 / 6 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Blood fibrinogen increased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Blood glucose increased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Body temperature increased			
subjects affected / exposed	1 / 7 (14.29%)	0 / 6 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Ejection fraction decreased			

subjects affected / exposed	1 / 7 (14.29%)	0 / 6 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Red blood cell sedimentation rate increased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Vitamin D decreased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	1 / 7 (14.29%)	0 / 6 (0.00%)	1 / 13 (7.69%)
occurrences (all)	1	0	1
Joint injury			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Post procedural haematuria			
subjects affected / exposed	0 / 7 (0.00%)	1 / 6 (16.67%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Wound			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	1 / 7 (14.29%)	0 / 6 (0.00%)	1 / 13 (7.69%)
occurrences (all)	1	0	1
Bradycardia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 6 (16.67%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Cardiac arrest			
subjects affected / exposed	0 / 7 (0.00%)	1 / 6 (16.67%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Left ventricular dysfunction			

subjects affected / exposed	1 / 7 (14.29%)	0 / 6 (0.00%)	1 / 13 (7.69%)
occurrences (all)	1	0	1
Sinus tachycardia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Tachycardia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 6 (16.67%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Ventricular extrasystoles			
subjects affected / exposed	1 / 7 (14.29%)	0 / 6 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
Burning sensation			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Carotid arteriosclerosis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Carotid artery stenosis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Carpal tunnel syndrome			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Cerebral haemorrhage			
subjects affected / exposed	1 / 7 (14.29%)	0 / 6 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Cerebrovascular accident			
subjects affected / exposed	1 / 7 (14.29%)	0 / 6 (0.00%)	1 / 13 (7.69%)
occurrences (all)	1	0	1
Circadian rhythm sleep disorder			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Dizziness			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0

Dysaesthesia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Haemorrhage intracranial			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Haemorrhagic stroke			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	3 / 7 (42.86%)	1 / 6 (16.67%)	2 / 13 (15.38%)
occurrences (all)	3	1	2
Memory impairment			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Partial seizures			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Psychomotor hyperactivity			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Sedation			
subjects affected / exposed	0 / 7 (0.00%)	1 / 6 (16.67%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Simple partial seizures			
subjects affected / exposed	1 / 7 (14.29%)	0 / 6 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Somnolence			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Stroke in evolution			
subjects affected / exposed	0 / 7 (0.00%)	1 / 6 (16.67%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Syncope			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0

Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 6 (16.67%)	2 / 13 (15.38%)
occurrences (all)	0	1	2
Hyperfibrinogenaemia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Leukocytosis			
subjects affected / exposed	1 / 7 (14.29%)	1 / 6 (16.67%)	1 / 13 (7.69%)
occurrences (all)	1	1	1
Thrombocytopenia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 6 (16.67%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Eye disorders			
Conjunctival haemorrhage			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Dry eye			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Vision blurred			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Constipation			
subjects affected / exposed	1 / 7 (14.29%)	2 / 6 (33.33%)	3 / 13 (23.08%)
occurrences (all)	1	2	3
Diarrhoea			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Dyspepsia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Dysphagia			

subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Nausea			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	2 / 13 (15.38%)
occurrences (all)	0	0	2
Toothache			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	0 / 7 (0.00%)	1 / 6 (16.67%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Hepatobiliary disorders			
Cholestasis			
subjects affected / exposed	0 / 7 (0.00%)	1 / 6 (16.67%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Hepatocellular injury			
subjects affected / exposed	0 / 7 (0.00%)	1 / 6 (16.67%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Skin and subcutaneous tissue disorders			
Angioedema			
subjects affected / exposed	1 / 7 (14.29%)	0 / 6 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Decubitis ulcer			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Erythema			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Petechiae			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Psoriasis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Swelling face			

subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Glycosuria			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Haematuria			
subjects affected / exposed	0 / 7 (0.00%)	1 / 6 (16.67%)	1 / 13 (7.69%)
occurrences (all)	0	1	1
Neurogenic bladder			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Renal failure acute			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Urethral pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Urinary incontinence			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Urinary retention			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	2 / 13 (15.38%)
occurrences (all)	0	0	2
Arthritis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Back pain			

subjects affected / exposed	0 / 7 (0.00%)	1 / 6 (16.67%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Muscle spasms			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Muscle spasticity			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Muscular weakness			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Neurological decompensation			
subjects affected / exposed	0 / 7 (0.00%)	1 / 6 (16.67%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Neurological symptom			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Osteoarthritis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Paraesthesia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Tendonitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Tenosynovitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Infections and infestations			
Bacterial disease carrier			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0

Bronchitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Clostridium difficile colitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Conjunctivitis bacterial			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Escherichia urinary tract infection			
subjects affected / exposed	0 / 7 (0.00%)	1 / 6 (16.67%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Hepatitis B			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Pneumonia			
subjects affected / exposed	1 / 7 (14.29%)	0 / 6 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Postoperative wound infection			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Pyuria			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Respiratory tract infection			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Upper respiratory tract infection			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0

Urosepsis			
subjects affected / exposed	0 / 7 (0.00%)	1 / 6 (16.67%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Metabolism and nutrition disorders			
Diabetes mellitus			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Dyslipidaemia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Electrolyte imbalance			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Fluid imbalance			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Hyperchloraemia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 6 (16.67%)	4 / 13 (30.77%)
occurrences (all)	0	1	4
Hypercholesterolaemia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Hyperglycaemia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Hyperlipidaemia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Hyperuricaemia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Hypoalbuminaemia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Hypocalcaemia			

subjects affected / exposed	1 / 7 (14.29%)	1 / 6 (16.67%)	2 / 13 (15.38%)
occurrences (all)	1	1	2
Hypoglycaemia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Hypokalaemia			
subjects affected / exposed	1 / 7 (14.29%)	2 / 6 (33.33%)	2 / 13 (15.38%)
occurrences (all)	1	2	2
Hypomagnesaemia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 6 (16.67%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Hyponatraemia			
subjects affected / exposed	1 / 7 (14.29%)	1 / 6 (16.67%)	0 / 13 (0.00%)
occurrences (all)	1	1	0
Malnutrition			
subjects affected / exposed	0 / 7 (0.00%)	1 / 6 (16.67%)	1 / 13 (7.69%)
occurrences (all)	0	1	1
Vitamin B12 deficiency			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Vitamin D deficiency			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1

Non-serious adverse events	Cohort 4: DS-1040 4.8 mg	Cohort 5: DS-1040b 7.2 mg	Cohort 6: DS-1040b 9.6 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	15 / 17 (88.24%)	14 / 18 (77.78%)	14 / 16 (87.50%)
Vascular disorders			
Arteriosclerosis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Haematoma			
subjects affected / exposed	1 / 17 (5.88%)	0 / 18 (0.00%)	1 / 16 (6.25%)
occurrences (all)	1	0	1
Hypertension			

subjects affected / exposed	3 / 17 (17.65%)	1 / 18 (5.56%)	0 / 16 (0.00%)
occurrences (all)	3	1	0
Hypotension			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Chest discomfort			
subjects affected / exposed	1 / 17 (5.88%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Chest pain			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	1 / 17 (5.88%)	1 / 18 (5.56%)	1 / 16 (6.25%)
occurrences (all)	1	1	1
Inflammation			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Influenza like illness			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Infusion site phlebitis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Pain			
subjects affected / exposed	1 / 17 (5.88%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Peripheral swelling			
subjects affected / exposed	1 / 17 (5.88%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Pyrexia			

subjects affected / exposed	1 / 17 (5.88%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Vessel puncture site pain			
subjects affected / exposed	1 / 17 (5.88%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
Bronchiectasis			
subjects affected / exposed	0 / 17 (0.00%)	1 / 18 (5.56%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Cough			
subjects affected / exposed	0 / 17 (0.00%)	2 / 18 (11.11%)	0 / 16 (0.00%)
occurrences (all)	0	2	0
Dyspnoea			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Hypoxia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Nasal obstruction			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Oropharyngeal pain			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Productive cough			
subjects affected / exposed	0 / 17 (0.00%)	1 / 18 (5.56%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Pulmonary mass			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Pulmonary oedema			
subjects affected / exposed	1 / 17 (5.88%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Respiratory failure			

subjects affected / exposed	0 / 17 (0.00%)	1 / 18 (5.56%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Rhinorrhoea			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Affective disorder			
subjects affected / exposed	1 / 17 (5.88%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Agitation			
subjects affected / exposed	0 / 17 (0.00%)	1 / 18 (5.56%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Anxiety			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	2 / 16 (12.50%)
occurrences (all)	0	0	2
Confusional state			
subjects affected / exposed	1 / 17 (5.88%)	0 / 18 (0.00%)	1 / 16 (6.25%)
occurrences (all)	1	0	1
Delirium			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Depressed mood			
subjects affected / exposed	1 / 17 (5.88%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Depression			
subjects affected / exposed	1 / 17 (5.88%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Hallucination			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Insomnia			
subjects affected / exposed	0 / 17 (0.00%)	1 / 18 (5.56%)	3 / 16 (18.75%)
occurrences (all)	0	1	3
Mood altered			
subjects affected / exposed	1 / 17 (5.88%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0

Sleep disorder			
subjects affected / exposed	0 / 17 (0.00%)	1 / 18 (5.56%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Investigations			
Activated partial thromboplastin time prolonged			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Biopsy bone			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Blood albumin decreased			
subjects affected / exposed	0 / 17 (0.00%)	1 / 18 (5.56%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Blood bicarbonate decreased			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Blood creatinine increased			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Blood fibrinogen increased			
subjects affected / exposed	1 / 17 (5.88%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Blood glucose increased			
subjects affected / exposed	1 / 17 (5.88%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Body temperature increased			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Ejection fraction decreased			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 17 (0.00%)	1 / 18 (5.56%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Red blood cell sedimentation rate increased			

subjects affected / exposed	1 / 17 (5.88%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Vitamin D decreased			
subjects affected / exposed	1 / 17 (5.88%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	1 / 17 (5.88%)	0 / 18 (0.00%)	1 / 16 (6.25%)
occurrences (all)	1	0	1
Joint injury			
subjects affected / exposed	0 / 17 (0.00%)	1 / 18 (5.56%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Post procedural haematuria			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Wound			
subjects affected / exposed	0 / 17 (0.00%)	1 / 18 (5.56%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 17 (0.00%)	1 / 18 (5.56%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Bradycardia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Cardiac arrest			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Left ventricular dysfunction			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Sinus tachycardia			
subjects affected / exposed	0 / 17 (0.00%)	1 / 18 (5.56%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Tachycardia			

subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Ventricular extrasystoles			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Burning sensation			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Carotid arteriosclerosis			
subjects affected / exposed	0 / 17 (0.00%)	1 / 18 (5.56%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Carotid artery stenosis			
subjects affected / exposed	0 / 17 (0.00%)	1 / 18 (5.56%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Carpal tunnel syndrome			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Cerebral haemorrhage			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Cerebrovascular accident			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Circadian rhythm sleep disorder			
subjects affected / exposed	0 / 17 (0.00%)	1 / 18 (5.56%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Dizziness			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Dysaesthesia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Haemorrhage intracranial			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1

Haemorrhagic stroke			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Headache			
subjects affected / exposed	2 / 17 (11.76%)	1 / 18 (5.56%)	4 / 16 (25.00%)
occurrences (all)	2	1	4
Memory impairment			
subjects affected / exposed	1 / 17 (5.88%)	1 / 18 (5.56%)	0 / 16 (0.00%)
occurrences (all)	1	1	0
Partial seizures			
subjects affected / exposed	1 / 17 (5.88%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Psychomotor hyperactivity			
subjects affected / exposed	1 / 17 (5.88%)	0 / 18 (0.00%)	1 / 16 (6.25%)
occurrences (all)	1	0	1
Sedation			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Simple partial seizures			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Somnolence			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Stroke in evolution			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Syncope			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 17 (0.00%)	1 / 18 (5.56%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Hyperfibrinogenaemia			

subjects affected / exposed	0 / 17 (0.00%)	1 / 18 (5.56%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Leukocytosis			
subjects affected / exposed	1 / 17 (5.88%)	2 / 18 (11.11%)	0 / 16 (0.00%)
occurrences (all)	1	2	0
Thrombocytopenia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Conjunctival haemorrhage			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Dry eye			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Vision blurred			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	0 / 17 (0.00%)	1 / 18 (5.56%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Constipation			
subjects affected / exposed	1 / 17 (5.88%)	5 / 18 (27.78%)	2 / 16 (12.50%)
occurrences (all)	1	5	2
Diarrhoea			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	2 / 16 (12.50%)
occurrences (all)	0	0	2
Dyspepsia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Dysphagia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Nausea			

subjects affected / exposed	2 / 17 (11.76%)	0 / 18 (0.00%)	2 / 16 (12.50%)
occurrences (all)	2	0	2
Toothache			
subjects affected / exposed	0 / 17 (0.00%)	1 / 18 (5.56%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Vomiting			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Hepatobiliary disorders			
Cholestasis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Hepatocellular injury			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Angioedema			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Decubitis ulcer			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Erythema			
subjects affected / exposed	1 / 17 (5.88%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Petechiae			
subjects affected / exposed	1 / 17 (5.88%)	1 / 18 (5.56%)	0 / 16 (0.00%)
occurrences (all)	1	1	0
Psoriasis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Swelling face			
subjects affected / exposed	1 / 17 (5.88%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Renal and urinary disorders			

Dysuria			
subjects affected / exposed	1 / 17 (5.88%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Glycosuria			
subjects affected / exposed	0 / 17 (0.00%)	1 / 18 (5.56%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Haematuria			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Neurogenic bladder			
subjects affected / exposed	0 / 17 (0.00%)	1 / 18 (5.56%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Renal failure acute			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	2 / 16 (12.50%)
occurrences (all)	0	0	2
Urethral pain			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Urinary incontinence			
subjects affected / exposed	1 / 17 (5.88%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Urinary retention			
subjects affected / exposed	0 / 17 (0.00%)	1 / 18 (5.56%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 17 (0.00%)	1 / 18 (5.56%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Arthritis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Back pain			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Muscle spasms			

subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Muscle spasticity			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Muscular weakness			
subjects affected / exposed	2 / 17 (11.76%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	2	0	0
Musculoskeletal pain			
subjects affected / exposed	1 / 17 (5.88%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Neurological decompensation			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Neurological symptom			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Osteoarthritis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Paraesthesia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Tendonitis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Tenosynovitis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Bacterial disease carrier			
subjects affected / exposed	0 / 17 (0.00%)	1 / 18 (5.56%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Bronchitis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0

Clostridium difficile colitis			
subjects affected / exposed	0 / 17 (0.00%)	1 / 18 (5.56%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Conjunctivitis bacterial			
subjects affected / exposed	1 / 17 (5.88%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Escherichia urinary tract infection			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Hepatitis B			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Nasopharyngitis			
subjects affected / exposed	1 / 17 (5.88%)	1 / 18 (5.56%)	0 / 16 (0.00%)
occurrences (all)	1	1	0
Pneumonia			
subjects affected / exposed	0 / 17 (0.00%)	2 / 18 (11.11%)	1 / 16 (6.25%)
occurrences (all)	0	2	1
Postoperative wound infection			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Pyuria			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Respiratory tract infection			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 17 (0.00%)	2 / 18 (11.11%)	0 / 16 (0.00%)
occurrences (all)	0	2	0
Urinary tract infection			
subjects affected / exposed	2 / 17 (11.76%)	3 / 18 (16.67%)	1 / 16 (6.25%)
occurrences (all)	2	3	1
Urosepsis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0

Metabolism and nutrition disorders			
Diabetes mellitus			
subjects affected / exposed	1 / 17 (5.88%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Dyslipidaemia			
subjects affected / exposed	0 / 17 (0.00%)	1 / 18 (5.56%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Electrolyte imbalance			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Fluid imbalance			
subjects affected / exposed	0 / 17 (0.00%)	1 / 18 (5.56%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Hyperchloraemia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Hypercholesterolaemia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 18 (0.00%)	2 / 16 (12.50%)
occurrences (all)	1	0	2
Hyperglycaemia			
subjects affected / exposed	1 / 17 (5.88%)	1 / 18 (5.56%)	0 / 16 (0.00%)
occurrences (all)	1	1	0
Hyperlipidaemia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Hyperuricaemia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Hypoalbuminaemia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Hypocalcaemia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Hypoglycaemia			

subjects affected / exposed	1 / 17 (5.88%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Hypokalaemia			
subjects affected / exposed	0 / 17 (0.00%)	2 / 18 (11.11%)	2 / 16 (12.50%)
occurrences (all)	0	2	2
Hypomagnesaemia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Hyponatraemia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Malnutrition			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Vitamin B12 deficiency			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Vitamin D deficiency			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Placebo	All DS-1040b	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	18 / 24 (75.00%)	63 / 77 (81.82%)	
Vascular disorders			
Arteriosclerosis			
subjects affected / exposed	0 / 24 (0.00%)	1 / 77 (1.30%)	
occurrences (all)	0	1	
Haematoma			
subjects affected / exposed	0 / 24 (0.00%)	2 / 77 (2.60%)	
occurrences (all)	0	2	
Hypertension			
subjects affected / exposed	3 / 24 (12.50%)	5 / 77 (6.49%)	
occurrences (all)	3	5	
Hypotension			

subjects affected / exposed	1 / 24 (4.17%)	1 / 77 (1.30%)	
occurrences (all)	1	1	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 24 (0.00%)	1 / 77 (1.30%)	
occurrences (all)	0	1	
Chest discomfort			
subjects affected / exposed	0 / 24 (0.00%)	1 / 77 (1.30%)	
occurrences (all)	0	1	
Chest pain			
subjects affected / exposed	0 / 24 (0.00%)	2 / 77 (2.60%)	
occurrences (all)	0	2	
Fatigue			
subjects affected / exposed	0 / 24 (0.00%)	4 / 77 (5.19%)	
occurrences (all)	0	4	
Inflammation			
subjects affected / exposed	0 / 24 (0.00%)	1 / 77 (1.30%)	
occurrences (all)	0	1	
Influenza like illness			
subjects affected / exposed	0 / 24 (0.00%)	1 / 77 (1.30%)	
occurrences (all)	0	1	
Infusion site phlebitis			
subjects affected / exposed	0 / 24 (0.00%)	1 / 77 (1.30%)	
occurrences (all)	0	1	
Pain			
subjects affected / exposed	0 / 24 (0.00%)	2 / 77 (2.60%)	
occurrences (all)	0	2	
Peripheral swelling			
subjects affected / exposed	0 / 24 (0.00%)	1 / 77 (1.30%)	
occurrences (all)	0	1	
Pyrexia			
subjects affected / exposed	3 / 24 (12.50%)	1 / 77 (1.30%)	
occurrences (all)	3	1	
Vessel puncture site pain			

subjects affected / exposed	0 / 24 (0.00%)	1 / 77 (1.30%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Bronchiectasis			
subjects affected / exposed	0 / 24 (0.00%)	1 / 77 (1.30%)	
occurrences (all)	0	1	
Cough			
subjects affected / exposed	1 / 24 (4.17%)	3 / 77 (3.90%)	
occurrences (all)	1	3	
Dyspnoea			
subjects affected / exposed	1 / 24 (4.17%)	1 / 77 (1.30%)	
occurrences (all)	1	1	
Hypoxia			
subjects affected / exposed	0 / 24 (0.00%)	1 / 77 (1.30%)	
occurrences (all)	0	1	
Nasal obstruction			
subjects affected / exposed	0 / 24 (0.00%)	1 / 77 (1.30%)	
occurrences (all)	0	1	
Oropharyngeal pain			
subjects affected / exposed	0 / 24 (0.00%)	1 / 77 (1.30%)	
occurrences (all)	0	1	
Productive cough			
subjects affected / exposed	0 / 24 (0.00%)	1 / 77 (1.30%)	
occurrences (all)	0	1	
Pulmonary mass			
subjects affected / exposed	0 / 24 (0.00%)	1 / 77 (1.30%)	
occurrences (all)	0	1	
Pulmonary oedema			
subjects affected / exposed	0 / 24 (0.00%)	1 / 77 (1.30%)	
occurrences (all)	0	1	
Respiratory failure			
subjects affected / exposed	0 / 24 (0.00%)	2 / 77 (2.60%)	
occurrences (all)	0	2	
Rhinorrhoea			

subjects affected / exposed	2 / 24 (8.33%)	0 / 77 (0.00%)	
occurrences (all)	2	0	
Psychiatric disorders			
Affective disorder			
subjects affected / exposed	0 / 24 (0.00%)	1 / 77 (1.30%)	
occurrences (all)	0	1	
Agitation			
subjects affected / exposed	0 / 24 (0.00%)	3 / 77 (3.90%)	
occurrences (all)	0	3	
Anxiety			
subjects affected / exposed	3 / 24 (12.50%)	3 / 77 (3.90%)	
occurrences (all)	3	3	
Confusional state			
subjects affected / exposed	0 / 24 (0.00%)	2 / 77 (2.60%)	
occurrences (all)	0	2	
Delirium			
subjects affected / exposed	2 / 24 (8.33%)	0 / 77 (0.00%)	
occurrences (all)	2	0	
Depressed mood			
subjects affected / exposed	0 / 24 (0.00%)	2 / 77 (2.60%)	
occurrences (all)	0	2	
Depression			
subjects affected / exposed	2 / 24 (8.33%)	2 / 77 (2.60%)	
occurrences (all)	2	2	
Hallucination			
subjects affected / exposed	0 / 24 (0.00%)	1 / 77 (1.30%)	
occurrences (all)	0	1	
Insomnia			
subjects affected / exposed	5 / 24 (20.83%)	5 / 77 (6.49%)	
occurrences (all)	5	5	
Mood altered			
subjects affected / exposed	0 / 24 (0.00%)	1 / 77 (1.30%)	
occurrences (all)	0	1	
Sleep disorder			
subjects affected / exposed	1 / 24 (4.17%)	1 / 77 (1.30%)	
occurrences (all)	1	1	

Investigations			
Activated partial thromboplastin time prolonged			
subjects affected / exposed	2 / 24 (8.33%)	0 / 77 (0.00%)	
occurrences (all)	2	0	
Biopsy bone			
subjects affected / exposed	0 / 24 (0.00%)	1 / 77 (1.30%)	
occurrences (all)	0	1	
Blood albumin decreased			
subjects affected / exposed	0 / 24 (0.00%)	1 / 77 (1.30%)	
occurrences (all)	0	1	
Blood bicarbonate decreased			
subjects affected / exposed	2 / 24 (8.33%)	0 / 77 (0.00%)	
occurrences (all)	2	0	
Blood creatinine increased			
subjects affected / exposed	0 / 24 (0.00%)	1 / 77 (1.30%)	
occurrences (all)	0	1	
Blood fibrinogen increased			
subjects affected / exposed	2 / 24 (8.33%)	1 / 77 (1.30%)	
occurrences (all)	2	1	
Blood glucose increased			
subjects affected / exposed	0 / 24 (0.00%)	1 / 77 (1.30%)	
occurrences (all)	0	1	
Body temperature increased			
subjects affected / exposed	0 / 24 (0.00%)	1 / 77 (1.30%)	
occurrences (all)	0	1	
Ejection fraction decreased			
subjects affected / exposed	0 / 24 (0.00%)	1 / 77 (1.30%)	
occurrences (all)	0	1	
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 24 (0.00%)	1 / 77 (1.30%)	
occurrences (all)	0	1	
Red blood cell sedimentation rate increased			
subjects affected / exposed	0 / 24 (0.00%)	1 / 77 (1.30%)	
occurrences (all)	0	1	
Vitamin D decreased			

subjects affected / exposed	0 / 24 (0.00%)	1 / 77 (1.30%)	
occurrences (all)	0	1	
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	1 / 24 (4.17%)	4 / 77 (5.19%)	
occurrences (all)	1	4	
Joint injury			
subjects affected / exposed	0 / 24 (0.00%)	1 / 77 (1.30%)	
occurrences (all)	0	1	
Post procedural haematuria			
subjects affected / exposed	0 / 24 (0.00%)	1 / 77 (1.30%)	
occurrences (all)	0	1	
Wound			
subjects affected / exposed	0 / 24 (0.00%)	1 / 77 (1.30%)	
occurrences (all)	0	1	
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	1 / 24 (4.17%)	4 / 77 (5.19%)	
occurrences (all)	1	4	
Bradycardia			
subjects affected / exposed	0 / 24 (0.00%)	2 / 77 (2.60%)	
occurrences (all)	0	2	
Cardiac arrest			
subjects affected / exposed	1 / 24 (4.17%)	1 / 77 (1.30%)	
occurrences (all)	1	1	
Left ventricular dysfunction			
subjects affected / exposed	0 / 24 (0.00%)	2 / 77 (2.60%)	
occurrences (all)	0	2	
Sinus tachycardia			
subjects affected / exposed	0 / 24 (0.00%)	1 / 77 (1.30%)	
occurrences (all)	0	1	
Tachycardia			
subjects affected / exposed	0 / 24 (0.00%)	1 / 77 (1.30%)	
occurrences (all)	0	1	
Ventricular extrasystoles			

subjects affected / exposed	0 / 24 (0.00%)	1 / 77 (1.30%)	
occurrences (all)	0	1	
Nervous system disorders			
Burning sensation			
subjects affected / exposed	0 / 24 (0.00%)	1 / 77 (1.30%)	
occurrences (all)	0	1	
Carotid arteriosclerosis			
subjects affected / exposed	0 / 24 (0.00%)	1 / 77 (1.30%)	
occurrences (all)	0	1	
Carotid artery stenosis			
subjects affected / exposed	0 / 24 (0.00%)	1 / 77 (1.30%)	
occurrences (all)	0	1	
Carpal tunnel syndrome			
subjects affected / exposed	0 / 24 (0.00%)	1 / 77 (1.30%)	
occurrences (all)	0	1	
Cerebral haemorrhage			
subjects affected / exposed	0 / 24 (0.00%)	1 / 77 (1.30%)	
occurrences (all)	0	1	
Cerebrovascular accident			
subjects affected / exposed	1 / 24 (4.17%)	2 / 77 (2.60%)	
occurrences (all)	1	2	
Circadian rhythm sleep disorder			
subjects affected / exposed	0 / 24 (0.00%)	1 / 77 (1.30%)	
occurrences (all)	0	1	
Dizziness			
subjects affected / exposed	1 / 24 (4.17%)	1 / 77 (1.30%)	
occurrences (all)	1	1	
Dysaesthesia			
subjects affected / exposed	0 / 24 (0.00%)	1 / 77 (1.30%)	
occurrences (all)	0	1	
Haemorrhage intracranial			
subjects affected / exposed	1 / 24 (4.17%)	1 / 77 (1.30%)	
occurrences (all)	1	1	
Haemorrhagic stroke			
subjects affected / exposed	0 / 24 (0.00%)	1 / 77 (1.30%)	
occurrences (all)	0	1	

Headache			
subjects affected / exposed	2 / 24 (8.33%)	13 / 77 (16.88%)	
occurrences (all)	2	13	
Memory impairment			
subjects affected / exposed	0 / 24 (0.00%)	2 / 77 (2.60%)	
occurrences (all)	0	2	
Partial seizures			
subjects affected / exposed	0 / 24 (0.00%)	1 / 77 (1.30%)	
occurrences (all)	0	1	
Psychomotor hyperactivity			
subjects affected / exposed	0 / 24 (0.00%)	3 / 77 (3.90%)	
occurrences (all)	0	3	
Sedation			
subjects affected / exposed	0 / 24 (0.00%)	1 / 77 (1.30%)	
occurrences (all)	0	1	
Simple partial seizures			
subjects affected / exposed	0 / 24 (0.00%)	1 / 77 (1.30%)	
occurrences (all)	0	1	
Somnolence			
subjects affected / exposed	0 / 24 (0.00%)	1 / 77 (1.30%)	
occurrences (all)	0	1	
Stroke in evolution			
subjects affected / exposed	0 / 24 (0.00%)	1 / 77 (1.30%)	
occurrences (all)	0	1	
Syncope			
subjects affected / exposed	0 / 24 (0.00%)	1 / 77 (1.30%)	
occurrences (all)	0	1	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 24 (8.33%)	4 / 77 (5.19%)	
occurrences (all)	2	4	
Hyperfibrinogenaemia			
subjects affected / exposed	0 / 24 (0.00%)	1 / 77 (1.30%)	
occurrences (all)	0	1	
Leukocytosis			

subjects affected / exposed	2 / 24 (8.33%)	6 / 77 (7.79%)	
occurrences (all)	2	6	
Thrombocytopenia			
subjects affected / exposed	3 / 24 (12.50%)	1 / 77 (1.30%)	
occurrences (all)	3	1	
Eye disorders			
Conjunctival haemorrhage			
subjects affected / exposed	0 / 24 (0.00%)	1 / 77 (1.30%)	
occurrences (all)	0	1	
Dry eye			
subjects affected / exposed	0 / 24 (0.00%)	1 / 77 (1.30%)	
occurrences (all)	0	1	
Vision blurred			
subjects affected / exposed	0 / 24 (0.00%)	1 / 77 (1.30%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	1 / 24 (4.17%)	1 / 77 (1.30%)	
occurrences (all)	1	1	
Constipation			
subjects affected / exposed	5 / 24 (20.83%)	14 / 77 (18.18%)	
occurrences (all)	5	14	
Diarrhoea			
subjects affected / exposed	1 / 24 (4.17%)	2 / 77 (2.60%)	
occurrences (all)	1	2	
Dyspepsia			
subjects affected / exposed	0 / 24 (0.00%)	1 / 77 (1.30%)	
occurrences (all)	0	1	
Dysphagia			
subjects affected / exposed	1 / 24 (4.17%)	2 / 77 (2.60%)	
occurrences (all)	1	2	
Nausea			
subjects affected / exposed	2 / 24 (8.33%)	6 / 77 (7.79%)	
occurrences (all)	2	6	
Toothache			

subjects affected / exposed	0 / 24 (0.00%)	1 / 77 (1.30%)	
occurrences (all)	0	1	
Vomiting			
subjects affected / exposed	3 / 24 (12.50%)	1 / 77 (1.30%)	
occurrences (all)	3	1	
Hepatobiliary disorders			
Cholestasis			
subjects affected / exposed	0 / 24 (0.00%)	1 / 77 (1.30%)	
occurrences (all)	0	1	
Hepatocellular injury			
subjects affected / exposed	0 / 24 (0.00%)	1 / 77 (1.30%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			
Angioedema			
subjects affected / exposed	0 / 24 (0.00%)	1 / 77 (1.30%)	
occurrences (all)	0	1	
Decubitis ulcer			
subjects affected / exposed	2 / 24 (8.33%)	0 / 77 (0.00%)	
occurrences (all)	2	0	
Erythema			
subjects affected / exposed	0 / 24 (0.00%)	2 / 77 (2.60%)	
occurrences (all)	0	2	
Petechiae			
subjects affected / exposed	0 / 24 (0.00%)	2 / 77 (2.60%)	
occurrences (all)	0	2	
Psoriasis			
subjects affected / exposed	0 / 24 (0.00%)	1 / 77 (1.30%)	
occurrences (all)	0	1	
Swelling face			
subjects affected / exposed	0 / 24 (0.00%)	1 / 77 (1.30%)	
occurrences (all)	0	1	
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	0 / 24 (0.00%)	1 / 77 (1.30%)	
occurrences (all)	0	1	
Glycosuria			

subjects affected / exposed	0 / 24 (0.00%)	1 / 77 (1.30%)	
occurrences (all)	0	1	
Haematuria			
subjects affected / exposed	2 / 24 (8.33%)	2 / 77 (2.60%)	
occurrences (all)	2	2	
Neurogenic bladder			
subjects affected / exposed	1 / 24 (4.17%)	1 / 77 (1.30%)	
occurrences (all)	1	1	
Renal failure acute			
subjects affected / exposed	0 / 24 (0.00%)	2 / 77 (2.60%)	
occurrences (all)	0	2	
Urethral pain			
subjects affected / exposed	0 / 24 (0.00%)	1 / 77 (1.30%)	
occurrences (all)	0	1	
Urinary incontinence			
subjects affected / exposed	1 / 24 (4.17%)	1 / 77 (1.30%)	
occurrences (all)	1	1	
Urinary retention			
subjects affected / exposed	0 / 24 (0.00%)	2 / 77 (2.60%)	
occurrences (all)	0	2	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 24 (8.33%)	3 / 77 (3.90%)	
occurrences (all)	2	3	
Arthritis			
subjects affected / exposed	0 / 24 (0.00%)	1 / 77 (1.30%)	
occurrences (all)	0	1	
Back pain			
subjects affected / exposed	1 / 24 (4.17%)	2 / 77 (2.60%)	
occurrences (all)	1	2	
Muscle spasms			
subjects affected / exposed	0 / 24 (0.00%)	1 / 77 (1.30%)	
occurrences (all)	0	1	
Muscle spasticity			

subjects affected / exposed	0 / 24 (0.00%)	1 / 77 (1.30%)	
occurrences (all)	0	1	
Muscular weakness			
subjects affected / exposed	1 / 24 (4.17%)	2 / 77 (2.60%)	
occurrences (all)	1	2	
Musculoskeletal pain			
subjects affected / exposed	2 / 24 (8.33%)	1 / 77 (1.30%)	
occurrences (all)	2	1	
Neurological decompensation			
subjects affected / exposed	0 / 24 (0.00%)	1 / 77 (1.30%)	
occurrences (all)	0	1	
Neurological symptom			
subjects affected / exposed	0 / 24 (0.00%)	1 / 77 (1.30%)	
occurrences (all)	0	1	
Osteoarthritis			
subjects affected / exposed	0 / 24 (0.00%)	1 / 77 (1.30%)	
occurrences (all)	0	1	
Paraesthesia			
subjects affected / exposed	0 / 24 (0.00%)	1 / 77 (1.30%)	
occurrences (all)	0	1	
Tendonitis			
subjects affected / exposed	0 / 24 (0.00%)	1 / 77 (1.30%)	
occurrences (all)	0	1	
Tenosynovitis			
subjects affected / exposed	0 / 24 (0.00%)	1 / 77 (1.30%)	
occurrences (all)	0	1	
Infections and infestations			
Bacterial disease carrier			
subjects affected / exposed	0 / 24 (0.00%)	1 / 77 (1.30%)	
occurrences (all)	0	1	
Bronchitis			
subjects affected / exposed	0 / 24 (0.00%)	1 / 77 (1.30%)	
occurrences (all)	0	1	
Clostridium difficile colitis			
subjects affected / exposed	0 / 24 (0.00%)	1 / 77 (1.30%)	
occurrences (all)	0	1	

Conjunctivitis bacterial			
subjects affected / exposed	0 / 24 (0.00%)	1 / 77 (1.30%)	
occurrences (all)	0	1	
Escherichia urinary tract infection			
subjects affected / exposed	0 / 24 (0.00%)	1 / 77 (1.30%)	
occurrences (all)	0	1	
Hepatitis B			
subjects affected / exposed	0 / 24 (0.00%)	1 / 77 (1.30%)	
occurrences (all)	0	1	
Nasopharyngitis			
subjects affected / exposed	0 / 24 (0.00%)	2 / 77 (2.60%)	
occurrences (all)	0	2	
Pneumonia			
subjects affected / exposed	1 / 24 (4.17%)	4 / 77 (5.19%)	
occurrences (all)	1	4	
Postoperative wound infection			
subjects affected / exposed	0 / 24 (0.00%)	1 / 77 (1.30%)	
occurrences (all)	0	1	
Pyuria			
subjects affected / exposed	0 / 24 (0.00%)	1 / 77 (1.30%)	
occurrences (all)	0	1	
Respiratory tract infection			
subjects affected / exposed	0 / 24 (0.00%)	1 / 77 (1.30%)	
occurrences (all)	0	1	
Upper respiratory tract infection			
subjects affected / exposed	0 / 24 (0.00%)	2 / 77 (2.60%)	
occurrences (all)	0	2	
Urinary tract infection			
subjects affected / exposed	1 / 24 (4.17%)	6 / 77 (7.79%)	
occurrences (all)	1	6	
Urosepsis			
subjects affected / exposed	1 / 24 (4.17%)	1 / 77 (1.30%)	
occurrences (all)	1	1	
Metabolism and nutrition disorders			
Diabetes mellitus			

subjects affected / exposed	0 / 24 (0.00%)	1 / 77 (1.30%)	
occurrences (all)	0	1	
Dyslipidaemia			
subjects affected / exposed	3 / 24 (12.50%)	2 / 77 (2.60%)	
occurrences (all)	3	2	
Electrolyte imbalance			
subjects affected / exposed	0 / 24 (0.00%)	1 / 77 (1.30%)	
occurrences (all)	0	1	
Fluid imbalance			
subjects affected / exposed	0 / 24 (0.00%)	1 / 77 (1.30%)	
occurrences (all)	0	1	
Hyperchloraemia			
subjects affected / exposed	2 / 24 (8.33%)	5 / 77 (6.49%)	
occurrences (all)	2	5	
Hypercholesterolaemia			
subjects affected / exposed	0 / 24 (0.00%)	3 / 77 (3.90%)	
occurrences (all)	0	3	
Hyperglycaemia			
subjects affected / exposed	3 / 24 (12.50%)	2 / 77 (2.60%)	
occurrences (all)	3	2	
Hyperlipidaemia			
subjects affected / exposed	1 / 24 (4.17%)	1 / 77 (1.30%)	
occurrences (all)	1	1	
Hyperuricaemia			
subjects affected / exposed	0 / 24 (0.00%)	1 / 77 (1.30%)	
occurrences (all)	0	1	
Hypoalbuminaemia			
subjects affected / exposed	2 / 24 (8.33%)	1 / 77 (1.30%)	
occurrences (all)	2	1	
Hypocalcaemia			
subjects affected / exposed	2 / 24 (8.33%)	4 / 77 (5.19%)	
occurrences (all)	2	4	
Hypoglycaemia			
subjects affected / exposed	1 / 24 (4.17%)	1 / 77 (1.30%)	
occurrences (all)	1	1	
Hypokalaemia			

subjects affected / exposed	6 / 24 (25.00%)	9 / 77 (11.69%)	
occurrences (all)	6	9	
Hypomagnesaemia			
subjects affected / exposed	0 / 24 (0.00%)	1 / 77 (1.30%)	
occurrences (all)	0	1	
Hyponatraemia			
subjects affected / exposed	2 / 24 (8.33%)	3 / 77 (3.90%)	
occurrences (all)	2	3	
Malnutrition			
subjects affected / exposed	0 / 24 (0.00%)	3 / 77 (3.90%)	
occurrences (all)	0	3	
Vitamin B12 deficiency			
subjects affected / exposed	3 / 24 (12.50%)	0 / 77 (0.00%)	
occurrences (all)	3	0	
Vitamin D deficiency			
subjects affected / exposed	0 / 24 (0.00%)	1 / 77 (1.30%)	
occurrences (all)	0	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
11 May 2015	Included an intermediate dose, updated number of sites, revised exclusion criteria, updated pharmacokinetics protocol, clarified dose escalation procedure, updated treatment details, and clarified purpose of assessments and details/timing of sample collection
01 October 2015	Updated secondary objectives, study duration, pharmacokinetic parameters, updated inclusion and exclusion criteria, and clarified rationale for assessments and details/timing of sample collection
12 July 2016	Revised inclusion and exclusion criteria, updated enrollment section and study duration, included exploratory assessments, updated primary objective, and clarified adverse event assessment
04 May 2018	Updated study rationale and number of subjects, revised cohort enrollment description, updated eligibility criteria, updated pharmacokinetic parameters, added exploratory assessments, extended study duration, clarified concomitant medications and procedures, and provided details of ECG assessment

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported