Clinical trial results:
Phase 1/2 Open-Label Study of the Safety, Pharmacokinetics, and Preliminary Activity of ASTX295 in Subjects with Wild-Type TP53 Advanced Solid Tumors

Summary

EudraCT number	2021-005033-16
Trial protocol	DE FR ES IT
Global end of trial date	15 August 2024

Results information

Result version number	v1 (current)
This version publication date	05 June 2025
First version publication date	05 June 2025

Trial information

Trial identification

Sponsor protocol code	ASTX295-01

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03975387
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Taiho Oncology, Inc.
Sponsor organisation address	101 Carnegie Center, Suite 101, Princeton, NJ, United States, 08540
Public contact	Senior Study Manager, Taiho Oncology, Inc., , 1 844-878-2446, medicalinformation@taihooncology.com
Scientific contact	Senior Study Manager, Taiho Oncology, Inc., +1 844-878-2446, medicalinformation@taihooncology.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	15 August 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	15 August 2024
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The main objective of this study was to assess safety and tolerability of ASTX295 including determination of maximum tolerated dose (MTD), and/or recommended dose for expansion (RDE) in Phase 1a (dose escalation) part of the study, and to determine the recommended Phase 2 dose (RP2D) and regimen of ASTX295 in Phase 1b (dose expansion) part of the study.

Protection of trial subjects:

All study subjects were required to read and sign an Informed Consent Form (ICF).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	05 July 2019
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 106
Worldwide total number of subjects	106
EEA total number of subjects	0

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)	67
From 65 to 84 years	38
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

Subjects were enrolled at 11 sites in the United States from 05 July 2019 to 15 August 2024.

Pre-assignment

Screening details:

A total of 106 subjects with wild-type TP53 advanced solid tumors were enrolled to receive ASTX295 in Phase 1 which consisted of 2 parts: Phase 1a (dose escalation) and Phase 1b (dose expansion). Phase 2 part of the study was terminated by the sponsor's strategic decision.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Dose Escalation: Phase 1a: Cohort 1

Arm description:

Subjects received ASTX295 at starting dose of 15 milligrams (mg), orally, administered once daily (QD) in each 28-day cycle under fasted condition, up to a maximum of 1.8 months.

Arm type	Experimental
Investigational medicinal product name	ASTX295
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

ASTX295 at an oral dose of 15 mg, administered QD in each 28-day cycle up to a maximum of 1.8 months.

Arm title	Dose Escalation: Phase 1a: Cohort 2

Arm description:

Subjects received ASTX295 at an oral dose of 45 mg, administered QD in each 28-day cycle under fasted condition, up to a maximum of 17.4 months.

Arm type	Experimental
Investigational medicinal product name	ASTX295
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

ASTX295 at an oral dose of 45 mg, administered QD in each 28-day cycle up to a maximum of 17.4 months.

Arm title	Dose Escalation: Phase 1a: Cohort 3

Arm description:

Subjects received ASTX295 at an oral dose of 120 mg, administered QD in each 28-day cycle under fasted condition, up to a maximum of 1.8 months.

Arm type	Experimental

Investigational medicinal product name	ASTX295
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

ASTX295 at an oral dose of 120 mg, administered QD in each 28-day cycle up to a maximum of 1.8 months.

Arm title	Dose Escalation: Phase 1a: Cohort 4

Arm description:

Subjects received ASTX295 at an oral dose of 240 mg, administered QD in each 28-day cycle under fasted condition, up to a maximum of 6.4 months.

Arm type	Experimental
Investigational medicinal product name	ASTX295
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

ASTX295 at an oral dose of 240 mg, administered QD in each 28-day cycle up to a maximum of 6.4 months.

Arm title	Dose Escalation: Phase 1a: Cohort 5

Arm description:

Subjects received ASTX295 at an oral dose of 420 mg, administered QD in each 28-day cycle under fasted condition, up to a maximum of 14.7 months.

Arm type	Experimental
Investigational medicinal product name	ASTX295
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

ASTX295 at an oral dose of 240 mg, administered QD in each 28-day cycle up to a maximum of 14.7 months.

Arm title	Dose Escalation: Phase 1a: Cohort 6

Arm description:

Subjects received ASTX295 at an oral dose of 520 mg, administered QD in each 28-day cycle under fasted condition, up to a maximum of 42.4 months.

Arm type	Experimental
Investigational medicinal product name	ASTX295
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

ASTX295 at an oral dose of 520 mg, administered QD in each 28-day cycle up to a maximum of 42.4 months.

Arm title	Dose Escalation: Phase 1a: Cohort 7

Arm description:

Subjects received ASTX295 at an oral dose of 415 mg, administered QD in each 28-day cycle under fed state, up to a maximum of 22.5 months.

Arm type	Experimental

Investigational medicinal product name	ASTX295
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

ASTX295 at an oral dose of 415 mg, administered QD in each 28-day cycle up to a maximum of 22.5 months.

Arm title	Dose Escalation: Phase 1a: Cohort 8

Arm description:

Subjects received ASTX295 at an oral dose of 200 mg, administered twice daily (BID) in each 28-day cycle under fasted condition, up to a maximum of 17.4 months.

Arm type	Experimental
Investigational medicinal product name	ASTX295
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

ASTX295 at an oral dose of 200 mg, administered BID in each 28-day cycle up to a maximum of 17.4 months.

Arm title	Dose Escalation: Phase 1a: Cohort 9

Arm description:

Subjects received ASTX295 at an oral dose of 320 mg, administered BID in each 28-day cycle under fasted condition, up to a maximum of 27.5 months.

Arm type	Experimental
Investigational medicinal product name	ASTX295
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

ASTX295 at an oral dose of 320 mg, administered BID in each 28-day cycle up to a maximum of 27.5 months.

Arm title	Dose Escalation: Phase 1a: Cohort 10

Arm description:

Subjects received ASTX295 at an oral dose of 520 mg (5 days on, 2 days off), administered QD in each 28-day cycle, with or without food, up to a maximum of 12 months.

Arm type	Experimental
Investigational medicinal product name	ASTX295
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

ASTX295 at an oral dose of 520 mg, administered QD, in each 28-day cycle up to a maximum of 12 months.

Arm title	Dose Escalation: Phase 1a: Cohort 11

Arm description:

Subjects received ASTX295 at an oral dose of 520 mg (3 days on, 4 days off), administered QD in each 28-day cycle, with or without food, up to a maximum of 1.8 months.

Arm type	Experimental

Investigational medicinal product name	ASTX295
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

ASTX295 at an oral dose of 520 mg, administered QD in each 28-day cycle up to a maximum of 1.8 months.

Arm title	Dose Escalation: Phase 1a: Cohort 12

Arm description:

Subjects received ASTX295 at an oral dose of 660 mg, administered QD, twice a week, in each 28-day cycle, with or without food, up to a maximum of 11.7 months.

Arm type	Experimental
Investigational medicinal product name	ASTX295
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

ASTX295 at an oral dose of 660 mg, administered QD, twice a week, in each 28-day cycle up to a maximum of 11.7 months.

Arm title	Dose Escalation: Phase 1a: Cohort 13

Arm description:

Subjects received ASTX295 at an oral dose of 660 mg (3 days on, 4 days off), administered QD, in each 28-day cycle, with or without food, up to a maximum of 18.5 months.

Arm type	Experimental
Investigational medicinal product name	ASTX295
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

ASTX295 at an oral dose of 660 mg, administered QD in each 28-day cycle up to a maximum of 18.5 months.

Arm title	Dose Escalation: Phase 1a: Cohort 14

Arm description:

Subjects received ASTX295 at an oral dose of 800 mg, administered QD, twice a week, in each 28-day cycle, with or without food, up to a maximum of 6 months.

Arm type	Experimental
Investigational medicinal product name	ASTX295
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

ASTX295 at an oral dose of 800 mg, administered QD, twice a week, in each 28-day cycle up to a maximum of 6 months.

Arm title	Dose Expansion: Phase 1b: Cohort 1

Arm description:

Subjects received ASTX295 at an oral dose of 400 mg, administered daily, in each 28-day cycle, with or without food, up to a maximum of 14.7 months.

Arm type	Experimental

Investigational medicinal product name	ASTX295
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

ASTX295 at an oral dose of 400 mg, administered daily, in each 28-day cycle up to a maximum of 14.7 months.

Arm title	Dose Expansion: Phase 1b: Cohort 2

Arm description:

Subjects received ASTX295 at an oral dose of 660 mg, administered QD, twice a week, in each 28-day cycle, with or without food, up to a maximum of 14.2 months.

Arm type	Experimental
Investigational medicinal product name	ASTX295
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

ASTX295 at an oral dose of 660 mg, administered QD, twice a week, in each 28-day cycle up to a maximum of 14.2 months.

Number of subjects in period 1	Dose Escalation: Phase 1a: Cohort 1	Dose Escalation: Phase 1a: Cohort 2	Dose Escalation: Phase 1a: Cohort 3
Started	1	3	4
Completed	0	0	0
Not completed	1	3	4
Death	1	-	2
Complete Consent Withdrawal	-	1	2
Study Terminated by Sponsor	-	1	-
Lost to follow-up	-	1	-

Number of subjects in period 1	Dose Escalation: Phase 1a: Cohort 4	Dose Escalation: Phase 1a: Cohort 5	Dose Escalation: Phase 1a: Cohort 6
Started	4	9	8
Completed	0	0	0
Not completed	4	9	8
Death	2	4	6
Complete Consent Withdrawal	-	1	1
Study Terminated by Sponsor	1	2	1
Lost to follow-up	1	2	-

Number of subjects in period 1	Dose Escalation: Phase 1a: Cohort 7	Dose Escalation: Phase 1a: Cohort 8	Dose Escalation: Phase 1a: Cohort 9
Started	5	6	7
Completed	0	0	0
Not completed	5	6	7

Death	3	4	3
Complete Consent Withdrawal	1	1	2
Study Terminated by Sponsor	1	1	2
Lost to follow-up	-	-	-

Number of subjects in period 1	Dose Escalation: Phase 1a: Cohort 10	Dose Escalation: Phase 1a: Cohort 11	Dose Escalation: Phase 1a: Cohort 12
Started	8	4	9
Completed	0	0	0
Not completed	8	4	9
Death	6	4	6
Complete Consent Withdrawal	-	-	-
Study Terminated by Sponsor	2	-	2
Lost to follow-up	-	-	1

Number of subjects in period 1	Dose Escalation: Phase 1a: Cohort 13	Dose Escalation: Phase 1a: Cohort 14	Dose Expansion: Phase 1b: Cohort 1
Started	8	6	12
Completed	0	0	0
Not completed	8	6	12
Death	5	5	4
Complete Consent Withdrawal	-	1	-
Study Terminated by Sponsor	2	-	7
Lost to follow-up	1	-	1

Number of subjects in period 1	Dose Expansion: Phase 1b: Cohort 2
Started	12
Completed	0
Not completed	12
Death	3
Complete Consent Withdrawal	1
Study Terminated by Sponsor	7
Lost to follow-up	1

Baseline characteristics

Reporting groups

Reporting group title	Dose Escalation: Phase 1a: Cohort 1
Reporting group description:	
Subjects received ASTX295 at starting dose of 15 milligrams (mg), orally, administered once daily (QD) in each 28-day cycle under fasted condition, up to a maximum of 1.8 months.	
Reporting group title	Dose Escalation: Phase 1a: Cohort 2
Reporting group description:	
Subjects received ASTX295 at an oral dose of 45 mg, administered QD in each 28-day cycle under fasted condition, up to a maximum of 17.4 months.	
Reporting group title	Dose Escalation: Phase 1a: Cohort 3
Reporting group description:	
Subjects received ASTX295 at an oral dose of 120 mg, administered QD in each 28-day cycle under fasted condition, up to a maximum of 1.8 months.	
Reporting group title	Dose Escalation: Phase 1a: Cohort 4
Reporting group description:	
Subjects received ASTX295 at an oral dose of 240 mg, administered QD in each 28-day cycle under fasted condition, up to a maximum of 6.4 months.	
Reporting group title	Dose Escalation: Phase 1a: Cohort 5
Reporting group description:	
Subjects received ASTX295 at an oral dose of 420 mg, administered QD in each 28-day cycle under fasted condition, up to a maximum of 14.7 months.	
Reporting group title	Dose Escalation: Phase 1a: Cohort 6
Reporting group description:	
Subjects received ASTX295 at an oral dose of 520 mg, administered QD in each 28-day cycle under fasted condition, up to a maximum of 42.4 months.	
Reporting group title	Dose Escalation: Phase 1a: Cohort 7
Reporting group description:	
Subjects received ASTX295 at an oral dose of 415 mg, administered QD in each 28-day cycle under fed state, up to a maximum of 22.5 months.	
Reporting group title	Dose Escalation: Phase 1a: Cohort 8
Reporting group description:	
Subjects received ASTX295 at an oral dose of 200 mg, administered twice daily (BID) in each 28-day cycle under fasted condition, up to a maximum of 17.4 months.	
Reporting group title	Dose Escalation: Phase 1a: Cohort 9
Reporting group description:	
Subjects received ASTX295 at an oral dose of 320 mg, administered BID in each 28-day cycle under fasted condition, up to a maximum of 27.5 months.	
Reporting group title	Dose Escalation: Phase 1a: Cohort 10
Reporting group description:	
Subjects received ASTX295 at an oral dose of 520 mg (5 days on, 2 days off), administered QD in each 28-day cycle, with or without food, up to a maximum of 12 months.	
Reporting group title	Dose Escalation: Phase 1a: Cohort 11
Reporting group description:	
Subjects received ASTX295 at an oral dose of 520 mg (3 days on, 4 days off), administered QD in each 28-day cycle, with or without food, up to a maximum of 1.8 months.	
Reporting group title	Dose Escalation: Phase 1a: Cohort 12
Reporting group description:	
Subjects received ASTX295 at an oral dose of 660 mg, administered QD, twice a week, in each 28-day cycle, with or without food, up to a maximum of 11.7 months.	
Reporting group title	Dose Escalation: Phase 1a: Cohort 13
Reporting group description:	
Subjects received ASTX295 at an oral dose of 660 mg (3 days on, 4 days off), administered QD, in each 28-day cycle, with or without food, up to a maximum of 18.5 months.	

Reporting group title	Dose Escalation: Phase 1a: Cohort 14
Reporting group description:	
Subjects received ASTX295 at an oral dose of 800 mg, administered QD, twice a week, in each 28-day cycle, with or without food, up to a maximum of 6 months.	

Reporting group title	Dose Expansion: Phase 1b: Cohort 1
Reporting group description:	
Subjects received ASTX295 at an oral dose of 400 mg, administered daily, in each 28-day cycle, with or without food, up to a maximum of 14.7 months.	

Reporting group title	Dose Expansion: Phase 1b: Cohort 2
Reporting group description:	
Subjects received ASTX295 at an oral dose of 660 mg, administered QD, twice a week, in each 28-day cycle, with or without food, up to a maximum of 14.2 months.	

Reporting group values	Dose Escalation: Phase 1a: Cohort 1	Dose Escalation: Phase 1a: Cohort 2	Dose Escalation: Phase 1a: Cohort 3
Number of subjects	1	3	4
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous			
Here, for Dose Escalation: Phase 1a: Cohort 1, "99999" represents that data for standard deviation could not be collected as only 1 subject was present in the cohort.			
Units: years arithmetic mean standard deviation	 41.0 ± 99999	 60.3 ± 2.31	 55.3 ± 10.78
Gender categorical Units: Subjects			
Female	0	1	1
Male	1	2	3
Race Units: Subjects			
Asian	0	0	1
American Indian or Alaska Native	0	0	0
Black or African American	0	0	0
Native Hawaiian	0	0	0
White	1	3	2
Other	0	0	0
Not Reported	0	0	1
Unknown	0	0	0
Ethnicity Units: Subjects			
Hispanic or Latino	1	0	1

Not Hispanic or Latino	0	3	3
Not Reported	0	0	0
Unknown	0	0	0

Reporting group values	Dose Escalation: Phase 1a: Cohort 4	Dose Escalation: Phase 1a: Cohort 5	Dose Escalation: Phase 1a: Cohort 6
Number of subjects	4	9	8
Age categorical			
Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			
85 years and over			
Age continuous			
Here, for Dose Escalation: Phase 1a: Cohort 1, "99999" represents that data for standard deviation could not be collected as only 1 subject was present in the cohort.			
Units: years			
arithmetic mean	63.8	65.6	61.0
standard deviation	± 7.04	± 6.67	± 8.30
Gender categorical			
Units: Subjects			
Female	2	3	2
Male	2	6	6
Race			
Units: Subjects			
Asian	0	0	0
American Indian or Alaska Native	0	0	0
Black or African American	1	0	1
Native Hawaiian	0	0	0
White	2	9	7
Other	0	0	0
Not Reported	1	0	0
Unknown	0	0	0
Ethnicity			
Units: Subjects			
Hispanic or Latino	1	1	2
Not Hispanic or Latino	3	8	5
Not Reported	0	0	0
Unknown	0	0	1

Reporting group values	Dose Escalation: Phase 1a: Cohort 7	Dose Escalation: Phase 1a: Cohort 8	Dose Escalation: Phase 1a: Cohort 9
Number of subjects	5	6	7
Age categorical			
Units: Subjects			
In utero			

Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous			
Here, for Dose Escalation: Phase 1a: Cohort 1, "99999" represents that data for standard deviation could not be collected as only 1 subject was present in the cohort.			
Units: years			
arithmetic mean	62.0	57.2	57.9
standard deviation	± 12.90	± 14.47	± 15.48
Gender categorical Units: Subjects			
Female	4	3	3
Male	1	3	4
Race Units: Subjects			
Asian	1	0	0
American Indian or Alaska Native	0	0	1
Black or African American	0	1	0
Native Hawaiian	0	0	0
White	4	4	6
Other	0	0	0
Not Reported	0	1	0
Unknown	0	0	0
Ethnicity Units: Subjects			
Hispanic or Latino	1	1	1
Not Hispanic or Latino	3	4	6
Not Reported	1	1	0
Unknown	0	0	0

Reporting group values	Dose Escalation: Phase 1a: Cohort 10	Dose Escalation: Phase 1a: Cohort 11	Dose Escalation: Phase 1a: Cohort 12
Number of subjects	8	4	9
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			

Age continuous			
Here, for Dose Escalation: Phase 1a: Cohort 1, "99999" represents that data for standard deviation could not be collected as only 1 subject was present in the cohort.			
Units: years			
arithmetic mean	57.6	60.8	52.1
standard deviation	± 11.55	± 4.35	± 16.84
Gender categorical			
Units: Subjects			
Female	4	2	4
Male	4	2	5
Race			
Units: Subjects			
Asian	0	0	0
American Indian or Alaska Native	0	0	0
Black or African American	2	1	1
Native Hawaiian	0	0	0
White	5	3	6
Other	0	0	2
Not Reported	0	0	0
Unknown	1	0	0
Ethnicity			
Units: Subjects			
Hispanic or Latino	0	1	3
Not Hispanic or Latino	7	3	6
Not Reported	0	0	0
Unknown	1	0	0

Reporting group values	Dose Escalation: Phase 1a: Cohort 13	Dose Escalation: Phase 1a: Cohort 14	Dose Expansion: Phase 1b: Cohort 1
Number of subjects	8	6	12
Age categorical			
Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			
85 years and over			
Age continuous			
Here, for Dose Escalation: Phase 1a: Cohort 1, "99999" represents that data for standard deviation could not be collected as only 1 subject was present in the cohort.			
Units: years			
arithmetic mean	67.6	60.3	61.0
standard deviation	± 12.70	± 11.09	± 12.25
Gender categorical			
Units: Subjects			
Female	5	3	8
Male	3	3	4

Race Units: Subjects			
Asian	0	0	0
American Indian or Alaska Native	0	0	0
Black or African American	1	1	0
Native Hawaiian	0	0	0
White	7	5	12
Other	0	0	0
Not Reported	0	0	0
Unknown	0	0	0
Ethnicity Units: Subjects			
Hispanic or Latino	0	1	0
Not Hispanic or Latino	8	4	12
Not Reported	0	1	0
Unknown	0	0	0

Reporting group values	Dose Expansion: Phase 1b: Cohort 2	Total	
Number of subjects	12	106	
Age categorical Units: Subjects			
In utero		0	
Preterm newborn infants (gestational age < 37 wks)		0	
Newborns (0-27 days)		0	
Infants and toddlers (28 days-23 months)		0	
Children (2-11 years)		0	
Adolescents (12-17 years)		0	
Adults (18-64 years)		0	
From 65-84 years		0	
85 years and over		0	
Age continuous			
Here, for Dose Escalation: Phase 1a: Cohort 1, "99999" represents that data for standard deviation could not be collected as only 1 subject was present in the cohort.			
Units: years			
arithmetic mean	58.4		
standard deviation	± 16.82	-	
Gender categorical Units: Subjects			
Female	9	54	
Male	3	52	
Race Units: Subjects			
Asian	2	4	
American Indian or Alaska Native	0	1	
Black or African American	0	9	
Native Hawaiian	0	0	
White	9	85	
Other	0	2	
Not Reported	1	4	
Unknown	0	1	

Ethnicity Units: Subjects			
Hispanic or Latino	2	16	
Not Hispanic or Latino	9	84	
Not Reported	1	4	
Unknown	0	2	

End points

End points reporting groups

Reporting group title	Dose Escalation: Phase 1a: Cohort 1
Reporting group description:	
Subjects received ASTX295 at starting dose of 15 milligrams (mg), orally, administered once daily (QD) in each 28-day cycle under fasted condition, up to a maximum of 1.8 months.	
Reporting group title	Dose Escalation: Phase 1a: Cohort 2
Reporting group description:	
Subjects received ASTX295 at an oral dose of 45 mg, administered QD in each 28-day cycle under fasted condition, up to a maximum of 17.4 months.	
Reporting group title	Dose Escalation: Phase 1a: Cohort 3
Reporting group description:	
Subjects received ASTX295 at an oral dose of 120 mg, administered QD in each 28-day cycle under fasted condition, up to a maximum of 1.8 months.	
Reporting group title	Dose Escalation: Phase 1a: Cohort 4
Reporting group description:	
Subjects received ASTX295 at an oral dose of 240 mg, administered QD in each 28-day cycle under fasted condition, up to a maximum of 6.4 months.	
Reporting group title	Dose Escalation: Phase 1a: Cohort 5
Reporting group description:	
Subjects received ASTX295 at an oral dose of 420 mg, administered QD in each 28-day cycle under fasted condition, up to a maximum of 14.7 months.	
Reporting group title	Dose Escalation: Phase 1a: Cohort 6
Reporting group description:	
Subjects received ASTX295 at an oral dose of 520 mg, administered QD in each 28-day cycle under fasted condition, up to a maximum of 42.4 months.	
Reporting group title	Dose Escalation: Phase 1a: Cohort 7
Reporting group description:	
Subjects received ASTX295 at an oral dose of 415 mg, administered QD in each 28-day cycle under fed state, up to a maximum of 22.5 months.	
Reporting group title	Dose Escalation: Phase 1a: Cohort 8
Reporting group description:	
Subjects received ASTX295 at an oral dose of 200 mg, administered twice daily (BID) in each 28-day cycle under fasted condition, up to a maximum of 17.4 months.	
Reporting group title	Dose Escalation: Phase 1a: Cohort 9
Reporting group description:	
Subjects received ASTX295 at an oral dose of 320 mg, administered BID in each 28-day cycle under fasted condition, up to a maximum of 27.5 months.	
Reporting group title	Dose Escalation: Phase 1a: Cohort 10
Reporting group description:	
Subjects received ASTX295 at an oral dose of 520 mg (5 days on, 2 days off), administered QD in each 28-day cycle, with or without food, up to a maximum of 12 months.	
Reporting group title	Dose Escalation: Phase 1a: Cohort 11
Reporting group description:	
Subjects received ASTX295 at an oral dose of 520 mg (3 days on, 4 days off), administered QD in each 28-day cycle, with or without food, up to a maximum of 1.8 months.	
Reporting group title	Dose Escalation: Phase 1a: Cohort 12
Reporting group description:	
Subjects received ASTX295 at an oral dose of 660 mg, administered QD, twice a week, in each 28-day cycle, with or without food, up to a maximum of 11.7 months.	
Reporting group title	Dose Escalation: Phase 1a: Cohort 13
Reporting group description:	
Subjects received ASTX295 at an oral dose of 660 mg (3 days on, 4 days off), administered QD, in each 28-day cycle, with or without food, up to a maximum of 18.5 months.	

Reporting group title	Dose Escalation: Phase 1a: Cohort 14

Reporting group description:

Subjects received ASTX295 at an oral dose of 800 mg, administered QD, twice a week, in each 28-day cycle, with or without food, up to a maximum of 6 months.

Reporting group title	Dose Expansion: Phase 1b: Cohort 1

Reporting group description:

Subjects received ASTX295 at an oral dose of 400 mg, administered daily, in each 28-day cycle, with or without food, up to a maximum of 14.7 months.

Reporting group title	Dose Expansion: Phase 1b: Cohort 2

Reporting group description:

Subjects received ASTX295 at an oral dose of 660 mg, administered QD, twice a week, in each 28-day cycle, with or without food, up to a maximum of 14.2 months.

Primary: Phase 1a and 1b: Number of Subjects with Treatment Emergent Adverse Events (TEAEs), and Serious TEAEs

End point title	Phase 1a and 1b: Number of Subjects with Treatment Emergent Adverse Events (TEAEs), and Serious TEAEs[1]

End point description:

An adverse event (AE) is any untoward medical occurrence in a subject or clinical study subject, temporally associated with the use of study treatment, whether or not considered related to the study treatment. TEAEs are defined as events that first occur or worsen on or after the date of the first study treatment Cycle 1 Day 1 (C1D1) until 30 days after the last dose of study treatment. Serious TEAE is defined as any untoward medical occurrence that, at any dose result in death, is life-threatening, requires inpatient hospitalization or prolongation of existing hospitalization, results in persistent disability/incapacity, or is a congenital anomaly/birth defect. Safety analysis set included all subjects who received at least one dose of study drug.

End point type	Primary

End point timeframe:

Up to approximately 61.3 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 statistics were provided for this endpoint.

End point values	Dose Escalation: Phase 1a: Cohort 1	Dose Escalation: Phase 1a: Cohort 2	Dose Escalation: Phase 1a: Cohort 3	Dose Escalation: Phase 1a: Cohort 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	1	3	4	4
Units: subjects				
TEAEs	1	3	4	4
SAEs	0	0	2	0

End point values	Dose Escalation: Phase 1a: Cohort 5	Dose Escalation: Phase 1a: Cohort 6	Dose Escalation: Phase 1a: Cohort 7	Dose Escalation: Phase 1a: Cohort 8
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9	8	5	6
Units: subjects				
TEAEs	9	8	5	6

SAEs	2	1	1	2

End point values	Dose Escalation: Phase 1a: Cohort 9	Dose Escalation: Phase 1a: Cohort 10	Dose Escalation: Phase 1a: Cohort 11	Dose Escalation: Phase 1a: Cohort 12
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	8	4	9
Units: subjects				
TEAEs	7	8	4	9
SAEs	0	1	0	4

End point values	Dose Escalation: Phase 1a: Cohort 13	Dose Escalation: Phase 1a: Cohort 14	Dose Expansion: Phase 1b: Cohort 1	Dose Expansion: Phase 1b: Cohort 2
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	6	12	12
Units: subjects				
TEAEs	8	6	12	12
SAEs	1	4	6	4

Statistical analyses

No statistical analyses for this end point

Primary: Phase 1a: Number of Subjects with Dose-limiting Toxicities (DLTs)

End point title	Phase 1a: Number of Subjects with Dose-limiting Toxicities (DLTs)[2][3]

End point description:

Dose-limiting toxicities (DLTs) were AEs graded by National Cancer Institute [NCI] Common Terminology Criteria for Adverse Events [CTCAE] version 5.0 criteria that occurred during first cycle of treatment & represent any 1 of the following: grade 4 thrombocytopenia of any duration; grade 3 thrombocytopenia lasting more than 7 days; ≥grade 3 hematologic toxicity with complications; febrile neutropenia of any duration; grade 4 neutropenia lasting more than 5 days; liver-associated abnormalities; ≥grade 3 nonhematologic AE; event leading to unacceptable risk after dose escalation as suggested by data and safety review committee (DSRC); clinically significant toxicities that persist or occur beyond Cycle 1. Dose escalation evaluable population included all subjects in the dose escalation who either experienced a DLT during the first cycle of treatment, or who completed the first cycle without experiencing a DLT and with at least 85% of planned study treatments administered.

End point type	Primary

End point timeframe:

During Cycle 1 (cycle length= 28 days)

Notes:

[2] - 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 statistics were provided for this endpoint.

[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 statistics were provided for this endpoint.

End point values	Dose Escalation: Phase 1a: Cohort 1	Dose Escalation: Phase 1a: Cohort 2	Dose Escalation: Phase 1a: Cohort 3	Dose Escalation: Phase 1a: Cohort 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	1	3	4	4
Units: subjects				
DLTs	0	0	0	0

End point values	Dose Escalation: Phase 1a: Cohort 5	Dose Escalation: Phase 1a: Cohort 6	Dose Escalation: Phase 1a: Cohort 7	Dose Escalation: Phase 1a: Cohort 8
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9	8	5	6
Units: subjects				
DLTs	0	1	1	1

End point values	Dose Escalation: Phase 1a: Cohort 9	Dose Escalation: Phase 1a: Cohort 10	Dose Escalation: Phase 1a: Cohort 11	Dose Escalation: Phase 1a: Cohort 12
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	8	4	9
Units: subjects				
DLTs	2	2	0	0

End point values	Dose Escalation: Phase 1a: Cohort 13	Dose Escalation: Phase 1a: Cohort 14		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	6		
Units: subjects				
DLTs	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1a and 1b: Disease Control Rate (DCR)

End point title	Phase 1a and 1b: Disease Control Rate (DCR)

End point description:

DCR was defined as proportion of subjects who have a complete response (CR), partial response (PR)/stable disease at Week 16 according to response evaluation criteria in solid tumors (RECIST) 1.1/modified RECIST (mRECIST) 1.1 (for malignant pleural mesothelioma [MPM]) as assessed by investigator. CR: Disappearance of all target lesions. Any pathological lymph nodes (whether target or nontarget) must have reduction in short axis to <10 mm. PR: At least 30% decrease in sum of diameters of target lesions, taking as reference baseline sum diameters. Stable disease: Neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for progressive disease, taking as reference smallest sum diameters while on study. Efficacy analysis set included all subjects who received any amount of study treatment. DCR was based on subjects who were in this set & who had disease assessment at baseline & at least 1 follow-up disease assessment/subjects who died/stopped treatment.

End point type	Secondary

End point timeframe:

Up to approximately 61.3 months

End point values	Dose Escalation: Phase 1a: Cohort 1	Dose Escalation: Phase 1a: Cohort 2	Dose Escalation: Phase 1a: Cohort 3	Dose Escalation: Phase 1a: Cohort 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	1	3	3	4
Units: percentage of subjects				
number (not applicable)	100	100	0	75.0

End point values	Dose Escalation: Phase 1a: Cohort 5	Dose Escalation: Phase 1a: Cohort 6	Dose Escalation: Phase 1a: Cohort 7	Dose Escalation: Phase 1a: Cohort 8
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	8	5	5
Units: percentage of subjects				
number (not applicable)	62.5	75.0	80.0	80.0

End point values	Dose Escalation: Phase 1a: Cohort 9	Dose Escalation: Phase 1a: Cohort 10	Dose Escalation: Phase 1a: Cohort 11	Dose Escalation: Phase 1a: Cohort 12
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	7	4	8
Units: percentage of subjects				
number (not applicable)	50.0	71.4	25.0	75.0

End point values	Dose Escalation: Phase 1a:	Dose Escalation: Phase 1a:	Dose Expansion: Phase 1b:	Dose Expansion: Phase 1b:

	Cohort 13	Cohort 14	Cohort 1	Cohort 2
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	5	11	10
Units: percentage of subjects				
number (not applicable)	71.4	60.0	72.7	50.0

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1a and 1b: Objective Response Rate (ORR)

End point title	Phase 1a and 1b: Objective Response Rate (ORR)

End point description:

ORR was defined as the proportion of subjects whose best response was CR or PR according to RECIST 1.1 or mRECIST 1.1 (for MPM) as assessed by the investigator. CR: Disappearance of all target lesions. Any pathological lymph nodes (whether target or nontarget) must have reduction in short axis to <10 mm. PR: At least a 30% decrease in the sum of diameters of target lesions, taking as reference the baseline sum diameters. Efficacy analysis set included all subjects who received any amount of study treatment. ORR was based on subjects who were in this set & who had disease assessment at baseline and at least 1 follow-up disease assessment or subjects who died or stopped treatment before the first scheduled disease assessment due to clinical progression or toxicity.

End point type	Secondary

End point timeframe:

Up to approximately 61.3 months

End point values	Dose Escalation: Phase 1a: Cohort 1	Dose Escalation: Phase 1a: Cohort 2	Dose Escalation: Phase 1a: Cohort 3	Dose Escalation: Phase 1a: Cohort 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	1	3	3	4
Units: percentage of subjects				
number (not applicable)	0	0	0	0

End point values	Dose Escalation: Phase 1a: Cohort 5	Dose Escalation: Phase 1a: Cohort 6	Dose Escalation: Phase 1a: Cohort 7	Dose Escalation: Phase 1a: Cohort 8
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	8	5	5
Units: percentage of subjects				
number (not applicable)	12.5	12.5	0	0

End point values	Dose Escalation:	Dose Escalation:	Dose Escalation:	Dose Escalation:

	Phase 1a: Cohort 9	Phase 1a: Cohort 10	Phase 1a: Cohort 11	Phase 1a: Cohort 12
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	7	4	8
Units: percentage of subjects				
number (not applicable)	0	0	0	12.5

End point values	Dose Escalation: Phase 1a: Cohort 13	Dose Escalation: Phase 1a: Cohort 14	Dose Expansion: Phase 1b: Cohort 1	Dose Expansion: Phase 1b: Cohort 2
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	5	11	10
Units: percentage of subjects				
number (not applicable)	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1a and 1b: Area Under the Concentration-time Curve From Time Zero to Time of Last Measurable Concentration (AUClast) of ASTX295

End point title	Phase 1a and 1b: Area Under the Concentration-time Curve From Time Zero to Time of Last Measurable Concentration (AUClast) of ASTX295[4]

End point description:

PK analysis set included all subjects who received the study drug and have post baseline plasma concentration data. Here, '99999' indicates that values were not measurable due to low number of subjects for the specified arms. ‘Subjects analysed’ indicates number of subjects with data available for analyses and 'n’ indicates number of subjects with data available for analyses at the specified timepoint.

End point type	Secondary

End point timeframe:

Pre-dose on Day 1 and Day 2 of Cycles 1 and 2, and at multiple timepoints post-dose on Day 1 of Cycles 1 and 2 (Cycle length = 28 days).

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 statistics were provided for this endpoint.

End point values	Dose Escalation: Phase 1a: Cohort 1	Dose Escalation: Phase 1a: Cohort 2	Dose Escalation: Phase 1a: Cohort 3	Dose Escalation: Phase 1a: Cohort 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	1	3	4	4
Units: hours*nanograms/millilitres (h*ng/mL)				
geometric mean (geometric coefficient of variation)				
C1D1 (n=1,3,4,4,9,8,5,5,7,8,4,9,8,6,12,12)	28.7 (± 99999)	60.0 (± 81.8)	1230 (± 222.2)	1140 (± 50.7)

C2D1 (n=1,3,2,3,7,5,1,5,2,7,3,6,6,4,11,9)	24.6 (± 99999)	113 (± 82.8)	1480 (± 77.2)	2270 (± 34.7)

End point values	Dose Escalation: Phase 1a: Cohort 5	Dose Escalation: Phase 1a: Cohort 6	Dose Escalation: Phase 1a: Cohort 8	Dose Escalation: Phase 1a: Cohort 9
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9	8	5	7
Units: hours*nanograms/millilitres (h*ng/mL)				
geometric mean (geometric coefficient of variation)				
C1D1 (n=1,3,4,4,9,8,5,5,7,8,4,9,8,6,12,12)	3850 (± 135.8)	3500 (± 140.7)	844 (± 82.8)	2180 (± 133.1)
C2D1 (n=1,3,2,3,7,5,1,5,2,7,3,6,6,4,11,9)	3540 (± 58.7)	1710 (± 180.2)	1790 (± 28.2)	4600 (± 65.3)

End point values	Dose Escalation: Phase 1a: Cohort 10	Dose Escalation: Phase 1a: Cohort 11	Dose Escalation: Phase 1a: Cohort 12	Dose Escalation: Phase 1a: Cohort 13
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	4	9	8
Units: hours*nanograms/millilitres (h*ng/mL)				
geometric mean (geometric coefficient of variation)				
C1D1 (n=1,3,4,4,9,8,5,5,7,8,4,9,8,6,12,12)	11200 (± 145.8)	3270 (± 64.4)	10600 (± 161.2)	7870 (± 222.9)
C2D1 (n=1,3,2,3,7,5,1,5,2,7,3,6,6,4,11,9)	12700 (± 131.5)	2890 (± 40.2)	10500 (± 237.4)	8640 (± 186.7)

End point values	Dose Escalation: Phase 1a: Cohort 14	Dose Expansion: Phase 1b: Cohort 1	Dose Expansion: Phase 1b: Cohort 2	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	12	12	
Units: hours*nanograms/millilitres (h*ng/mL)				
geometric mean (geometric coefficient of variation)				
C1D1 (n=1,3,4,4,9,8,5,5,7,8,4,9,8,6,12,12)	9310 (± 102.1)	3020 (± 72.4)	11600 (± 200.3)	
C2D1 (n=1,3,2,3,7,5,1,5,2,7,3,6,6,4,11,9)	11000 (± 52.2)	4440 (± 50.9)	4730 (± 262.4)	

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1a and 1b: Maximum Observed Plasma Concentration (Cmax) of ASTX295

End point title	Phase 1a and 1b: Maximum Observed Plasma Concentration (Cmax) of ASTX295[5]

End point description:

PK analysis set included all subjects who received the study drug and have post baseline plasma concentration data. Here, '99999' indicates that dispersion values were not measurable due to low number of subjects for the specified arms. 'Subjects analysed' indicates number of subjects with data available for analyses and 'n' indicates number of subjects with data available for analyses at the specified timepoint.

End point type	Secondary

End point timeframe:

Pre-dose on Day 1 and Day 2 of Cycles 1 and 2, and at multiple timepoints post-dose on Day 1 of Cycles 1 and 2 (Cycle length = 28 days).

Notes:

[5] - 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 statistics were provided for this endpoint.

End point values	Dose Escalation: Phase 1a: Cohort 1	Dose Escalation: Phase 1a: Cohort 2	Dose Escalation: Phase 1a: Cohort 3	Dose Escalation: Phase 1a: Cohort 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	1	3	4	4
Units: nanogram(s)/millilitre (ng/mL)				
geometric mean (geometric coefficient of variation)				
C1D1 (n=1,3,4,4,9,8,5,7,8,4,9,8,6,12,12)	19.1 (± 99999)	27.3 (± 9.2)	367 (± 189.9)	448 (± 69.7)
C2D1 (n=1,3,2,3,7,5,5,2,7,4,5,6,4,11,9)	15.3 (± 99999)	40.4 (± 108.1)	318 (± 49.7)	937 (± 63.3)

End point values	Dose Escalation: Phase 1a: Cohort 5	Dose Escalation: Phase 1a: Cohort 6	Dose Escalation: Phase 1a: Cohort 8	Dose Escalation: Phase 1a: Cohort 9
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9	8	5	7
Units: nanogram(s)/millilitre (ng/mL)				
geometric mean (geometric coefficient of variation)				
C1D1 (n=1,3,4,4,9,8,5,7,8,4,9,8,6,12,12)	963 (± 109.0)	758 (± 224.2)	307 (± 67.6)	924 (± 123.5)
C2D1 (n=1,3,2,3,7,5,5,2,7,4,5,6,4,11,9)	963 (± 81.8)	497 (± 196.3)	544 (± 52.2)	1800 (± 54.8)

End point values	Dose	Dose	Dose	Dose

	Escalation: Phase 1a: Cohort 10	Escalation: Phase 1a: Cohort 11	Escalation: Phase 1a: Cohort 12	Escalation: Phase 1a: Cohort 13
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	4	9	8
Units: nanogram(s)/millilitre (ng/mL)				
geometric mean (geometric coefficient of variation)				
C1D1 (n=1,3,4,4,9,8,5,7,8,4,9,8,6,12,12)	2670 (± 133.0)	936 (± 70.9)	2210 (± 189.7)	1830 (± 228.8)
C2D1 (n=1,3,2,3,7,5,5,2,7,4,5,6,4,11,9)	2870 (± 87.6)	1010 (± 89.3)	1620 (± 334)	2100 (± 165.2)

End point values	Dose Escalation: Phase 1a: Cohort 14	Dose Expansion: Phase 1b: Cohort 1	Dose Expansion: Phase 1b: Cohort 2	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	12	12	
Units: nanogram(s)/millilitre (ng/mL)				
geometric mean (geometric coefficient of variation)				
C1D1 (n=1,3,4,4,9,8,5,7,8,4,9,8,6,12,12)	2600 (± 90.3)	786 (± 63.0)	3010 (± 207.2)	
C2D1 (n=1,3,2,3,7,5,5,2,7,4,5,6,4,11,9)	3490 (± 53.8)	942 (± 50.8)	1370 (± 192.1)	

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1a and 1b: Minimum Observed Plasma Concentration (Cmin) of ASTX295

End point title	Phase 1a and 1b: Minimum Observed Plasma Concentration (Cmin) of ASTX295[6]

End point description:

PK analysis set included all subjects who received the study drug and have post baseline plasma concentration data. Here, '99999' indicates that dispersion values were not measurable due to low number of subjects for the specified arms. ‘Subjects analysed’ indicates number of subjects with data available for analyses.

End point type	Secondary

End point timeframe:

Pre-dose on Day 1 and Day 2 of Cycles 1 and 2, and at multiple timepoints post-dose on Day 1 of Cycles 1 and 2 (Cycle length = 28 days).

Notes:

[6] - 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 statistics were provided for this endpoint.

End point values	Dose Escalation: Phase 1a: Cohort 1	Dose Escalation: Phase 1a: Cohort 2	Dose Escalation: Phase 1a: Cohort 3	Dose Escalation: Phase 1a: Cohort 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	1	3	2	3
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
C2D1	99999 (± 99999)	99999 (± 99999)	14.17 (± 151.8)	33.56 (± 48.7)

End point values	Dose Escalation: Phase 1a: Cohort 5	Dose Escalation: Phase 1a: Cohort 6	Dose Escalation: Phase 1a: Cohort 8	Dose Escalation: Phase 1a: Cohort 9
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	7	5	2
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
C2D1	40.00 (± 67.3)	99999 (± 99999)	59.04 (± 64.0)	129.4 (± 6.0)

End point values	Dose Escalation: Phase 1a: Cohort 10	Dose Escalation: Phase 1a: Cohort 11	Dose Escalation: Phase 1a: Cohort 12	Dose Escalation: Phase 1a: Cohort 13
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	4	7	6
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
C2D1	134 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)

End point values	Dose Escalation: Phase 1a: Cohort 14	Dose Expansion: Phase 1b: Cohort 1	Dose Expansion: Phase 1b: Cohort 2	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	5	11	10	
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
C2D1	14.44 (± 113.3)	99999 (± 99999)	26.78 (± 256.5)	

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1a and 1b: Time to Maximum Observed Plasma Concentration (Tmax) of ASTX295

End point title	Phase 1a and 1b: Time to Maximum Observed Plasma Concentration (Tmax) of ASTX295[7]

End point description:

PK analysis set included all subjects who received the study drug and have post baseline plasma concentration data. Here, '99999' indicates that dispersion values were not measurable due to low number of subjects for the specified arms. 'Subjects analysed' indicates number of subjects with data available for analyses and 'n' indicates number of subjects with data available for analyses at the specified timepoint.

End point type	Secondary

End point timeframe:

Pre-dose on Day 1 and Day 2 of Cycles 1 and 2, and at multiple timepoints post-dose on Day 1 of Cycles 1 and 2 (Cycle length = 28 days).

Notes:

[7] - 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 statistics were provided for this endpoint.

End point values	Dose Escalation: Phase 1a: Cohort 1	Dose Escalation: Phase 1a: Cohort 2	Dose Escalation: Phase 1a: Cohort 3	Dose Escalation: Phase 1a: Cohort 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	1	3	4	4
Units: hours				
median (full range (min-max))				
C1D1 (n=1,3,4,4,9,8,5,5,7,8,4,9,8,6,12,12)	0.95 (-99999 to 99999)	1.00 (1.00 to 3.83)	1.52 (1.00 to 3.83)	1.47 (1.00 to 2.00)
C2D1 (n=1,3,2,3,7,5,1,5,2,7,4,6,6,4,11,9)	1.00 (-99999 to 99999)	3.08 (0.50 to 3.92)	1.51 (1.00 to 2.02)	2.83 (1.97 to 2.90)

End point values	Dose Escalation: Phase 1a: Cohort 5	Dose Escalation: Phase 1a: Cohort 6	Dose Escalation: Phase 1a: Cohort 8	Dose Escalation: Phase 1a: Cohort 9
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9	8	5	7
Units: hours				
median (full range (min-max))				
C1D1 (n=1,3,4,4,9,8,5,5,7,8,4,9,8,6,12,12)	3.95 (2.00 to 4.00)	3.01 (2.93 to 4.15)	2.97 (1.98 to 5.7)	3.02 (2.13 to 4.17)

C2D1 (n=1,3,2,3,7,5,1,5,2,7,4,6,6,4,11,9)	2.85 (2.00 to 3.02)	3.02 (1.00 to 4.03)	2.90 (2.05 to 3.88)	2.42 (2.17 to 2.67)

End point values	Dose Escalation: Phase 1a: Cohort 10	Dose Escalation: Phase 1a: Cohort 11	Dose Escalation: Phase 1a: Cohort 12	Dose Escalation: Phase 1a: Cohort 13
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	4	9	8
Units: hours				
median (full range (min-max))				
C1D1 (n=1,3,4,4,9,8,5,5,7,8,4,9,8,6,12,12)	3.00 (0.52 to 6.03)	2.46 (1.00 to 3.17)	2.98 (1.02 to 6.00)	2.93 (1.98 to 5.85)
C2D1 (n=1,3,2,3,7,5,1,5,2,7,4,6,6,4,11,9)	3.05 (2.07 to 5.67)	2.55 (1.97 to 3.22)	3.48 (2.00 to 4.05)	3.45 (1.98 to 5.9)

End point values	Dose Escalation: Phase 1a: Cohort 14	Dose Expansion: Phase 1b: Cohort 1	Dose Expansion: Phase 1b: Cohort 2	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	12	12	
Units: hours				
median (full range (min-max))				
C1D1 (n=1,3,4,4,9,8,5,5,7,8,4,9,8,6,12,12)	3.49 (1.98 to 3.97)	3.42 (0.97 to 6.02)	2.92 (1.02 to 5.77)	
C2D1 (n=1,3,2,3,7,5,1,5,2,7,4,6,6,4,11,9)	3.39 (1.98 to 3.98)	3.00 (1.02 to 5.98)	2.97 (1.92 to 5.82)	

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1a and 1b: Elimination Half-life (t1/2) of ASTX295

End point title	Phase 1a and 1b: Elimination Half-life (t1/2) of ASTX295[8]

End point description:

PK analysis set included all subjects who received the study drug and have post baseline plasma concentration data. Here, '99999' indicates that dispersion values were not measurable due to low number of subjects for the specified arms. ‘Subjects analysed’ indicates number of subjects with data available for analyses and ‘n’ indicates number of subjects with data available for analyses at the specified timepoint.

End point type	Secondary

End point timeframe:

Pre-dose on Day 1 and Day 2 of Cycles 1 and 2, and at multiple timepoints post-dose on Day 1 of Cycles 1 and 2 (Cycle length = 28 days).

Notes:

[8] - 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 statistics were provided for this endpoint.

End point values	Dose Escalation: Phase 1a: Cohort 1	Dose Escalation: Phase 1a: Cohort 2	Dose Escalation: Phase 1a: Cohort 3	Dose Escalation: Phase 1a: Cohort 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[9]	1	2	4
Units: hours				
geometric mean (geometric coefficient of variation)				
C1D1 (n=0,0,2,4,5,7,3,3,3,6,4,6,7,6,7,9)	()	99999 (± 99999)	3.14 (± 37.8)	2.42 (± 68.9)
C2D1 (n=0,1,2,2,6,4,0,1,2,4,3,3,4,4,7,5)	()	3.14 (± 99999)	7.86 (± 46.7)	4.46 (± 268.9)

Notes:

[9] - Data was not reported as no subjects were available for analyses at the specified timepoint.

End point values	Dose Escalation: Phase 1a: Cohort 5	Dose Escalation: Phase 1a: Cohort 6	Dose Escalation: Phase 1a: Cohort 8	Dose Escalation: Phase 1a: Cohort 9
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	7	3	3
Units: hours				
geometric mean (geometric coefficient of variation)				
C1D1 (n=0,0,2,4,5,7,3,3,3,6,4,6,7,6,7,9)	4.50 (± 35.0)	4.86 (± 66.4)	1.73 (± 39.5)	1.35 (± 16.7)
C2D1 (n=0,1,2,2,6,4,0,1,2,4,3,3,4,4,7,5)	4.50 (± 106.4)	3.81 (± 52.3)	1.93 (± 99999)	2.49 (± 68.4)

End point values	Dose Escalation: Phase 1a: Cohort 10	Dose Escalation: Phase 1a: Cohort 11	Dose Escalation: Phase 1a: Cohort 12	Dose Escalation: Phase 1a: Cohort 13
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	4	6	7
Units: hours				
geometric mean (geometric coefficient of variation)				
C1D1 (n=0,0,2,4,5,7,3,3,3,6,4,6,7,6,7,9)	3.74 (± 74.9)	5.55 (± 15.1)	4.39 (± 28.8)	5.10 (± 39.6)
C2D1 (n=0,1,2,2,6,4,0,1,2,4,3,3,4,4,7,5)	3.59 (± 116.8)	8.06 (± 3.6)	4.48 (± 19.8)	4.44 (± 20.0)

End point values	Dose Escalation: Phase 1a: Cohort 14	Dose Expansion: Phase 1b: Cohort 1	Dose Expansion: Phase 1b: Cohort 2	

Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	7	9	
Units: hours				
geometric mean (geometric coefficient of variation)				
C1D1 (n=0,0,2,4,5,7,3,3,3,6,4,6,7,6,7,9)	3.52 (± 60.0)	4.99 (± 58.8)	3.32 (± 58.3)	
C2D1 (n=0,1,2,2,6,4,0,1,2,4,3,3,4,4,7,5)	3.60 (± 14.4)	6.01 (± 18.7)	4.20 (± 23.2)	

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1a and 1b: Area Under the Concentration-time Curve From Time Zero to 24 Hours (AUC0-24) of ASTX295

End point title	Phase 1a and 1b: Area Under the Concentration-time Curve From Time Zero to 24 Hours (AUC0-24) of ASTX295[10]

End point description:

Pharmacokinetics (PK) analysis set included all subjects who received the study drug and have post baseline plasma concentration data. Here, C1D1 represents Cycle 1 Day 1, and C2D1 represents Cycle 2 Day 1, '99999' indicates that values were not measurable due to low number of subjects for the specified arms. 'Subjects analysed' indicates number of subjects with data available for analyses and 'n' indicates number of subjects with data available for analyses at the specified timepoint.

End point type	Secondary

End point timeframe:

Pre-dose on Day 1 and 2 of Cycles 1 and 2, and at multiple timepoints post-dose on Day 1 of Cycles 1 and 2 (Cycle length = 28 days).

Notes:

[10] - 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 statistics were provided for this endpoint.

End point values	Dose Escalation: Phase 1a: Cohort 1	Dose Escalation: Phase 1a: Cohort 2	Dose Escalation: Phase 1a: Cohort 3	Dose Escalation: Phase 1a: Cohort 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	1	0[11]	4	4
Units: hours*nanograms/millilitres (h*ng/mL)				
geometric mean (geometric coefficient of variation)				
C1D1 (n=0,0,3,3,7,8,5,0,0,8,4,8,8,6,11,12)	99999 (± 99999)	()	2040 (± 148.9)	1380 (± 53.6)
C2D1 (n=1,0,2,2,7,4,0,0,0,7,3,6,4,4,9,6)	27.7 (± 99999)	()	1500 (± 76.3)	2170 (± 39.8)

Notes:

[11] - Data was not reported as AUC(0-24) could not be calculated.

End point values	Dose Escalation: Phase 1a: Cohort 5	Dose Escalation: Phase 1a: Cohort 6	Dose Escalation: Phase 1a: Cohort 8	Dose Escalation: Phase 1a: Cohort 9

Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9	8	0[12]	0[13]
Units: hours*nanograms/millilitres (h*ng/mL)				
geometric mean (geometric coefficient of variation)				
C1D1 (n=0,0,3,3,7,8,5,0,0,8,4,8,8,6,11,12)	4450 (± 59.0)	3520 (± 140.5)	()	()
C2D1 (n=1,0,2,2,7,4,0,0,0,7,3,6,4,4,9,6)	3610 (± 60.4)	2760 (± 82.8)	()	()

Notes:

[12] - Since this cohort was dosed every 12 hours, therefore AUC0-24 could not be calculated.

[13] - Since this cohort was dosed every 12 hours, therefore AUC0-24 could not be calculated.

End point values	Dose Escalation: Phase 1a: Cohort 10	Dose Escalation: Phase 1a: Cohort 11	Dose Escalation: Phase 1a: Cohort 12	Dose Escalation: Phase 1a: Cohort 13
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	4	8	8
Units: hours*nanograms/millilitres (h*ng/mL)				
geometric mean (geometric coefficient of variation)				
C1D1 (n=0,0,3,3,7,8,5,0,0,8,4,8,8,6,11,12)	11300 (± 137.8)	3280 (± 64.4)	11500 (± 173.4)	7860 (± 223.2)
C2D1 (n=1,0,2,2,7,4,0,0,0,7,3,6,4,4,9,6)	12700 (± 129.8)	2890 (± 40.2)	10500 (± 238.6)	10400 (± 175.0)

End point values	Dose Escalation: Phase 1a: Cohort 14	Dose Expansion: Phase 1b: Cohort 1	Dose Expansion: Phase 1b: Cohort 2	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	12	12	
Units: hours*nanograms/millilitres (h*ng/mL)				
geometric mean (geometric coefficient of variation)				
C1D1 (n=0,0,3,3,7,8,5,0,0,8,4,8,8,6,11,12)	9360 (± 101.3)	2930 (± 74.3)	11800 (± 195.7)	
C2D1 (n=1,0,2,2,7,4,0,0,0,7,3,6,4,4,9,6)	11000 (± 52.5)	4180 (± 52.6)	8940 (± 203.4)	

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1a and 1b: Area Under the Concentration-time Curve From Time Zero to Infinity (AUC0-inf) of ASTX295

End point title	Phase 1a and 1b: Area Under the Concentration-time Curve From Time Zero to Infinity (AUC0-inf) of ASTX295[14]

End point description:

PK analysis set included all subjects who received the study drug and have post baseline plasma concentration data. Here, '99999' indicates that values were not measurable due to low number of subjects for the specified arms. ‘Subjects analysed’ indicates number of subjects with data available for analyses and ‘n’ indicates number of subjects with data available for analyses at the specified timepoint.

End point type	Secondary

End point timeframe:

Pre-dose on Day 1 and Day 2 of Cycles 1 and 2, and at multiple timepoints post-dose on Day 1 of Cycles 1 and 2 (Cycle length = 28 days).

Notes:

[14] - 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 statistics were provided for this endpoint.

End point values	Dose Escalation: Phase 1a: Cohort 1	Dose Escalation: Phase 1a: Cohort 2	Dose Escalation: Phase 1a: Cohort 3	Dose Escalation: Phase 1a: Cohort 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[15]	1	4	4
Units: h*ng/mL				
geometric mean (geometric coefficient of variation)				
C1D1 (n=0,0,2,4,5,7,3,3,3,6,4,6,7,6,7,9)	()	99999 (± 99999)	1550 (± 986.8)	1250 (± 42.5)
C2D1 (n=0,1,2,2,6,4,0,1,2,4,3,3,4,4,7,5)	()	261 (± 99999)	1660 (± 90.1)	2330 (± 51.5)

Notes:

[15] - Data was not reported as no subjects were available for analyses at the specified timepoint.

End point values	Dose Escalation: Phase 1a: Cohort 5	Dose Escalation: Phase 1a: Cohort 6	Dose Escalation: Phase 1a: Cohort 8	Dose Escalation: Phase 1a: Cohort 9
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9	8	5	7
Units: h*ng/mL				
geometric mean (geometric coefficient of variation)				
C1D1 (n=0,0,2,4,5,7,3,3,3,6,4,6,7,6,7,9)	3670 (± 40.8)	3300 (± 138.5)	1190 (± 43.0)	4350 (± 211.2)
C2D1 (n=0,1,2,2,6,4,0,1,2,4,3,3,4,4,7,5)	4400 (± 50.6)	2820 (± 83.3)	2160 (± 99999)	5250 (± 49.4)

End point values	Dose Escalation: Phase 1a: Cohort 10	Dose Escalation: Phase 1a: Cohort 11	Dose Escalation: Phase 1a: Cohort 12	Dose Escalation: Phase 1a: Cohort 13
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	4	9	8
Units: h*ng/mL				
geometric mean (geometric coefficient of variation)				

C1D1 (n=0,0,2,4,5,7,3,3,3,6,4,6,7,6,7,9)	13000 (± 190.6)	3380 (± 63.3)	10200 (± 215.9)	9680 (± 221.2)
C2D1 (n=0,1,2,2,6,4,0,1,2,4,3,3,4,4,7,5)	16700 (± 112.8)	3150 (± 36.1)	13500 (± 75.4)	10800 (± 179.3)

End point values	Dose Escalation: Phase 1a: Cohort 14	Dose Expansion: Phase 1b: Cohort 1	Dose Expansion: Phase 1b: Cohort 2	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	12	12	
Units: h*ng/mL				
geometric mean (geometric coefficient of variation)				
C1D1 (n=0,0,2,4,5,7,3,3,3,6,4,6,7,6,7,9)	9540 (± 101.0)	2390 (± 74.6)	13500 (± 176.3)	
C2D1 (n=0,1,2,2,6,4,0,1,2,4,3,3,4,4,7,5)	11200 (± 51.8)	4590 (± 46.1)	12400 (± 169.9)	

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1a: AUC0-24 of ASTX295 Under Fed State

End point title	Phase 1a: AUC0-24 of ASTX295 Under Fed State[16]

End point description:

PK analysis set included all subjects who received the study drug and have post baseline plasma concentration data. Here, '99999' indicates that values were not measurable due to low number of subjects for the specified arms. ‘Subjects analysed’ indicates number of subjects with data available for analyses and 'n’ indicates number of subjects with data available for analyses at the specified timepoint.

End point type	Secondary

End point timeframe:

Pre-dose on Day 1 and Day 2 of Cycles 1 and 2, and at multiple timepoints post-dose on Day 1 of Cycles 1 and 2 (Cycle length = 28 days).

Notes:

[16] - 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 statistics were provided for this endpoint.

End point values	Dose Escalation: Phase 1a: Cohort 7			
Subject group type	Reporting group			
Number of subjects analysed	5			
Units: h*ng/mL				
geometric mean (geometric coefficient of variation)				
C1D1 (n=5)	5730 (± 57.9)			
C2D1 (n=0)	99999 (± 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1a: AUClast of ASTX295 Under Fed State

End point title	Phase 1a: AUClast of ASTX295 Under Fed State[17]

End point description:

PK analysis set included all subjects who received the study drug and have post baseline plasma concentration data. Here, '99999' indicates that values were not measurable due to low number of subjects for the specified arms. ‘Subjects analysed’ indicates number of subjects with data available for analyses and 'n’ indicates number of subjects with data available for analyses at the specified timepoint.

End point type	Secondary

End point timeframe:

Pre-dose on Day 1 and Day 2 of Cycles 1 and 2, and at multiple timepoints post-dose on Day 1 of Cycles 1 and 2 (Cycle length = 28 days).

Notes:

[17] - 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 statistics were provided for this endpoint.

End point values	Dose Escalation: Phase 1a: Cohort 7			
Subject group type	Reporting group			
Number of subjects analysed	5			
Units: h*ng/mL				
geometric mean (geometric coefficient of variation)				
C1D1 (n=5) C2D1 (n=1)	5720 (± 58.3) 427 (± 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1a: AUC0-inf of ASTX295 Under Fed State

End point title	Phase 1a: AUC0-inf of ASTX295 Under Fed State[18]

End point description:

PK analysis set included all subjects who received the study drug and have post baseline plasma concentration data. Here, '99999' indicates that values were not measurable due to low number of subjects for the specified arms. ‘Subjects analysed’ indicates number of subjects with data available for analyses and ‘n’ indicates number of subjects with data available for analyses at the specified timepoint.

End point type	Secondary

End point timeframe:

Pre-dose on Day 1 and Day 2 of Cycles 1 and 2, and at multiple timepoints post-dose on Day 1 of Cycles 1 and 2 (Cycle length = 28 days).

Notes:

[18] - 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 statistics were provided for this endpoint.

End point values	Dose Escalation: Phase 1a: Cohort 7			
Subject group type	Reporting group			
Number of subjects analysed	5			
Units: h*ng/mL				
geometric mean (geometric coefficient of variation)				
C1D1 (n=3) C2D1 (n=0)	7200 (± 26.9) 99999 (± 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1a: Cmax of ASTX295 Under Fed State

End point title	Phase 1a: Cmax of ASTX295 Under Fed State[19]

End point description:

PK analysis set included all subjects who received the study drug and have post baseline plasma concentration data. Here, '99999' indicates that dispersion values were not measurable due to low number of subjects for the specified arms. ‘Subjects analysed’ indicates number of subjects with data available for analyses and ‘n’ indicates number of subjects with data available for analyses at the specified timepoint.

End point type	Secondary

End point timeframe:

Pre-dose on Day 1 and Day 2 of Cycles 1 and 2, and at multiple timepoints post-dose on Day 1 of Cycles 1 and 2 (Cycle length = 28 days).

Notes:

[19] - 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 statistics were provided for this endpoint.

End point values	Dose Escalation: Phase 1a: Cohort 7			
Subject group type	Reporting group			
Number of subjects analysed	5			
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
C1D1 (n=5) C2D1 (n=1)	1970 (± 88.4) 43.1 (± 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1a: Cmin of ASTX295 Under Fed State

End point title	Phase 1a: Cmin of ASTX295 Under Fed State[20]

End point description:

PK analysis set included all subjects who received the study drug and have post baseline plasma concentration data. Here, '99999' indicates that dispersion values were not measurable due to low number of subjects. 'Subjects analysed' indicates number of subjects with data available for analyses.

End point type	Secondary

End point timeframe:

Pre-dose on Day 1 and Day 2 of Cycles 1 and 2, and at multiple timepoints post-dose on Day 1 of Cycles 1 and 2 (Cycle length = 28 days).

Notes:

[20] - 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 statistics were provided for this endpoint.

End point values	Dose Escalation: Phase 1a: Cohort 7			
Subject group type	Reporting group			
Number of subjects analysed	1			
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
C2D1	5.88 (± 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1a: Tmax of ASTX295 Under Fed State

End point title	Phase 1a: Tmax of ASTX295 Under Fed State[21]

End point description:

PK analysis set included all subjects who received the study drug and have post baseline plasma concentration data. Here, '99999' indicates that dispersion values were not measurable due to low number of subjects for the specified arms. 'Subjects analysed' indicates number of subjects with data available for analyses and 'n' indicates number of subjects with data available for analyses at the specified timepoint.

End point type	Secondary

End point timeframe:

Pre-dose on Day 1 and Day 2 of Cycles 1 and 2, and at multiple timepoints post-dose on Day 1 of Cycles 1 and 2 (Cycle length = 28 days).

Notes:

[21] - 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 statistics were provided for this endpoint.

End point values	Dose Escalation: Phase 1a: Cohort 7			
Subject group type	Reporting group			
Number of subjects analysed	5			
Units: hours				
median (full range (min-max))				
C1D1 (n=5) C2D1 (n=1)	3.87 (1.02 to 4.17) 7.33 (-99999 to 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1a: The t1/2 of ASTX295 Under Fed State

End point title	Phase 1a: The t1/2 of ASTX295 Under Fed State[22]

End point description:

PK analysis set included all subjects who received the study drug and have post baseline plasma concentration data. Here, '99999' indicates that dispersion values were not measurable due to low number of subjects for the specified arms. ‘Subjects analysed’ indicates number of subjects with data available for analyses and ‘n’ indicates number of subjects with data available for analyses at the specified timepoint.

End point type	Secondary

End point timeframe:

Pre-dose on Day 1 and Day 2 of Cycles 1 and 2, and at multiple timepoints post-dose on Day 1 of Cycles 1 and 2 (Cycle length = 28 days).

Notes:

[22] - 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 statistics were provided for this endpoint.

End point values	Dose Escalation: Phase 1a: Cohort 7			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: hours				
geometric mean (geometric coefficient of variation)				
C1D1 (n=3) C2D1 (n=0)	6.55 (± 36.7) 99999 (± 99999)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to approximately 61.3 months

Adverse event reporting additional description:

Safety analysis set included all subjects who received at least one dose of study drug.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	27.0

Reporting groups

Reporting group title	Dose Escalation: Phase 1a: Cohort 1

Reporting group description:

Subjects received ASTX295 at starting dose of 15 milligrams (mg), orally, administered once daily (QD) in each 28-day cycle under fasted condition, up to a maximum of 1.8 months.

Reporting group title	Dose Escalation: Phase 1a: Cohort 2

Reporting group description:

Subjects received ASTX295 at an oral dose of 45 mg, administered QD in each 28-day cycle under fasted condition, up to a maximum of 17.4 months.

Reporting group title	Dose Escalation: Phase 1a: Cohort 3

Reporting group description:

Subjects received ASTX295 at an oral dose of 120 mg, administered QD in each 28-day cycle under fasted condition, up to a maximum of 1.8 months.

Reporting group title	Dose Escalation: Phase 1a: Cohort 4

Reporting group description:

Subjects received ASTX295 at an oral dose of 240 mg, administered QD in each 28-day cycle under fasted condition, up to a maximum of 6.4 months.

Reporting group title	Dose Escalation: Phase 1a: Cohort 5

Reporting group description:

Subjects received ASTX295 at an oral dose of 420 mg, administered QD in each 28-day cycle under fasted condition, up to a maximum of 14.7 months.

Reporting group title	Dose Escalation: Phase 1a: Cohort 6

Reporting group description:

Subjects received ASTX295 at an oral dose of 520 mg, administered QD in each 28-day cycle under fasted condition, up to a maximum of 42.4 months.

Reporting group title	Dose Escalation: Phase 1a: Cohort 7

Reporting group description:

Subjects received ASTX295 at an oral dose of 415 mg, administered QD in each 28-day cycle under fed state, up to a maximum of 22.5 months.

Reporting group title	Dose Escalation: Phase 1a: Cohort 8

Reporting group description:

Subjects received ASTX295 at an oral dose of 200 mg, administered twice daily (BID) in each 28-day cycle under fasted condition, up to a maximum of 17.4 months.

Reporting group title	Dose Escalation: Phase 1a: Cohort 9

Reporting group description:

Subjects received ASTX295 at an oral dose of 320 mg, administered BID in each 28-day cycle under fasted condition, up to a maximum of 27.5 months.

Reporting group title	Dose Escalation: Phase 1a: Cohort 10

Reporting group description:

Subjects received ASTX295 at an oral dose of 520 mg (5 days on, 2 days off), administered QD in each 28-day cycle, with or without food, up to a maximum of 12 months.

Reporting group title	Dose Escalation: Phase 1a: Cohort 11

Reporting group description:	
Subjects received ASTX295 at an oral dose of 520 mg (3 days on, 4 days off), administered QD in each 28-day cycle, with or without food, up to a maximum of 1.8 months.	
Reporting group title	Dose Escalation: Phase 1a: Cohort 12
Reporting group description:	
Subjects received ASTX295 at an oral dose of 660 mg, administered QD, twice a week, in each 28-day cycle, with or without food, up to a maximum of 11.7 months.	
Reporting group title	Dose Escalation: Phase 1a: Cohort 13
Reporting group description:	
Subjects received ASTX295 at an oral dose of 660 mg (3 days on, 4 days off), administered QD, in each 28-day cycle, with or without food, up to a maximum of 18.5 months.	
Reporting group title	Dose Escalation: Phase 1a: Cohort 14
Reporting group description:	
Subjects received ASTX295 at an oral dose of 800 mg, administered QD, twice a week, in each 28-day cycle, with or without food, up to a maximum of 6 months.	
Reporting group title	Dose Expansion: Phase 1b: Cohort 1
Reporting group description:	
Subjects received ASTX295 at an oral dose of 400 mg, administered daily, in each 28-day cycle, with or without food, up to a maximum of 14.7 months.	
Reporting group title	Dose Expansion: Phase 1b: Cohort 2
Reporting group description:	
Subjects received ASTX295 at an oral dose of 660 mg, administered QD, twice a week, in each 28-day cycle, with or without food, up to a maximum of 14.2 months.	

Serious adverse events	Dose Escalation: Phase 1a: Cohort 1	Dose Escalation: Phase 1a: Cohort 2	Dose Escalation: Phase 1a: Cohort 3
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	2 / 4 (50.00%)
number of deaths (all causes)	1	0	2
number of deaths resulting from adverse events	0	0	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal wall wound			

subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	1 / 4 (25.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericardial effusion			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (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			
Loss of consciousnes			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seizure			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (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
Hemiparesis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Asthenia			

subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (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
Oedema			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal obstruction			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (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
Oesophageal obstruction			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (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
Haemoperitoneum			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (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			

Hyperbilirubinaemia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (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			
Haemoptysis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	1 / 4 (25.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (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
Dyspnoea			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (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
Tracheal fistula			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (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 haemorrhage			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (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			
Pneumonia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	1 / 4 (25.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal abscess			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic shock			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin bacterial infection			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (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 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (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	Dose Escalation: Phase 1a: Cohort 4	Dose Escalation: Phase 1a: Cohort 5	Dose Escalation: Phase 1a: Cohort 6
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 4 (0.00%)	2 / 9 (22.22%)	1 / 8 (12.50%)
number of deaths (all causes)	2	4	6
number of deaths resulting from adverse events	0	0	0
Investigations			
Alanine aminotransferase increased			

subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	1 / 8 (12.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	1 / 8 (12.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal wall wound			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (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			
Atrial fibrillation			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericardial effusion			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (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			
Loss of consciousnes			
subjects affected / exposed	0 / 4 (0.00%)	1 / 9 (11.11%)	0 / 8 (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
Seizure			

subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (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
Hemiparesis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (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
Oedema			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal obstruction			
subjects affected / exposed	0 / 4 (0.00%)	1 / 9 (11.11%)	0 / 8 (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
Abdominal pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	1 / 8 (12.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Oesophageal obstruction			
subjects affected / exposed	0 / 4 (0.00%)	1 / 9 (11.11%)	0 / 8 (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
Haemoperitoneum			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (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			
Hyperbilirubinaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	1 / 8 (12.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Haemoptysis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (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
Pleural effusion			
subjects affected / exposed	0 / 4 (0.00%)	1 / 9 (11.11%)	0 / 8 (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
Dyspnoea			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (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
Tracheal fistula			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (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 haemorrhage			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (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			
Pneumonia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal abscess			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic shock			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin bacterial infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (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 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (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	Dose Escalation: Phase 1a: Cohort 7	Dose Escalation: Phase 1a: Cohort 8	Dose Escalation: Phase 1a: Cohort 9
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 5 (20.00%)	2 / 6 (33.33%)	0 / 7 (0.00%)
number of deaths (all causes)	3	4	3
number of deaths resulting from adverse events	1	1	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal wall wound			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (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			
Atrial fibrillation			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericardial effusion			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (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			

Loss of consciousnes			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seizure			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (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
Hemiparesis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (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
Oedema			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Gastrointestinal haemorrhage			
subjects affected / exposed	1 / 5 (20.00%)	0 / 6 (0.00%)	0 / 7 (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
Small intestinal obstruction			

subjects affected / exposed	1 / 5 (20.00%)	1 / 6 (16.67%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (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
Oesophageal obstruction			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (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
Haemoperitoneum			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (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			
Hyperbilirubinaemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (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			
Haemoptysis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (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
Pleural effusion			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (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
Dyspnoea			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	0 / 7 (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

Tracheal fistula			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Pulmonary embolism			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (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 haemorrhage			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (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			
Pneumonia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal abscess			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic shock			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin bacterial infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Urinary tract infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (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 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (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	Dose Escalation: Phase 1a: Cohort 10	Dose Escalation: Phase 1a: Cohort 11	Dose Escalation: Phase 1a: Cohort 12
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 8 (12.50%)	0 / 4 (0.00%)	4 / 9 (44.44%)
number of deaths (all causes)	6	4	6
number of deaths resulting from adverse events	0	0	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal wall wound			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (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			
Atrial fibrillation			

subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericardial effusion			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Loss of consciousnes			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seizure			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (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
Hemiparesis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (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
Oedema			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Gastrointestinal disorders			
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal obstruction			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (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
Oesophageal obstruction			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (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
Haemoperitoneum			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (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			
Hyperbilirubinaemia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (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			
Haemoptysis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (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
Pleural effusion			

subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tracheal fistula			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (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 haemorrhage			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (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			
Pneumonia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 4 (0.00%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal abscess			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic shock			

subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin bacterial infection			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (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 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (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	Dose Escalation: Phase 1a: Cohort 13	Dose Escalation: Phase 1a: Cohort 14	Dose Expansion: Phase 1b: Cohort 1
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 8 (12.50%)	4 / 6 (66.67%)	6 / 12 (50.00%)
number of deaths (all causes)	5	5	4
number of deaths resulting from adverse events	0	1	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	1 / 12 (8.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal wall wound			

subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	1 / 12 (8.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	1 / 12 (8.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	1 / 12 (8.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericardial effusion			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (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			
Loss of consciousnes			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seizure			
subjects affected / exposed	0 / 8 (0.00%)	1 / 6 (16.67%)	0 / 12 (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
Hemiparesis			
subjects affected / exposed	1 / 8 (12.50%)	0 / 6 (0.00%)	0 / 12 (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
General disorders and administration site conditions			
Asthenia			

subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	1 / 12 (8.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oedema			
subjects affected / exposed	0 / 8 (0.00%)	1 / 6 (16.67%)	0 / 12 (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
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 8 (0.00%)	1 / 6 (16.67%)	0 / 12 (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
Small intestinal obstruction			
subjects affected / exposed	0 / 8 (0.00%)	1 / 6 (16.67%)	1 / 12 (8.33%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (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
Oesophageal obstruction			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (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
Haemoperitoneum			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (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			

Hyperbilirubinaemia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (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			
Haemoptysis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (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
Pleural effusion			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (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
Dyspnoea			
subjects affected / exposed	0 / 8 (0.00%)	1 / 6 (16.67%)	0 / 12 (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
Tracheal fistula			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	2 / 12 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	2 / 12 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal haemorrhage			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (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			
Pneumonia			
subjects affected / exposed	0 / 8 (0.00%)	1 / 6 (16.67%)	0 / 12 (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
Abdominal abscess			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic shock			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin bacterial infection			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	1 / 12 (8.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	1 / 12 (8.33%)
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 / 8 (0.00%)	0 / 6 (0.00%)	1 / 12 (8.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Dose Expansion: Phase 1b: Cohort 2		
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 12 (33.33%)		
number of deaths (all causes)	3		
number of deaths resulting from adverse events	0		
Investigations			
Alanine aminotransferase increased			

subjects affected / exposed	0 / 12 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Abdominal wall wound			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pericardial effusion			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Loss of consciousnes			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Seizure			

subjects affected / exposed	0 / 12 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hemiparesis				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
General disorders and administration site conditions				
Asthenia				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Oedema				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Blood and lymphatic system disorders				
Anaemia				
subjects affected / exposed	1 / 12 (8.33%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
Gastrointestinal haemorrhage				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Small intestinal obstruction				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Abdominal pain				
subjects affected / exposed	1 / 12 (8.33%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

Oesophageal obstruction				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Haemoperitoneum				
subjects affected / exposed	1 / 12 (8.33%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hepatobiliary disorders				
Hyperbilirubinaemia				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Haemoptysis				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pleural effusion				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Dyspnoea				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Tracheal fistula				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pulmonary embolism				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal haemorrhage			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Pneumonia			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Abdominal abscess			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Septic shock			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Skin bacterial infection			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Urosepsis			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Dose Escalation: Phase 1a: Cohort 1	Dose Escalation: Phase 1a: Cohort 2	Dose Escalation: Phase 1a: Cohort 3
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 1 (100.00%)	3 / 3 (100.00%)	4 / 4 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cancer pain			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	2 / 4 (50.00%)
occurrences (all)	0	0	2
Tumour pain			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Deep vein thrombosis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Hypertension			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Embolism			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Hot flush			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Pallor			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Peripheral embolism			

subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Fatigue			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	2 / 4 (50.00%)
occurrences (all)	0	0	4
Asthenia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Gait disturbance			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Influenza like illness			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Non-cardiac chest pain			
subjects affected / exposed	0 / 1 (0.00%)	1 / 3 (33.33%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Oedema peripheral			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Chest discomfort			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Chest pain			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Chills			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Early satiety			

subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Infusion site extravasation			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Pain			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Performance status decreased			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Physical deconditioning			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Peripheral swelling			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Contrast media reaction			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Erectile dysfunction			
subjects affected / exposed	1 / 1 (100.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Vaginal haemorrhage			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Dyspnoea			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Oropharyngeal pain			

subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Wheezing			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Atelectasis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Pleural effusion			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Acute respiratory distress syndrome			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Nasal congestion			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Pulmonary embolism			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Rhinorrhoea			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract congestion			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Increased viscosity of upper respiratory secretion			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Pneumothorax			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Productive cough			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0

Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Hallucination, auditory			
subjects affected / exposed	0 / 1 (0.00%)	1 / 3 (33.33%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Insomnia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Anxiety			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Confusional state			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Irritability			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Product issues			
Device breakage			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Investigations			
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Blood creatinine increased			
subjects affected / exposed	0 / 1 (0.00%)	1 / 3 (33.33%)	0 / 4 (0.00%)
occurrences (all)	0	2	0
Alanine aminotransferase increased			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1

Blood bilirubin increased			
subjects affected / exposed	0 / 1 (0.00%)	1 / 3 (33.33%)	1 / 4 (25.00%)
occurrences (all)	0	1	1
Blood cholesterol increased			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Blood lactate dehydrogenase decreased			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Blood phosphorus decreased			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Electrocardiogram QT interval abnormal			
subjects affected / exposed	0 / 1 (0.00%)	1 / 3 (33.33%)	0 / 4 (0.00%)
occurrences (all)	0	2	0
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 1 (0.00%)	1 / 3 (33.33%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Lymphocyte count decreased			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Neutrophil count decreased			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Weight decreased			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Weight increased			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
White blood cell count decreased			

subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Blood creatinine decreased			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Blood sodium decreased			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Eosinophil count decreased			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Platelet count decreased			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
White blood cell count increased			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Ejection fraction decreased			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Blood albumin decreased			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Carbon dioxide decreased			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			

Spinal compression fracture			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Contusion			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Fall			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Stoma prolapse			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Skin laceration			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Pelvic fracture			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Procedural pain			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Rib fracture			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Ulna fracture			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Sinus tachycardia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Atrial fibrillation			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Palpitations			

subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Pericardial effusion			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Sinus bradycardia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Atrial thrombosis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Atrioventricular block first degree			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Tachycardia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Ageusia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Anosmia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Dysgeusia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Hypoaesthesia			
subjects affected / exposed	0 / 1 (0.00%)	1 / 3 (33.33%)	0 / 4 (0.00%)
occurrences (all)	0	1	0

Sensory loss			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Syncope			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Paraesthesia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Brain oedema			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Neuropathy peripheral			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Post herpetic neuralgia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Taste disorder			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Tremor			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Coordination abnormal			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Cognitive disorder			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Disturbance in attention			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Parosmia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0

Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Leukocytosis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Leukopenia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Thrombocytopenia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Lymphopenia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Neutropenia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Tinnitus			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Hyperacusis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Vision blurred			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Conjunctival haemorrhage			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Eye pain			
subjects affected / exposed	0 / 1 (0.00%)	1 / 3 (33.33%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Vitreous floaters			

subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Diplopia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	0 / 1 (0.00%)	1 / 3 (33.33%)	2 / 4 (50.00%)
occurrences (all)	0	1	2
Vomiting			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	2
Abdominal pain			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Constipation			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
subjects affected / exposed	1 / 1 (100.00%)	1 / 3 (33.33%)	1 / 4 (25.00%)
occurrences (all)	1	2	1
Abdominal distension			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Dry mouth			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Haematochezia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Retching			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Anal incontinence			
subjects affected / exposed	1 / 1 (100.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0

Dyspepsia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Dysphagia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Faeces soft			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Flatulence			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Salivary hypersecretion			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Stomatitis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Abdominal pain upper			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Colitis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Food poisoning			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Tooth discolouration			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Ascites			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0

Parotid gland enlargement			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Rectal haemorrhage			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Tooth erosion			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Tooth loss			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Hepatobiliary disorders			
Hyperbilirubinaemia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	2
Hepatitis acute			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Biliary dilatation			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Dermatitis acneiform			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Rash maculo-papular			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Dermatitis contact			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Night sweats			

subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Rash macular			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Skin lesion			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Hyperhidrosis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Ketonuria			
subjects affected / exposed	0 / 1 (0.00%)	1 / 3 (33.33%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Urinary incontinence			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Haematuria			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Proteinuria			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Renal colic			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Glycosuria			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Endocrine disorders			
Pituitary-dependent Cushing's syndrome			

subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Hypothyroidism			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 1 (100.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Myalgia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Arthralgia			
subjects affected / exposed	0 / 1 (0.00%)	1 / 3 (33.33%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Groin pain			
subjects affected / exposed	0 / 1 (0.00%)	1 / 3 (33.33%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Muscle spasms			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal pain			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Osteoarthritis			
subjects affected / exposed	0 / 1 (0.00%)	1 / 3 (33.33%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Fistula			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Osteoporosis			

subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Coccydynia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
COVID-19			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Pneumonia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Respiratory tract infection			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Cellulitis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Onychomycosis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Oral candidiasis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Pneumonia aspiration			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Skin infection			
subjects affected / exposed	1 / 1 (100.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0

Upper respiratory tract infection			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Candida infection			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Herpes zoster			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Vaginal infection			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Coronavirus infection			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Influenza			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 1 (0.00%)	1 / 3 (33.33%)	1 / 4 (25.00%)
occurrences (all)	0	1	1
Hypercalcaemia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Hyperkalaemia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Hypomagnesaemia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Dehydration			

subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Gout			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Hyperglycaemia			
subjects affected / exposed	0 / 1 (0.00%)	1 / 3 (33.33%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Hyperlipidaemia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Hypokalaemia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Hyponatraemia			
subjects affected / exposed	0 / 1 (0.00%)	1 / 3 (33.33%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Hypophosphataemia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Vitamin B12 deficiency			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Vitamin D deficiency			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Hypoalbuminaemia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Hypocalcaemia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Hypoglycaemia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Hyperuricaemia			

subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Malnutrition			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Dose Escalation: Phase 1a: Cohort 4	Dose Escalation: Phase 1a: Cohort 5	Dose Escalation: Phase 1a: Cohort 6
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 4 (100.00%)	9 / 9 (100.00%)	8 / 8 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cancer pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Tumour pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 4 (0.00%)	1 / 9 (11.11%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Deep vein thrombosis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Hypertension			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Embolism			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Hot flush			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Pallor			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Peripheral embolism			

subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Fatigue			
subjects affected / exposed	2 / 4 (50.00%)	3 / 9 (33.33%)	4 / 8 (50.00%)
occurrences (all)	2	3	10
Asthenia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 9 (11.11%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Gait disturbance			
subjects affected / exposed	0 / 4 (0.00%)	1 / 9 (11.11%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Influenza like illness			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Non-cardiac chest pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Oedema peripheral			
subjects affected / exposed	0 / 4 (0.00%)	1 / 9 (11.11%)	2 / 8 (25.00%)
occurrences (all)	0	1	2
Chest discomfort			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Chest pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Chills			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Early satiety			

subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Infusion site extravasation			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Performance status decreased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Physical deconditioning			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Peripheral swelling			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Contrast media reaction			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Erectile dysfunction			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Vaginal haemorrhage			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Dyspnoea			
subjects affected / exposed	1 / 4 (25.00%)	1 / 9 (11.11%)	1 / 8 (12.50%)
occurrences (all)	1	1	1
Oropharyngeal pain			

subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Wheezing			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Atelectasis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Pleural effusion			
subjects affected / exposed	0 / 4 (0.00%)	1 / 9 (11.11%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Acute respiratory distress syndrome			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Nasal congestion			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Pulmonary embolism			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Rhinorrhoea			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract congestion			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Increased viscosity of upper respiratory secretion			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Pneumothorax			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Productive cough			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0

Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 4 (0.00%)	1 / 9 (11.11%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Hallucination, auditory			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Insomnia			
subjects affected / exposed	0 / 4 (0.00%)	2 / 9 (22.22%)	0 / 8 (0.00%)
occurrences (all)	0	2	0
Anxiety			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Confusional state			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Irritability			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Product issues			
Device breakage			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Investigations			
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Blood creatinine increased			
subjects affected / exposed	1 / 4 (25.00%)	1 / 9 (11.11%)	1 / 8 (12.50%)
occurrences (all)	1	1	1
Alanine aminotransferase increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	4
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	6

Blood bilirubin increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Blood cholesterol increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Blood lactate dehydrogenase decreased			
subjects affected / exposed	0 / 4 (0.00%)	1 / 9 (11.11%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Blood phosphorus decreased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Electrocardiogram QT interval abnormal			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 4 (0.00%)	2 / 9 (22.22%)	0 / 8 (0.00%)
occurrences (all)	0	3	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	2
Lymphocyte count decreased			
subjects affected / exposed	0 / 4 (0.00%)	1 / 9 (11.11%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Neutrophil count decreased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	2
Weight decreased			
subjects affected / exposed	1 / 4 (25.00%)	0 / 9 (0.00%)	2 / 8 (25.00%)
occurrences (all)	1	0	2
Weight increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
White blood cell count decreased			

subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	2 / 8 (25.00%)
occurrences (all)	0	0	4
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Blood creatinine decreased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Blood sodium decreased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Eosinophil count decreased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Platelet count decreased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
White blood cell count increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Ejection fraction decreased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Blood albumin decreased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Carbon dioxide decreased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			

Spinal compression fracture			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Contusion			
subjects affected / exposed	0 / 4 (0.00%)	1 / 9 (11.11%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Fall			
subjects affected / exposed	0 / 4 (0.00%)	1 / 9 (11.11%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Stoma prolapse			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Skin laceration			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Pelvic fracture			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Procedural pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Rib fracture			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Ulna fracture			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Sinus tachycardia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Atrial fibrillation			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Palpitations			

subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Pericardial effusion			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Sinus bradycardia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Atrial thrombosis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Atrioventricular block first degree			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Tachycardia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Ageusia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 9 (11.11%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Anosmia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Dysgeusia			
subjects affected / exposed	1 / 4 (25.00%)	2 / 9 (22.22%)	0 / 8 (0.00%)
occurrences (all)	1	3	0
Headache			
subjects affected / exposed	0 / 4 (0.00%)	1 / 9 (11.11%)	1 / 8 (12.50%)
occurrences (all)	0	2	2
Hypoaesthesia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 9 (11.11%)	0 / 8 (0.00%)
occurrences (all)	0	1	0

Sensory loss			
subjects affected / exposed	0 / 4 (0.00%)	1 / 9 (11.11%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Syncope			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Paraesthesia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Brain oedema			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Neuropathy peripheral			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Post herpetic neuralgia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Taste disorder			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Tremor			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Coordination abnormal			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Cognitive disorder			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Disturbance in attention			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Parosmia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0

Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Leukocytosis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Leukopenia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 9 (11.11%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Thrombocytopenia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 9 (11.11%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Lymphopenia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Neutropenia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Tinnitus			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Hyperacusis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Vision blurred			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Conjunctival haemorrhage			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Eye pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Vitreous floaters			

subjects affected / exposed	0 / 4 (0.00%)	1 / 9 (11.11%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Diplopia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	3 / 4 (75.00%)	7 / 9 (77.78%)	5 / 8 (62.50%)
occurrences (all)	4	16	13
Vomiting			
subjects affected / exposed	2 / 4 (50.00%)	5 / 9 (55.56%)	4 / 8 (50.00%)
occurrences (all)	2	10	5
Abdominal pain			
subjects affected / exposed	0 / 4 (0.00%)	1 / 9 (11.11%)	2 / 8 (25.00%)
occurrences (all)	0	1	2
Constipation			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Diarrhoea			
subjects affected / exposed	4 / 4 (100.00%)	9 / 9 (100.00%)	7 / 8 (87.50%)
occurrences (all)	10	15	17
Abdominal distension			
subjects affected / exposed	0 / 4 (0.00%)	1 / 9 (11.11%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Dry mouth			
subjects affected / exposed	1 / 4 (25.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Haematochezia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Retching			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Anal incontinence			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0

Dyspepsia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 9 (11.11%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Dysphagia			
subjects affected / exposed	0 / 4 (0.00%)	2 / 9 (22.22%)	0 / 8 (0.00%)
occurrences (all)	0	2	0
Faeces soft			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Flatulence			
subjects affected / exposed	0 / 4 (0.00%)	2 / 9 (22.22%)	0 / 8 (0.00%)
occurrences (all)	0	2	0
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 4 (25.00%)	1 / 9 (11.11%)	1 / 8 (12.50%)
occurrences (all)	1	1	1
Salivary hypersecretion			
subjects affected / exposed	0 / 4 (0.00%)	1 / 9 (11.11%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Stomatitis			
subjects affected / exposed	0 / 4 (0.00%)	1 / 9 (11.11%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Abdominal pain upper			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Colitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Food poisoning			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Tooth discolouration			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Ascites			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0

Parotid gland enlargement			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Rectal haemorrhage			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Tooth erosion			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Tooth loss			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Hepatobiliary disorders			
Hyperbilirubinaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Hepatitis acute			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Biliary dilatation			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Dermatitis acneiform			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Rash maculo-papular			
subjects affected / exposed	0 / 4 (0.00%)	1 / 9 (11.11%)	1 / 8 (12.50%)
occurrences (all)	0	1	1
Dermatitis contact			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Night sweats			

subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Rash macular			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Skin lesion			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Hyperhidrosis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Ketonuria			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Urinary incontinence			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Haematuria			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Proteinuria			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Renal colic			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Glycosuria			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Endocrine disorders			
Pituitary-dependent Cushing's syndrome			

subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Hypothyroidism			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Myalgia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Arthralgia			
subjects affected / exposed	1 / 4 (25.00%)	1 / 9 (11.11%)	0 / 8 (0.00%)
occurrences (all)	1	1	0
Groin pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	2 / 8 (25.00%)
occurrences (all)	0	0	2
Musculoskeletal pain			
subjects affected / exposed	0 / 4 (0.00%)	1 / 9 (11.11%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Osteoarthritis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Fistula			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Osteoporosis			

subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Coccydynia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
COVID-19			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Pneumonia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Respiratory tract infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Cellulitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Onychomycosis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Oral candidiasis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	2
Pneumonia aspiration			
subjects affected / exposed	0 / 4 (0.00%)	1 / 9 (11.11%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Skin infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0

Upper respiratory tract infection			
subjects affected / exposed	0 / 4 (0.00%)	1 / 9 (11.11%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Candida infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Herpes zoster			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Vaginal infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Coronavirus infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Influenza			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	3 / 4 (75.00%)	3 / 9 (33.33%)	3 / 8 (37.50%)
occurrences (all)	3	3	3
Hypercalcaemia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 9 (11.11%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Hyperkalaemia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 9 (11.11%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Hypomagnesaemia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 9 (11.11%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Dehydration			

subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	2 / 8 (25.00%)
occurrences (all)	0	0	2
Gout			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Hyperglycaemia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 9 (11.11%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Hyperlipidaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Hypokalaemia			
subjects affected / exposed	0 / 4 (0.00%)	3 / 9 (33.33%)	1 / 8 (12.50%)
occurrences (all)	0	3	1
Hyponatraemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Hypophosphataemia			
subjects affected / exposed	0 / 4 (0.00%)	2 / 9 (22.22%)	1 / 8 (12.50%)
occurrences (all)	0	2	1
Vitamin B12 deficiency			
subjects affected / exposed	0 / 4 (0.00%)	1 / 9 (11.11%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Vitamin D deficiency			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Hypoalbuminaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Hypocalcaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Hypoglycaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Hyperuricaemia			

subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Malnutrition			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Dose Escalation: Phase 1a: Cohort 7	Dose Escalation: Phase 1a: Cohort 8	Dose Escalation: Phase 1a: Cohort 9
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 5 (100.00%)	6 / 6 (100.00%)	7 / 7 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cancer pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Tumour pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Hypotension			
subjects affected / exposed	1 / 5 (20.00%)	1 / 6 (16.67%)	1 / 7 (14.29%)
occurrences (all)	1	1	1
Deep vein thrombosis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Hypertension			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Embolism			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Hot flush			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Pallor			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Peripheral embolism			

subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	2 / 5 (40.00%)	0 / 6 (0.00%)	1 / 7 (14.29%)
occurrences (all)	2	0	1
Fatigue			
subjects affected / exposed	1 / 5 (20.00%)	5 / 6 (83.33%)	3 / 7 (42.86%)
occurrences (all)	2	5	6
Asthenia			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Gait disturbance			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Influenza like illness			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Non-cardiac chest pain			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	1 / 7 (14.29%)
occurrences (all)	0	1	1
Oedema peripheral			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Chest discomfort			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Chest pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Chills			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	1 / 7 (14.29%)
occurrences (all)	0	1	1
Early satiety			

subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Infusion site extravasation			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Pain			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Performance status decreased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Physical deconditioning			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Peripheral swelling			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Contrast media reaction			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Erectile dysfunction			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Vaginal haemorrhage			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 5 (20.00%)	0 / 6 (0.00%)	2 / 7 (28.57%)
occurrences (all)	1	0	2
Dyspnoea			
subjects affected / exposed	1 / 5 (20.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Oropharyngeal pain			

subjects affected / exposed	1 / 5 (20.00%)	0 / 6 (0.00%)	1 / 7 (14.29%)
occurrences (all)	1	0	1
Wheezing			
subjects affected / exposed	1 / 5 (20.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Atelectasis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Pleural effusion			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Acute respiratory distress syndrome			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Nasal congestion			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Pulmonary embolism			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Rhinorrhoea			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract congestion			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Increased viscosity of upper respiratory secretion			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Pneumothorax			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Productive cough			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0

Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Hallucination, auditory			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Insomnia			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	2 / 7 (28.57%)
occurrences (all)	0	1	2
Anxiety			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Confusional state			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Irritability			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Product issues			
Device breakage			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Investigations			
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 5 (20.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Blood creatinine increased			
subjects affected / exposed	1 / 5 (20.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Alanine aminotransferase increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0

Blood bilirubin increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Blood cholesterol increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Blood lactate dehydrogenase decreased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Blood phosphorus decreased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Electrocardiogram QT interval abnormal			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Lymphocyte count decreased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	2
Neutrophil count decreased			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Weight decreased			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	1 / 7 (14.29%)
occurrences (all)	0	2	1
Weight increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
White blood cell count decreased			

subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Blood creatinine decreased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Blood sodium decreased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Eosinophil count decreased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Platelet count decreased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
White blood cell count increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Ejection fraction decreased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Blood albumin decreased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Carbon dioxide decreased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			

Spinal compression fracture			
subjects affected / exposed	1 / 5 (20.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Contusion			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Fall			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Stoma prolapse			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Skin laceration			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Pelvic fracture			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Procedural pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Rib fracture			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Ulna fracture			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Sinus tachycardia			
subjects affected / exposed	1 / 5 (20.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Atrial fibrillation			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Palpitations			

subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Pericardial effusion			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Sinus bradycardia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Atrial thrombosis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Atrioventricular block first degree			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Tachycardia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	2 / 5 (40.00%)	1 / 6 (16.67%)	0 / 7 (0.00%)
occurrences (all)	2	1	0
Ageusia			
subjects affected / exposed	1 / 5 (20.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Anosmia			
subjects affected / exposed	1 / 5 (20.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Dysgeusia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	1 / 7 (14.29%)
occurrences (all)	0	1	1
Hypoaesthesia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0

Sensory loss			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Syncope			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	1 / 7 (14.29%)
occurrences (all)	0	1	1
Paraesthesia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Brain oedema			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Neuropathy peripheral			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Post herpetic neuralgia			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Taste disorder			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Tremor			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Coordination abnormal			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Cognitive disorder			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Disturbance in attention			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Parosmia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0

Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 5 (20.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	8	0	0
Leukocytosis			
subjects affected / exposed	1 / 5 (20.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	2	0	0
Leukopenia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Thrombocytopenia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Lymphopenia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Neutropenia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Tinnitus			
subjects affected / exposed	1 / 5 (20.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Hyperacusis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Vision blurred			
subjects affected / exposed	1 / 5 (20.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Conjunctival haemorrhage			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Eye pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Vitreous floaters			

subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Diplopia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	5 / 5 (100.00%)	5 / 6 (83.33%)	7 / 7 (100.00%)
occurrences (all)	19	8	15
Vomiting			
subjects affected / exposed	5 / 5 (100.00%)	3 / 6 (50.00%)	6 / 7 (85.71%)
occurrences (all)	12	5	10
Abdominal pain			
subjects affected / exposed	1 / 5 (20.00%)	1 / 6 (16.67%)	1 / 7 (14.29%)
occurrences (all)	4	3	1
Constipation			
subjects affected / exposed	2 / 5 (40.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	3	0	0
Diarrhoea			
subjects affected / exposed	2 / 5 (40.00%)	6 / 6 (100.00%)	7 / 7 (100.00%)
occurrences (all)	4	8	11
Abdominal distension			
subjects affected / exposed	1 / 5 (20.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	2	0	0
Dry mouth			
subjects affected / exposed	1 / 5 (20.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Haematochezia			
subjects affected / exposed	1 / 5 (20.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Retching			
subjects affected / exposed	1 / 5 (20.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Anal incontinence			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0

Dyspepsia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Dysphagia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Faeces soft			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Flatulence			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Salivary hypersecretion			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Stomatitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Abdominal pain upper			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	0 / 7 (0.00%)
occurrences (all)	0	4	0
Colitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Food poisoning			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Tooth discolouration			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Ascites			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0

Parotid gland enlargement			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Rectal haemorrhage			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Tooth erosion			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Tooth loss			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Hepatobiliary disorders			
Hyperbilirubinaemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Hepatitis acute			
subjects affected / exposed	1 / 5 (20.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Biliary dilatation			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
Dermatitis acneiform			
subjects affected / exposed	1 / 5 (20.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Pruritus			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Rash maculo-papular			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Dermatitis contact			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Night sweats			

subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Rash macular			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Skin lesion			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Hyperhidrosis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Ketonuria			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Urinary incontinence			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Haematuria			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Proteinuria			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Renal colic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Glycosuria			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Endocrine disorders			
Pituitary-dependent Cushing's syndrome			

subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Hypothyroidism			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 5 (20.00%)	1 / 6 (16.67%)	1 / 7 (14.29%)
occurrences (all)	1	1	1
Myalgia			
subjects affected / exposed	1 / 5 (20.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Arthralgia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Groin pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Osteoarthritis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Fistula			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Osteoporosis			

subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Pain in extremity			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Coccydynia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
COVID-19			
subjects affected / exposed	1 / 5 (20.00%)	1 / 6 (16.67%)	1 / 7 (14.29%)
occurrences (all)	1	1	1
Pneumonia			
subjects affected / exposed	2 / 5 (40.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	2	0	0
Urinary tract infection			
subjects affected / exposed	2 / 5 (40.00%)	0 / 6 (0.00%)	1 / 7 (14.29%)
occurrences (all)	2	0	1
Respiratory tract infection			
subjects affected / exposed	1 / 5 (20.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Cellulitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Onychomycosis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Oral candidiasis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Pneumonia aspiration			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Skin infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0

Upper respiratory tract infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Candida infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Herpes zoster			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Nasopharyngitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Vaginal infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Coronavirus infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Influenza			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 5 (20.00%)	1 / 6 (16.67%)	2 / 7 (28.57%)
occurrences (all)	1	1	2
Hypercalcaemia			
subjects affected / exposed	1 / 5 (20.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Hyperkalaemia			
subjects affected / exposed	1 / 5 (20.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Hypomagnesaemia			
subjects affected / exposed	1 / 5 (20.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Dehydration			

subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Gout			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Hyperglycaemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Hyperlipidaemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Hypokalaemia			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	1 / 7 (14.29%)
occurrences (all)	0	1	6
Hyponatraemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Hypophosphataemia			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	1 / 7 (14.29%)
occurrences (all)	0	1	1
Vitamin B12 deficiency			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Vitamin D deficiency			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Hypoalbuminaemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Hypocalcaemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Hypoglycaemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Hyperuricaemia			

subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Malnutrition			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Dose Escalation: Phase 1a: Cohort 10	Dose Escalation: Phase 1a: Cohort 11	Dose Escalation: Phase 1a: Cohort 12
Total subjects affected by non-serious adverse events			
subjects affected / exposed	8 / 8 (100.00%)	4 / 4 (100.00%)	9 / 9 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cancer pain			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Tumour pain			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Deep vein thrombosis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Hypertension			
subjects affected / exposed	1 / 8 (12.50%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	2	0	0
Embolism			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Hot flush			
subjects affected / exposed	0 / 8 (0.00%)	1 / 4 (25.00%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Pallor			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Peripheral embolism			

subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 4 (0.00%)	2 / 9 (22.22%)
occurrences (all)	2	0	4
Fatigue			
subjects affected / exposed	5 / 8 (62.50%)	3 / 4 (75.00%)	6 / 9 (66.67%)
occurrences (all)	9	3	11
Asthenia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	3	0	0
Gait disturbance			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Influenza like illness			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Non-cardiac chest pain			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Oedema peripheral			
subjects affected / exposed	2 / 8 (25.00%)	0 / 4 (0.00%)	2 / 9 (22.22%)
occurrences (all)	2	0	3
Chest discomfort			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Chest pain			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Chills			
subjects affected / exposed	1 / 8 (12.50%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Early satiety			

subjects affected / exposed	1 / 8 (12.50%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	2	0	0
Infusion site extravasation			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Pain			
subjects affected / exposed	1 / 8 (12.50%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Performance status decreased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Physical deconditioning			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Peripheral swelling			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Contrast media reaction			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Reproductive system and breast disorders			
Erectile dysfunction			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Vaginal haemorrhage			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 8 (25.00%)	1 / 4 (25.00%)	2 / 9 (22.22%)
occurrences (all)	2	2	2
Dyspnoea			
subjects affected / exposed	1 / 8 (12.50%)	1 / 4 (25.00%)	2 / 9 (22.22%)
occurrences (all)	2	1	5
Oropharyngeal pain			

subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Wheezing			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Atelectasis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Pleural effusion			
subjects affected / exposed	1 / 8 (12.50%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Acute respiratory distress syndrome			
subjects affected / exposed	1 / 8 (12.50%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Nasal congestion			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	2 / 9 (22.22%)
occurrences (all)	0	0	2
Pulmonary embolism			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Rhinorrhoea			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Upper respiratory tract congestion			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	2
Increased viscosity of upper respiratory secretion			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Pneumothorax			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Productive cough			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0

Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Hallucination, auditory			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Insomnia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Anxiety			
subjects affected / exposed	1 / 8 (12.50%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Confusional state			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Irritability			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Product issues			
Device breakage			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Investigations			
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 8 (12.50%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Blood creatinine increased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Alanine aminotransferase increased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0

Blood bilirubin increased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Blood cholesterol increased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Blood lactate dehydrogenase decreased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Blood phosphorus decreased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Electrocardiogram QT interval abnormal			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 8 (12.50%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Lymphocyte count decreased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Neutrophil count decreased			
subjects affected / exposed	2 / 8 (25.00%)	1 / 4 (25.00%)	0 / 9 (0.00%)
occurrences (all)	4	1	0
Weight decreased			
subjects affected / exposed	2 / 8 (25.00%)	0 / 4 (0.00%)	1 / 9 (11.11%)
occurrences (all)	2	0	1
Weight increased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
White blood cell count decreased			

subjects affected / exposed	1 / 8 (12.50%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Blood creatine phosphokinase increased			
subjects affected / exposed	1 / 8 (12.50%)	0 / 4 (0.00%)	1 / 9 (11.11%)
occurrences (all)	1	0	1
Blood creatinine decreased			
subjects affected / exposed	1 / 8 (12.50%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Blood lactate dehydrogenase increased			
subjects affected / exposed	1 / 8 (12.50%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Blood sodium decreased			
subjects affected / exposed	1 / 8 (12.50%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Eosinophil count decreased			
subjects affected / exposed	1 / 8 (12.50%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Platelet count decreased			
subjects affected / exposed	1 / 8 (12.50%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	5	0	0
White blood cell count increased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	2
Ejection fraction decreased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Blood albumin decreased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Carbon dioxide decreased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			

Spinal compression fracture			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Contusion			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Fall			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	2 / 9 (22.22%)
occurrences (all)	0	0	2
Stoma prolapse			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Skin laceration			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Pelvic fracture			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Procedural pain			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Rib fracture			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Ulna fracture			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Sinus tachycardia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Atrial fibrillation			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Palpitations			

subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Pericardial effusion			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Sinus bradycardia			
subjects affected / exposed	0 / 8 (0.00%)	1 / 4 (25.00%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Atrial thrombosis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Atrioventricular block first degree			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Tachycardia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Ageusia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Anosmia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Dysgeusia			
subjects affected / exposed	0 / 8 (0.00%)	1 / 4 (25.00%)	1 / 9 (11.11%)
occurrences (all)	0	1	1
Headache			
subjects affected / exposed	2 / 8 (25.00%)	0 / 4 (0.00%)	3 / 9 (33.33%)
occurrences (all)	2	0	3
Hypoaesthesia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0

Sensory loss			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Syncope			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Paraesthesia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Brain oedema			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Neuropathy peripheral			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Post herpetic neuralgia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Taste disorder			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Tremor			
subjects affected / exposed	1 / 8 (12.50%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Coordination abnormal			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Cognitive disorder			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Disturbance in attention			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Parosmia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0

Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 4 (0.00%)	1 / 9 (11.11%)
occurrences (all)	8	0	3
Leukocytosis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Leukopenia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Thrombocytopenia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	4	0	0
Lymphopenia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	5	0	0
Neutropenia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Ear and labyrinth disorders			
Tinnitus			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Hyperacusis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Vision blurred			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Conjunctival haemorrhage			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Eye pain			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Vitreous floaters			

subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Diplopia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	7 / 8 (87.50%)	4 / 4 (100.00%)	7 / 9 (77.78%)
occurrences (all)	14	5	19
Vomiting			
subjects affected / exposed	6 / 8 (75.00%)	1 / 4 (25.00%)	3 / 9 (33.33%)
occurrences (all)	7	2	6
Abdominal pain			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Constipation			
subjects affected / exposed	2 / 8 (25.00%)	1 / 4 (25.00%)	0 / 9 (0.00%)
occurrences (all)	3	1	0
Diarrhoea			
subjects affected / exposed	6 / 8 (75.00%)	3 / 4 (75.00%)	6 / 9 (66.67%)
occurrences (all)	25	3	11
Abdominal distension			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Dry mouth			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Haematochezia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Retching			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Anal incontinence			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0

Dyspepsia			
subjects affected / exposed	0 / 8 (0.00%)	1 / 4 (25.00%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Dysphagia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Faeces soft			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Flatulence			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Salivary hypersecretion			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Stomatitis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Abdominal pain upper			
subjects affected / exposed	0 / 8 (0.00%)	1 / 4 (25.00%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Colitis			
subjects affected / exposed	1 / 8 (12.50%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Food poisoning			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Tooth discolouration			
subjects affected / exposed	0 / 8 (0.00%)	1 / 4 (25.00%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Ascites			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0

Parotid gland enlargement			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Rectal haemorrhage			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Tooth erosion			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Tooth loss			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Hepatobiliary disorders			
Hyperbilirubinaemia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	2	0	0
Hepatitis acute			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Biliary dilatation			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Dermatitis acneiform			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Rash maculo-papular			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Dermatitis contact			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Night sweats			

subjects affected / exposed	1 / 8 (12.50%)	1 / 4 (25.00%)	0 / 9 (0.00%)
occurrences (all)	1	1	0
Rash			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Rash macular			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Skin lesion			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Hyperhidrosis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Ketonuria			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Urinary incontinence			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Haematuria			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Proteinuria			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Renal colic			
subjects affected / exposed	0 / 8 (0.00%)	1 / 4 (25.00%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Glycosuria			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Endocrine disorders			
Pituitary-dependent Cushing's syndrome			

subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Hypothyroidism			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 8 (12.50%)	1 / 4 (25.00%)	0 / 9 (0.00%)
occurrences (all)	1	1	0
Myalgia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Arthralgia			
subjects affected / exposed	0 / 8 (0.00%)	1 / 4 (25.00%)	1 / 9 (11.11%)
occurrences (all)	0	2	2
Groin pain			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal pain			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Osteoarthritis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Fistula			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Musculoskeletal chest pain			
subjects affected / exposed	1 / 8 (12.50%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	2	0	0
Osteoporosis			

subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	2 / 9 (22.22%)
occurrences (all)	0	0	2
Coccydynia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
COVID-19			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	3 / 9 (33.33%)
occurrences (all)	0	0	3
Pneumonia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 4 (0.00%)	1 / 9 (11.11%)
occurrences (all)	1	0	1
Urinary tract infection			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Respiratory tract infection			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Cellulitis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Onychomycosis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Oral candidiasis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Pneumonia aspiration			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Skin infection			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0

Upper respiratory tract infection			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	2
Candida infection			
subjects affected / exposed	1 / 8 (12.50%)	0 / 4 (0.00%)	1 / 9 (11.11%)
occurrences (all)	1	0	1
Herpes zoster			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Vaginal infection			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Coronavirus infection			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Influenza			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	3 / 8 (37.50%)	1 / 4 (25.00%)	2 / 9 (22.22%)
occurrences (all)	6	1	4
Hypercalcaemia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Hyperkalaemia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Hypomagnesaemia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Dehydration			

subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Gout			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Hyperglycaemia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	2
Hyperlipidaemia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Hypokalaemia			
subjects affected / exposed	3 / 8 (37.50%)	0 / 4 (0.00%)	1 / 9 (11.11%)
occurrences (all)	3	0	3
Hyponatraemia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 4 (0.00%)	1 / 9 (11.11%)
occurrences (all)	1	0	3
Hypophosphataemia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 4 (0.00%)	4 / 9 (44.44%)
occurrences (all)	2	0	5
Vitamin B12 deficiency			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Vitamin D deficiency			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Hypoalbuminaemia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Hypocalcaemia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Hypoglycaemia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Hyperuricaemia			

subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Malnutrition			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Dose Escalation: Phase 1a: Cohort 13	Dose Escalation: Phase 1a: Cohort 14	Dose Expansion: Phase 1b: Cohort 1
Total subjects affected by non-serious adverse events			
subjects affected / exposed	8 / 8 (100.00%)	6 / 6 (100.00%)	12 / 12 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cancer pain			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Tumour pain			
subjects affected / exposed	0 / 8 (0.00%)	1 / 6 (16.67%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Deep vein thrombosis			
subjects affected / exposed	0 / 8 (0.00%)	1 / 6 (16.67%)	1 / 12 (8.33%)
occurrences (all)	0	1	2
Hypertension			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Embolism			
subjects affected / exposed	0 / 8 (0.00%)	1 / 6 (16.67%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Hot flush			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Pallor			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Peripheral embolism			

subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Fatigue			
subjects affected / exposed	4 / 8 (50.00%)	3 / 6 (50.00%)	8 / 12 (66.67%)
occurrences (all)	4	3	12
Asthenia			
subjects affected / exposed	0 / 8 (0.00%)	1 / 6 (16.67%)	1 / 12 (8.33%)
occurrences (all)	0	1	1
Gait disturbance			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Influenza like illness			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Non-cardiac chest pain			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Oedema peripheral			
subjects affected / exposed	0 / 8 (0.00%)	1 / 6 (16.67%)	2 / 12 (16.67%)
occurrences (all)	0	1	2
Chest discomfort			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Chest pain			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Chills			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Early satiety			

subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Infusion site extravasation			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Pain			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Performance status decreased			
subjects affected / exposed	1 / 8 (12.50%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Physical deconditioning			
subjects affected / exposed	1 / 8 (12.50%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Peripheral swelling			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Contrast media reaction			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Erectile dysfunction			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Vaginal haemorrhage			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 8 (0.00%)	1 / 6 (16.67%)	3 / 12 (25.00%)
occurrences (all)	0	1	4
Dyspnoea			
subjects affected / exposed	2 / 8 (25.00%)	1 / 6 (16.67%)	2 / 12 (16.67%)
occurrences (all)	2	1	2
Oropharyngeal pain			

subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Wheezing			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Atelectasis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Pleural effusion			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Acute respiratory distress syndrome			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Nasal congestion			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Pulmonary embolism			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Rhinorrhoea			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract congestion			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Increased viscosity of upper respiratory secretion			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Pneumothorax			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Productive cough			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1

Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Hallucination, auditory			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Insomnia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Anxiety			
subjects affected / exposed	0 / 8 (0.00%)	1 / 6 (16.67%)	1 / 12 (8.33%)
occurrences (all)	0	1	1
Confusional state			
subjects affected / exposed	1 / 8 (12.50%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Irritability			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Product issues			
Device breakage			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Investigations			
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 8 (12.50%)	0 / 6 (0.00%)	1 / 12 (8.33%)
occurrences (all)	3	0	1
Blood creatinine increased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Alanine aminotransferase increased			
subjects affected / exposed	1 / 8 (12.50%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	2	0	0
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 8 (12.50%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	3	0	0

Blood bilirubin increased			
subjects affected / exposed	1 / 8 (12.50%)	0 / 6 (0.00%)	1 / 12 (8.33%)
occurrences (all)	2	0	1
Blood cholesterol increased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Blood lactate dehydrogenase decreased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Blood phosphorus decreased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Electrocardiogram QT interval abnormal			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Lymphocyte count decreased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Neutrophil count decreased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Weight decreased			
subjects affected / exposed	1 / 8 (12.50%)	1 / 6 (16.67%)	2 / 12 (16.67%)
occurrences (all)	1	1	2
Weight increased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
White blood cell count decreased			

subjects affected / exposed	1 / 8 (12.50%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Blood creatinine decreased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Blood lactate dehydrogenase increased			
subjects affected / exposed	1 / 8 (12.50%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Blood sodium decreased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Eosinophil count decreased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Platelet count decreased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
White blood cell count increased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Ejection fraction decreased			
subjects affected / exposed	0 / 8 (0.00%)	1 / 6 (16.67%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Blood albumin decreased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Carbon dioxide decreased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Injury, poisoning and procedural complications			

Spinal compression fracture			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Contusion			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Fall			
subjects affected / exposed	1 / 8 (12.50%)	1 / 6 (16.67%)	0 / 12 (0.00%)
occurrences (all)	2	1	0
Stoma prolapse			
subjects affected / exposed	0 / 8 (0.00%)	1 / 6 (16.67%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Skin laceration			
subjects affected / exposed	1 / 8 (12.50%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Pelvic fracture			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Procedural pain			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Rib fracture			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Ulna fracture			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Cardiac disorders			
Sinus tachycardia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Atrial fibrillation			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Palpitations			

subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Pericardial effusion			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Sinus bradycardia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Atrial thrombosis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Atrioventricular block first degree			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Tachycardia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	2 / 12 (16.67%)
occurrences (all)	0	0	2
Ageusia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Anosmia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Dysgeusia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 6 (0.00%)	4 / 12 (33.33%)
occurrences (all)	1	0	4
Headache			
subjects affected / exposed	1 / 8 (12.50%)	1 / 6 (16.67%)	0 / 12 (0.00%)
occurrences (all)	1	1	0
Hypoaesthesia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0

Sensory loss			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Syncope			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Paraesthesia			
subjects affected / exposed	0 / 8 (0.00%)	1 / 6 (16.67%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Brain oedema			
subjects affected / exposed	1 / 8 (12.50%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Neuropathy peripheral			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Post herpetic neuralgia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Taste disorder			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Tremor			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Coordination abnormal			
subjects affected / exposed	0 / 8 (0.00%)	1 / 6 (16.67%)	0 / 12 (0.00%)
occurrences (all)	0	2	0
Cognitive disorder			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Disturbance in attention			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Parosmia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1

Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Leukocytosis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Leukopenia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Thrombocytopenia			
subjects affected / exposed	2 / 8 (25.00%)	1 / 6 (16.67%)	0 / 12 (0.00%)
occurrences (all)	3	1	0
Lymphopenia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Neutropenia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	2	0	0
Ear and labyrinth disorders			
Tinnitus			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Hyperacusis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Vision blurred			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Conjunctival haemorrhage			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Eye pain			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Vitreous floaters			

subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Diplopia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	5 / 8 (62.50%)	4 / 6 (66.67%)	10 / 12 (83.33%)
occurrences (all)	10	8	14
Vomiting			
subjects affected / exposed	5 / 8 (62.50%)	3 / 6 (50.00%)	5 / 12 (41.67%)
occurrences (all)	8	5	11
Abdominal pain			
subjects affected / exposed	1 / 8 (12.50%)	1 / 6 (16.67%)	3 / 12 (25.00%)
occurrences (all)	1	1	3
Constipation			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Diarrhoea			
subjects affected / exposed	7 / 8 (87.50%)	3 / 6 (50.00%)	9 / 12 (75.00%)
occurrences (all)	12	6	22
Abdominal distension			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Dry mouth			
subjects affected / exposed	0 / 8 (0.00%)	1 / 6 (16.67%)	1 / 12 (8.33%)
occurrences (all)	0	1	1
Haematochezia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Retching			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Anal incontinence			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1

Dyspepsia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Dysphagia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Faeces soft			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Flatulence			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Salivary hypersecretion			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Stomatitis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Abdominal pain upper			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	2 / 12 (16.67%)
occurrences (all)	0	0	2
Colitis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Food poisoning			
subjects affected / exposed	1 / 8 (12.50%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Tooth discolouration			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Ascites			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1

Parotid gland enlargement			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Rectal haemorrhage			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Tooth erosion			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Tooth loss			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	2
Hepatobiliary disorders			
Hyperbilirubinaemia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Hepatitis acute			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Biliary dilatation			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Dermatitis acneiform			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Rash maculo-papular			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Dermatitis contact			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Night sweats			

subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Rash macular			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Skin lesion			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Hyperhidrosis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Renal and urinary disorders			
Ketonuria			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Urinary incontinence			
subjects affected / exposed	0 / 8 (0.00%)	1 / 6 (16.67%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Haematuria			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Proteinuria			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Renal colic			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Glycosuria			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Endocrine disorders			
Pituitary-dependent Cushing's syndrome			

subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Hypothyroidism			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 8 (12.50%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Myalgia			
subjects affected / exposed	0 / 8 (0.00%)	1 / 6 (16.67%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Arthralgia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Groin pain			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal pain			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Osteoarthritis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Fistula			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Osteoporosis			

subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Coccydynia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Infections and infestations			
COVID-19			
subjects affected / exposed	0 / 8 (0.00%)	2 / 6 (33.33%)	0 / 12 (0.00%)
occurrences (all)	0	2	0
Pneumonia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	3 / 12 (25.00%)
occurrences (all)	0	0	4
Respiratory tract infection			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Cellulitis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Onychomycosis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Oral candidiasis			
subjects affected / exposed	0 / 8 (0.00%)	1 / 6 (16.67%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Pneumonia aspiration			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Skin infection			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0

Upper respiratory tract infection			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	2 / 12 (16.67%)
occurrences (all)	0	0	2
Candida infection			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Herpes zoster			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Vaginal infection			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Coronavirus infection			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Influenza			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 8 (12.50%)	1 / 6 (16.67%)	6 / 12 (50.00%)
occurrences (all)	2	2	10
Hypercalcaemia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Hyperkalaemia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Hypomagnesaemia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Dehydration			

subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	4 / 12 (33.33%)
occurrences (all)	0	0	5
Gout			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Hyperglycaemia			
subjects affected / exposed	0 / 8 (0.00%)	1 / 6 (16.67%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Hyperlipidaemia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Hypokalaemia			
subjects affected / exposed	2 / 8 (25.00%)	2 / 6 (33.33%)	0 / 12 (0.00%)
occurrences (all)	2	2	0
Hyponatraemia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Hypophosphataemia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	2 / 12 (16.67%)
occurrences (all)	0	0	2
Vitamin B12 deficiency			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Vitamin D deficiency			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Hypoalbuminaemia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Hypocalcaemia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Hypoglycaemia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 6 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Hyperuricaemia			

subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Malnutrition			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1

Non-serious adverse events	Dose Expansion: Phase 1b: Cohort 2		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	12 / 12 (100.00%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cancer pain			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Tumour pain			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Deep vein thrombosis			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Hypertension			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Embolism			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Hot flush			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Pallor			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Peripheral embolism			

subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Fatigue			
subjects affected / exposed	7 / 12 (58.33%)		
occurrences (all)	11		
Asthenia			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Gait disturbance			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Influenza like illness			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Non-cardiac chest pain			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Oedema peripheral			
subjects affected / exposed	2 / 12 (16.67%)		
occurrences (all)	2		
Chest discomfort			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Chest pain			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Chills			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Early satiety			

subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Infusion site extravasation			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Pain			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Performance status decreased			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Physical deconditioning			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Peripheral swelling			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Immune system disorders			
Contrast media reaction			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Reproductive system and breast disorders			
Erectile dysfunction			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Vaginal haemorrhage			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	3 / 12 (25.00%)		
occurrences (all)	4		
Dyspnoea			
subjects affected / exposed	2 / 12 (16.67%)		
occurrences (all)	2		
Oropharyngeal pain			

subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Wheezing				
subjects affected / exposed	1 / 12 (8.33%)			
occurrences (all)	1			
Atelectasis				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Pleural effusion				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Acute respiratory distress syndrome				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Nasal congestion				
subjects affected / exposed	1 / 12 (8.33%)			
occurrences (all)	1			
Pulmonary embolism				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Rhinorrhoea				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Upper respiratory tract congestion				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Increased viscosity of upper respiratory secretion				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Pneumothorax				
subjects affected / exposed	1 / 12 (8.33%)			
occurrences (all)	1			
Productive cough				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			

Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Hallucination, auditory			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Insomnia			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Anxiety			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Confusional state			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Irritability			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Product issues			
Device breakage			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Investigations			
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Blood creatinine increased			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	2		
Alanine aminotransferase increased			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		

Blood bilirubin increased				
subjects affected / exposed	1 / 12 (8.33%)			
occurrences (all)	1			
Blood cholesterol increased				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Blood lactate dehydrogenase decreased				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Blood phosphorus decreased				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Electrocardiogram QT interval abnormal				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Electrocardiogram QT prolonged				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Gamma-glutamyltransferase increased				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Lymphocyte count decreased				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Neutrophil count decreased				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Weight decreased				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Weight increased				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
White blood cell count decreased				

subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	7		
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Blood creatinine decreased			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Blood sodium decreased			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Eosinophil count decreased			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Platelet count decreased			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	2		
White blood cell count increased			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Ejection fraction decreased			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Blood albumin decreased			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Carbon dioxide decreased			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Injury, poisoning and procedural complications			

Spinal compression fracture subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0		
Contusion subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0		
Fall subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0		
Stoma prolapse subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0		
Skin laceration subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0		
Pelvic fracture subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0		
Procedural pain subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1		
Rib fracture subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1		
Ulna fracture subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0		
Cardiac disorders Sinus tachycardia subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0		
Atrial fibrillation subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1		
Palpitations			

subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Pericardial effusion			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Sinus bradycardia			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Atrial thrombosis			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Atrioventricular block first degree			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Tachycardia			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Ageusia			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Anosmia			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Dysgeusia			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Headache			
subjects affected / exposed	2 / 12 (16.67%)		
occurrences (all)	2		
Hypoaesthesia			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		

Sensory loss				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Syncope				
subjects affected / exposed	1 / 12 (8.33%)			
occurrences (all)	2			
Paraesthesia				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Brain oedema				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Neuropathy peripheral				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Post herpetic neuralgia				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Taste disorder				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Tremor				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Coordination abnormal				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Cognitive disorder				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Disturbance in attention				
subjects affected / exposed	1 / 12 (8.33%)			
occurrences (all)	1			
Parosmia				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			

Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 12 (16.67%)		
occurrences (all)	2		
Leukocytosis			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Leukopenia			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Thrombocytopenia			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	5		
Lymphopenia			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Neutropenia			
subjects affected / exposed	2 / 12 (16.67%)		
occurrences (all)	5		
Ear and labyrinth disorders			
Tinnitus			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Hyperacusis			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Eye disorders			
Vision blurred			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Conjunctival haemorrhage			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Eye pain			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Vitreous floaters			

subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Diplopia			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	7 / 12 (58.33%)		
occurrences (all)	13		
Vomiting			
subjects affected / exposed	5 / 12 (41.67%)		
occurrences (all)	7		
Abdominal pain			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Constipation			
subjects affected / exposed	3 / 12 (25.00%)		
occurrences (all)	3		
Diarrhoea			
subjects affected / exposed	6 / 12 (50.00%)		
occurrences (all)	15		
Abdominal distension			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Dry mouth			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Haematochezia			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Retching			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	2		
Anal incontinence			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		

Dyspepsia				
subjects affected / exposed	1 / 12 (8.33%)			
occurrences (all)	1			
Dysphagia				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Faeces soft				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Flatulence				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Gastrooesophageal reflux disease				
subjects affected / exposed	1 / 12 (8.33%)			
occurrences (all)	1			
Salivary hypersecretion				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Stomatitis				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Abdominal pain upper				
subjects affected / exposed	1 / 12 (8.33%)			
occurrences (all)	1			
Colitis				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Food poisoning				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Tooth discolouration				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Ascites				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			

Parotid gland enlargement subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0		
Rectal haemorrhage subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0		
Tooth erosion subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0		
Tooth loss subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0		
Hepatobiliary disorders Hyperbilirubinaemia subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 2		
Hepatitis acute subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0		
Biliary dilatation subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0		
Skin and subcutaneous tissue disorders Dermatitis acneiform subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0		
Pruritus subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0		
Rash maculo-papular subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0		
Dermatitis contact subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0		
Night sweats			

subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Rash			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Rash macular			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Skin lesion			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Hyperhidrosis			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Renal and urinary disorders			
Ketonuria			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Urinary incontinence			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Haematuria			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Proteinuria			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Renal colic			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Glycosuria			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Endocrine disorders			
Pituitary-dependent Cushing's syndrome			

subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Hypothyroidism			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Myalgia			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Arthralgia			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Groin pain			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Muscle spasms			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Musculoskeletal pain			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Osteoarthritis			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Fistula			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Musculoskeletal chest pain			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Osteoporosis			

subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Pain in extremity			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Coccydynia			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Infections and infestations			
COVID-19			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Pneumonia			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Urinary tract infection			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Respiratory tract infection			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Cellulitis			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Onychomycosis			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Oral candidiasis			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Pneumonia aspiration			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Skin infection			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		

Upper respiratory tract infection			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Candida infection			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Herpes zoster			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Nasopharyngitis			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Vaginal infection			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Coronavirus infection			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Influenza			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Hypercalcaemia			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Hyperkalaemia			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Hypomagnesaemia			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Dehydration			

subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Gout				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Hyperglycaemia				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Hyperlipidaemia				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Hypokalaemia				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Hyponatraemia				
subjects affected / exposed	1 / 12 (8.33%)			
occurrences (all)	1			
Hypophosphataemia				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Vitamin B12 deficiency				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Vitamin D deficiency				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Hypoalbuminaemia				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Hypocalcaemia				
subjects affected / exposed	1 / 12 (8.33%)			
occurrences (all)	1			
Hypoglycaemia				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Hyperuricaemia				

subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Malnutrition			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
01 May 2020	The following changes were made as per Amendment 1: 1. A nonclinical rationale for each new Phase 2 cohort (sarcoma with murine Double minute 2 [MDM2] amplification [Cohort 2], CDKN2A loss [Cohort 3], and molecular features that may confer sensitivity to ASTX295 [Cohort 4]) was provided in addition to the previously defined malignant pleural mesothelioma (MPM) cohort [Cohort 1]. 2. The number of overall subjects and the duration of study was updated based on the additional Phase 2 cohorts. 3. The Phase 2 study design description was updated to define the new cohorts, Cohorts 2-4. 4. Scientific rationale for study design was updated to reflect the new cohorts added for Phase 2. 5. The inclusion and exclusion criteria were updated. 6. In the statistical hypotheses section for Phase 2, hypotheses were included for the new Phase 2 cohorts. 7. The sample size was calculated for new Cohorts 2, 3, and 4.
21 October 2020	The following changes were made as per Amendment 2: 1. A secondary objective was added regarding PK parameters of ASTX295 after administration with food. 2. A concomitant change was made regarding the ASTX295 plasma concentration profiles and PK parameters in the fed state. 3. Figure was updated to add a food-effect cohort. 4. The addition of a window to activities occurring beyond Cycle 6. 5. Study rationale section was updated to add the rationale for a food bridging cohort. 6. Background section was updated to include information from a nonclinical PK food-effect study. 7. Objectives and endpoints were updated to include the determination of PK parameters of ASTX295 when administered with food. 8. Overall design section was updated to add the rationale for a food bridging cohort. This section was updated with language to address the impact and changes resulting from the coronavirus disease of 2019 (COVID-19) health emergency. 9. Scientific rational for study design was updated to add the rationale for a food bridging cohort. 10. The "drug administration under fed state" section was added to provide meal requirements and procedures for subjects enrolled into the food-bridging cohort. 11. Study treatments administered section updated to provide information on alternative dispensing of study drug under extenuating circumstances, such as the COVID-19 health emergency. 12. Appendix was added to provide information and guidance to continue study during the COVID-19 emergency.
15 June 2021	The following changes were made as per Amendment 3: 1. Allowed an alternate dosing regimen (i.e., BID administration) to enhance exposure and based on the latest research findings. These include BID dosing or administration with food based on results from a food-bridging cohort (Amendment #2). 2. The study numbers were corrected (255 should have read 239) and increased from 28 to 60 for Phase 1a and up to an additional 15 to 20 subjects for Phase 1b. 3. For BID cohorts under fasting conditions, meals and dietary restrictions were updated. 4. Details of alternate dose regimen was updated in drug administration under fed conditions section.

21 March 2022	The following changes were made as per Amendment 4: 1. The duration of the study was increased. 2. Intermittent dosing was added to the possible dosing schedule modifications for Phase 1a. 3. The expected total numbers of screened and treated subjects in all phases were increased, and all numbers by phase were specified as approximate. 4. Up to an additional 14 days (up to 35 total screening days) was specified as being allowed for acquisition of archived tissue slides or a fresh biopsy for prospective eligibility confirmation in Phase 2. 5. "Fasting conditions" was deleted from the description of the last safe dose as determined by the DSRC for the description of Amendment 2, Phase 1, Cohort 7. 6. Consideration of twice daily dosing or intermittent dose schedules or meal options for improvement of tolerability while allowing for additional dose escalation was added. 7. The location of Phase 1b was changed from "North America" to "United States; same centers initiated in Phase 1a." 8. The expected total numbers of screened and treated subjects in all phases were increased, and all numbers by phase were specified as approximate. 9. Inclusion and exclusion criteria were modified.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Phase 2 was not conducted due to Sponsor's strategic decision.

Notes: